A New Speckle Tracking Algorithm can Accurately Analyze Left Ventricular Wall Motion - a Multicenter Study by the Israeli Echocardiography Research Group

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Introduction: Left ventricular wall (WM) motion assessment is crucial in echocardiogram interpretation, but despite technology improvements no automatic tool yet replaced visual reading. We hypothesized that 2D strain, a new speckle-tracking technique, can assess WM automatically with high concordance to visual assessment.

Methods: Echocardiograms (3 apical views, 18 segments) of 105 patients (ten duplicated), (28 healthy, 62 AMI, 15 dilated cardiomyopathy) were blindly read by 10 readers. Segments were scored: normal-dyskinetic (1-4). Segmental "gold-standard" for visual scoring (VSS) was computed using majority score assigned to each segment. 2DS was applied and segmental peak systolic strain (PSS) determined [Vivid 7, AFI(GE)]. PSS scores were divided: <-14% normal, -14 to -11% hypokinetic, - 11 to 2% akinetic, >2% dyskinetic.

Results: 1890 segments were analyzed, 66% categorized by VSS as normal and 30% as abnormal (13.5% hypokinetic, 12.1% akinetic and 1.7% dyskinetic), (4% unscorable). The sensitivity and specificity of PSS vs. VSS for identifying normal vs. abnormal segments was 88% and 85%. 85% of normal and 88% of akinetic segments were correctly identified by PSS. Kappa values for VSS inter and intra observer variability (4 categories): 0.50 and 0.57. When dichotomized into normal (score 1) and abnormal (2-4), inter and intra observer variabilities were 0.65 and 0.71. For PSS, Kappa values for inter and intra observer variability were 0.71 and 0.77, and when dichotomized, 0.79 and 0.83.

Conclusions: Automated PSS can accurately distinguish normally and abnormally contracting segments with good agreement to visual assessment by experienced echocardiographers, thus may assist WM analysis performed by less experienced readers.

Reduction in Mitral Regurgitation in Patients Undergoing Cardiac Resynchronization Treatment: Assessment of Predictors by Two Dimensional Radial Strain Echocardiography

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Background. Cardiac resynchronization treatment (CRT) is associated with reduction in mitral regurgitation (MR), however few studies have defined specific predictors of acute MR reduction. We hypothesized that left ventricular (LV) mechanical dyssynchrony in mid-LV segments corresponding to papillary muscles insertion sites can predict early MR reduction post CRT, due to improved synchrony in papillary muscle contraction. We utilized the novel approach of 2-D radial strain (2-DRS) to evaluate our hypothesis.

Methods. We evaluated 32 pts undergoing CRT (mean age 64±17 years, 54% male) with MR grade ≥3 determined by MR jet area/left atrial area ratio (JA/LAA) (grade 1, MRJA/LAA <20% to grade 4, MRJA/LAA >40%). Radial mechanical activation sequence maps were constructed using 2-DRS from mid-LV circumferential sites. Responders were defined as patients with post-CRT (1.9±1.0 months) reduction in MR to MRJA/LAA < 25%.

Results. The percent reduction in LV end-systolic volume was significantly higher in responders (p=0.03), as was improvement in LVEF (p=0.007). Post CRT, 67% of responders had mild or no MR and 33% had mild to moderate MR, while 70% of non-responders had grade 3 or 4 MR (p=0.0001). Significant delay of time-to-peak 2-DRS in the mid posterior and inferior segments prior to CRT was found in responders compared with non-responders (580±58 vs. 486±94, p=0.002 and 596±79 vs. 478±127 ms, p=0.005, respectively). Responders also had higher peak positive systolic 2-DRS in the posterior and inferior segments compared to non- responders (22±13 vs. 12±7%, p=0.01 and 17±9 vs. 9±7%, p=0.02, respectively). Logistic regression analysis showed that the difference in pre-CRT infero-anterior time-to-peak radial strain of >110 ms and MRJA/LAA <40% as well as 2-DRS >18% in the posterior wall were significant predictors of post-CRT improvement in MR.

Conclusion. 2-D radial strain can quantify LV dyssynchrony and predict post- CRT improvement in MR. Presence of a significant time-to-peak delay on 2-DRS between inferior and anterior LV segments, preserved strain of posterior wall and MRJA/LAA <40% were found to be associated with significant MR reduction in patients post CRT.

Is Left Ventricular Diastolic Dysfunction Associated with Elevated Pulmonary Artery Pressure in Patients with Preserved Left Ventricular Ejection Fraction?

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Background and Objectives: The role of isolated left ventricular (LV) diastolic dysfunction (DDFx) as a cause of pulmonary hypertension is unclear. The objectives of our study were: 1) to determine the distribution of pulmonary artery systolic pressure (PAP) in patients with advanced LV DDFx and preserved LV ejection fraction (LVEF); 2) to examine whether the severity of LV DDFx is related to PAP.

Methods: The computerized database of the echocardiography laboratory at our institution was used to identify consecutive patients with preserved LVEF (≥50%), advanced LV DDFx (pseudonormal or restrictive LV filling patterns), and no significant left-sided valve disease, in whom PAP was estimated. Advanced LV DDFx was defined as mitral inflow E/A ratio ≥1.0 *and* echocardiographic evidence of elevated LV filling pressures (at least one of the following: pulmonary venous systolic/diastolic flow ratio [PV S/D] <1, mitral inflow E/mitral annular e' ratio ≥15 [septal aspect of annulus], or E/e' ratio ≥10 [lateral annulus]).

Results: During the study period (44 months) – 407 patients fulfilled the inclusion criteria (age: 70±10 yrs; 43% male). PAP was <35 mmHg in 57 (14%) patients, 35-49 mmHg in 201 (49%) patients, 50-69 mmHg in 133 (33%) patients, and ≥70 mmHg in 16 (4%) patients. The PAP in patients with variable degrees of LV diastolic filling abnormalities is presented in the Table.

	Terciles of Diastolic Parameters			
Diastolic parameters	**I**	**II**	**III**	***P* for trend**
Mitral inflow E/A ratio				
Tertiles (ranges)	<1.4	1.4-1.7	>1.7	
PAP	43 ± 11	46 ± 11	48 ± 13	<0.0001
E wave deceleration time (DT)				
Tertiles (ranges)	<170	170-200	>200	
PAP	50 ± 14	46 ± 11	43 ± 9	<0.0001
PV S/D ratio				
Tertiles (ranges)	<0.6	0.6-0.8	>0.8	
PAP	51 ± 14	46 ± 13	44 ± 10	<0.0001
Left atrial (LA) diameter				
Tertiles (ranges)	<4.3	4.3-4.7	>4.7	
PAP	42 ± 11	45 ± 11	48 ± 14	0.01

Greater abnormalities of LV filling (increasing values of E/A ratio and LA diameter and decreasing values of DT and PV S/D ratio) were associated with higher PAP. Female gender was associated with higher PAP (*P*=0.002) and there was an interaction between gender, the severity of DDFx, and its association with PAP. For example - PAP in the 3rd tertile of E/A ratio was higher in women (50±13 mmHg) than in men (45±13 mmHg).

Conclusions: PAP is significantly elevated in a large proportion of patients with advanced LV DDFx and preserved LVEF. More severe abnormalities of LV filling (reflecting more severe LV DDFx) are associated with higher PAP, suggesting a cause-and-effect relationship. Gender appears to modify this relationship, suggesting that women are more prone to developing pulmonary hypertension under these circumstances.

Differential Effects of Afterload on Left Ventricular Long-Axis and Short-Axis Function: Insights from a Clinical Model of Patients with Aortic Valve Stenosis Undergoing Aortic Valve Replacement

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Background and Objective: The differential effects of left ventricular (LV) afterload on longitudinal versus circumferential ventricular mechanics is largely unknown. The objective of our study was to examine the changes in LV deformation early after aortic valve replacement (AVR) in patients with aortic valve stenosis (AS), using 2-D myocardial strain imaging.

Methods: Paired echocardiographic studies before and early [7±3 days] after AVR, were analyzed in 29 patients (age: 72±9 yrs, 45% men) with severe AS. All patients had normal LV ejection fraction (LVEF) and no segmental wall motion abnormalities. Long-axis (longitudinal) myocardial function was assessed from 3 apical views (average of 18 segments from 4-chamber, 2-chamber, and long-axis views). Short-axis (circumferential) function was assessed from mid-LV and apical short-axis views (separate averages of 6 segments in each view). Myocardial deformation (strain), strain rate (SR), and LV twist (counterclockwise systolic rotation of apex relative to mid-LV) were measured using the 2-D Velocity Vector Imaging software (VVI, Siemens, Mountainview, CA).

Results: AVR resulted in a significant drop in transaortic pressure gradients (peak and mean gradients dropped from 93±13 to 35±1 and from 55±12 to 18±6 mmHg, respectively, p<0.001 for both), whereas LV size and LVEF did not change early post-AVR. The changes in myocardial longitudinal and circumferential function are listed in the Table.

	Pre-AVR	**Post-AVR**	**p**
Peak systolic strain (%)			
Longitudinal	-12.1±2.9	-15.3±3.4	<0.001
Circumferential			
Mid-LV	-27.6±6.2	-24.1±3.9	<0.001
Apex	-31.3±8.4	-31.6±6.3	NS
Early diastolic SR (%/sec)			
Longitudinal	0.49±0.16	0.65±0.22	<0.001
Circumferential			
Mid-LV	1.31±0.58	1.06±0.27	<0.001
Apex	1.44±0.54	1.53±0.46	NS
LV twist (°)	3.1±2.6	5.3±2.7	<0.001

Following AVR: 1) longitudinal systolic strain increased, whereas mid-LV circumferential strain decreased; 2) longitudinal early diastolic SR increased, whereas mid-LV circumferential strain decreased; 3) LV twist increased.

Conclusions: In this clinical model of significant afterload reduction (patients with severe AS undergoing AVR), afterload reduction resulted in differential effects on LV long-axis versus short-axis function (systolic and diastolic) without a change in overall LV performance (LVEF). These findings provide new insights into the mechanical adaptation of the LV to chronic afterload elevation and its response to acute unloading.

Strain Imaging Improves the Accuracy of Dipyridamole Stress Echocardiography in Detecting Coronary Artery Disease

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Stress echocardiography is a cost-effective tool for noninvasive diagnosis of coronary artery disease. Several physical and pharmacological stresses have been used in combination with echocardiographic imaging including exercise, dobutamine and dipyridamole. The use of dipyridamole stress echocardiography (DE) for the diagnosis of mild to moderate coronary artery disease is controversial since dipyridamole stress is believed to mainly produce flow heterogenisity rather than ischemia. Myocardial strain imaging provides quantitative segmental analysis of myocardial function. It has been shown recently that segmental analysis of systolic strain rate has prognostic information that is independent and incremental to standard wall motion score index in dobutamine echocardiography. We sought to determine whether segmental quantification of DE using strain imaging improves the accuracy of standard DE in detecting coronary artery disease as defined by stress perfusion scintigraphy. We performed DE and Th-201 gated SPECT simultaneously in 73 patients with suspected or known coronary artery disease. DE images were analyzed using customized software to measure peak systolic longitudinal strain. Fifty-one patients had abnormal perfusion by SPECT. Standard DE reviled wall motion abnormalities in 24 patients while 57 patients had abnormal longitudinal systolic strain. The overall concordance between SPECT and wall motion assessment was 57% (k=0.30). The concordance between SPECT and DE using strain imaging was 80% (k=0.52). Analysis of agreement between SPECT and DE using strain imaging by coronary territory (n=218) revealed concordance of 82% at the LAD territory, 84% at the RCA territory and 68% at the circumflex territory. We conclude that myocardial strain imaging improves the accuracy of standard DE in detecting coronary artery disease. DE with strain imaging allows routine use of vasodilators in stress echocardiography.

Ultrasound Echocardiographic Assessment of Transmural Inhomogeneity of the Left Ventricular Contraction during the Heart Cycle

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Objectives: The normal adult left ventricle (LV) is characterized by regional nonuniformity. A spiral structure of the fibers around the LV generates rotation of the LV during contraction and relaxation. The inhomogenity of the human heart was investigated better with magnetic resonance tagging. We evaluated rotation and circumferential strain over the LV in normal subjects using novel echocardiography based signal processing method.

Methods: Circumferential strain and the myocardial rotation were calculated at 3 levels (apical, papillary muscle and mitral valve) from short-axis ultrasound echo cines in 11 normal subjects, utilizing speckle tracking imaging (UFI, GE Healthcare Inc., and Technion, Israel) and a novel signal processing method. This new method enabled high temporal and spatial resolution measurements of the myocardial velocities, so that the circumferential strain and the myocardial rotation were evaluated during a full heart cycle for 3 myocardial layers.

Results: A significant transmural difference was found in the myocardial rotation and circumferential strain. The rotation is larger in the endocardium and decreases towards the epicardium, while the apex and base rotate in counter directions (apex level: endocardium 7.7±3.4 [deg], midwall 5.0±2.3 [deg], epicardium 3.6±2.0 [deg], Papillary muscle level: endocardium 1.4±2.4 [deg], midwall 1.8±2.1 [deg], epicardium 2.3±1.3 [deg], mitral valve level: endocardium -4.4±2.0 [deg], midwall -1.9±2.4 [deg], epicardium -0.5±2.1 [deg]). Similarly, the circumferential strain is larger at the endocardium than at the epicardium. Furthermore, the circumferential strain is larger at the apex level than at the base level.

Conclusion: Transmural inhomogeneities of the left ventricular rotation and of the circumferential strain can be evaluated by echocardiography based method, and may serve as a simple, affordable and commonly available diagnostic modality.

Successful Restoration of Function of Frozen/Thawed Isolated Rat Hearts

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Introduction Long-term organ preservation for transplantation may allow optimal donor-recipient matching with potential reduction in the incidence and severity of rejection. Complete cessation of metabolism may be obtained by freezing. Previous attempts to freeze intact mammalian hearts were limited to -3.6°C, restricting tissue ice content to 34%. We hypothesized that our freezing method will allow recovery of function of the intact rat heart after freezing to -8°C, a temperature at which most of the tissue water is frozen. **Methods** Isolated rat hearts were attached to a Langendorff apparatus. After normothermic perfusion, cold cardioplegia was induced followed by perfusion with a cryoprotecting agent. Hearts were than frozen to -8°C; thawed, and reperfused for 1hr. Recovery was tested by means of haemodynamic parameters, ATP and phosphocreatine content and electron microscopy scanning. **Results** All frozen/thawed hearts regained normal electric activity. At -8°C, ice content was over 64%. The hearts maintained over 80% viability although energy stores, as represented by ATP and phosphocreatine were depleted compared to the control hearts. Integrity of muscle fibers and intracellular organelles after thawing and reperfusion, as demonstrated by electron microscopy, was maintained. **Conclusion** We demonstrate for the first time, the feasibility of functional recovery following freezing and thawing of the isolated rat heart while maintaining structural integrity and viability.

Repair of Ischemic Mitral Regurgitation: Comparison Between Flexible and Rigid Annuloplasty Rings

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Introduction: The surgical treatment of ischemic mitral valve regurgitation (IMR) usually involves implantation of an annuloplasty ring. We compared results of mitral valve repair using a flexible or a rigid annuloplasty ring in patients with IMR undergoing coronary artery bypass grafting (CABG) and mitral valve repair.

Methods: One hundred and seventy patients underwent CABG with mitral valve annuloplasty. A flexible ring was implanted in 118 and a rigid ring in 52. Age and clinical profile, degree of left ventricular dysfunction and degree of MR (mean 3.2) were similar between both groups.

Results: Operative mortality was 9% in each group. Late follow-up (58+30 months for flexible and 14+7 months for rigid groups) was available in 88%. For the flexible and rigid ring group respectively: mean NYHA class was 1.9 and 1.6, with 33% and 14% in NYHA class III-IV ($p=0.03$). There was no difference in LV function or dimensions. Mean MR grade was 1.3 and 0.7 respectively for flexible and rigid ring groups ($p=0.006$). At late follow-up, 29 patients (34%) in the flexible group had residual MR of moderate degree or greater compared with 6 (15%) in the rigid group ($p=0.03$). TI gradient was 39 and 34 mmHg (p=ns), however the degree of reduction was greater in the rigid group ($p<0.001$). Late mortality was observed in 33 patients, all in the flexible group.

Conclusions: Clinical and hemodynamic results are better with rigid mitral annuloplasty rings compared to flexible rings. This may be due to ring design which dictates not only the annular diameter, but also annular configuration. Longer follow-up is needed to determine differences in survival.

Multiple Arterial Revascularization Using the Tangential K-Graft Technique

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BACKGROUND: Complete arterial revascularization of the left ventricle with two conduits can be achieved even in triple vessel disease, using a T-configuration. However, kinks, tension and technical errors in constructing this end-to-side anastomosis can jeopardize the entire revascularization. Hypoperfusion and ignored diagonal branches are also troublesome. The tangential K-graft composite technique attempts to resolve these issues. We present our new surgical technique - Tangential (K-graft) and its intermediate clinical and physiological outcome.

METHODS: From July 2002 to September 2007, 194 consecutive patients underwent multiple arterial grafting using the Tangential K-graft technique. One end of the free graft is anastomosed end-to-side, the other sequential side-to-side anastomoses are constructed parallel to the coronary artery, and the other end of the free arterial conduit is anastomosed end-to-side to a diagonal or intermediate branch. After the left internal thoracic artery (LITA) is attached to the left anterior descending artery (LAD), a wide-open side-to-side free right ITA or radial artery (RA) to LITA anastomosis - resembling the letter "K" – is constructed.

RESULTS: Mean age was 66 (range 31 to 81). 74 patients (38%) were older then 70, 70 patients (36%) suffered from diabetes mellitus. 17 (8.8%) cases were emergent. Left ventricle ejection fraction (EF) ranged from 18% to 72% (mean 52 ± 13%). The number of distal anastomoses of the left ventricle per patient was averaged 3.9(mean). In 167patients (86 %) both IMA's and in 27 patients (17%) any IMA and RA were used. 15 patients (7.7%) were undergoing first-time reoperation. Eighteen patients (8.7%) were operated on by off-pump coronary arteries bypass (OPCAB) technique. Cross-clamp was 79±13 minutes, and bypass time was 98±16 minutes. Operative mortality was 1.55% (n=3). There was 1.55% (n=3) perioperative myocardial infarction, and one patient (0.79%) sustained permanent stroke. Deep sternal wound infection occurred in 4 patients (2 %) and six (3%) had superficial wound infections. During the follow-up in 27 arbitrary patients studied early postoperatively no of them had recurrent angina or intervention. Newly released 64-slice multidetector CT scanner verified patency in all 27 patients.

CONCLUSIONS: The K-grafting technique was found to be safe, and has the potential of increasing the ease and versatility with which the surgeon can perform total grafting to the left system using only two arterial conduits.

Neontal Brain Protection Using Innominate Artery Cannulation for Continuous Brain Perfusion in Complex Aortic Arch Repairs

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Introduction: Traditionally, deep hypothermic circulatory arrest has been used when complex neonatal arch surgery was performed. Recently, the use of antegrade cerebral perfusion (ACP) has been advocated as means of brain protection. Two basic techniques have been used; either suturing a gortex shunt to the innomonate artery, or direct cannulation of the ascending aorta with sliding of the cannula to the innominate artery when ACP is performed. Both techniques require additional surgical maneuvers to complete. For the last year we have been using direct innominate artery cannulation when ACP is performed.

Materials and Methods: During 2007, 6 neonates [Norwood (3), IAA VSD (2), severe coarctation (1)], and 1 child [intracardiac Willms tumor] underwent complex arch surgery using innomonate artery cannulation and ACP. Median age was 1 week (range- 1week-3.5yrs), median weight was 3 kg (range 2.4-12kg). Innominate artery cannulation was accomplished using 8 french modified cannula inserted 3 mm into the innominate artery and directed into the ascending aorta enabling 200cc/kg flow. CPB times: mean 176±66 min, median 221and ranges were104-268 minutes. ACP times: mean 49±27 minutes,median 40minutes, range 26-84 minutes.

Results: All patients survived the operation without neorologic damage, there were no clinical seizures. Innomoinate artery cannulation accommodated appropriate flows and de-cannulation was performed without complications.

Conclusion: Innominate artery cannulation and ACP is a safe and effective technique for brain protection in neonates and infants undergoing complex arch surgery.

Phrenic Nerve Paralysis after Pediatric Cardiac Surgery: Role of Diaphragmatic Plication

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Background: Diaphragmatic paralysis complicating cardiac surgery in children continues to occur with significant impact on morbidity.

Methods: From 2003 to 2007 our institution screened pediatric patients for phrenic nerve paralysis (PNP) following cardiac surgery. The diagnosis was suspected if difficulty was experienced in weaning the patient from the ventilator with respiratory failure. PNP was established by ultrasound screening of the diaphragm together with chest x-ray. Indications for placation were reintubation, failure to wean from ventilator, recurrent lung infection and persistent respiratory distress. Abnormal elevation of the hemidiaphragm was present in eight patients and a modified technique of transthoracic diaphragmatic plication was performed. Echocardiography was used to assess subsequent return of diaphragmatic function.

Results: Median age at diaphragmatic placation was 10.6 months. Median time from cardiac surgery to surgical placation was 12 days. Incidences of PNP were observed after Blalock-Taussig shunt, Fontan procedure, repair of coarctation and arterial switch. There were no deaths. All patients after placation were weaned from ventilation. Position of plicated diaphragm was normal in all patients.

Conclusion: Our method of transthoracic diaphragmatic placation is a simple and effective means of treatment for PNP and effectively reduced the duration of ventilation, morbidity and ICU stay.

Ligation of Patent Ductus Arteriosus for Premature Infants in the Intensive Care Units in the North of Israel

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Purpose: Patent ductus arteriosus (PDA) is common in preterm babies and persists in 15% to 80% of infants, depending on the gestational age and birth weight. The purpose was to review the results of ligation of patent ductus arteriosus in premature babies in an intensive care unit in the North of Israel.

Method: Retrospective review of premature babies who underwent ligation of patent ductus arteriosus in the intensive care units (Carmel Hospital, Bnai Zion Hospital, Ha'emek Medical Center, Western Galilee Hospital) during the period from December, 1984 to August, 2006.

Results: A total of 72 premature babies were recruited. 44 male and 28 female babies with a mean gestation of 25.7 weeks (ranged from 24 to 30 weeks) and a mean birth weight of 835 grams (ranged from 625 to 2650 gram) underwent ligation of patent ductus arteriosus via a left thoracotomy in the intensive units. The mean body weight at the time of operation was 1154 grams with a range of 570 to 3010 grams. The indications were respiratory failure and congestive heart failure. The babies were from 4 different hospitals. All except 18 babies had a trial of indomethacin induction for closure of patent ductus arteriosus (18 infants were operated before era of indomethacin treatment). The mean ductal size was 3 mm with a range of 2 to 5 mm. Until 1991 in-hospital-mortality in premature infants that underwent PDA closure was very high and reached 85% because lack of experience and technologies in treatment of this kind of patients. After 1991 only one patient died. There was no operative-mortality. Blood loss was minimal and there was no empyema or wound dehiscence. In two patients the operation was discontinued after exposure and recognition of additional congenital pathology.

Conclusion: Ligation of patent ductus arteriosus in the intensive units is safe and effective procedure. Risks, including hypothermia, encountered during transfer of preterm infants to the operating theatre can be avoided when patent ductus arteriosus is ligated in the intensive unit.

Impact of Red Blood Cell Transfusion on Clinical Outcomes in Patients with Acute Myocardial Infarction

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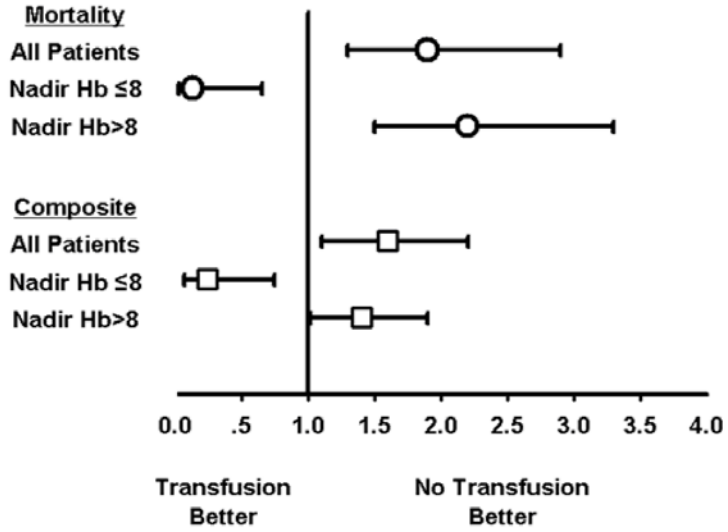
Background: There remain divergent views regarding the safety of treating anemia with red blood cell (RBC) transfusions in patients (pts) with acute coronary syndrome (ACS).
Methods: We used a prospective database to study the effect of RBC transfusion in pts with acute MI (n = 2358). Cox models were used to determine the association between RBC transfusion and 6-months outcomes. The models adjusted for baseline variables, propensity score for transfusion, and nadir hemoglobin (Hb) prior to the transfusion.
Results: One hundred and ninety two patients (8.1%) received RBC transfusion. Six-month mortality rates were higher in pts receiving transfusion (28.2% vs. 11.7%, $P<0.0001$). The adjusted hazard ratio [HR] for mortality was 1.9 in transfused patients (95% 1.3-2.9). There was a significant interaction between RBC transfusion and nadir Hb with respect to mortality ($P=0.004$). Stratified analyses showed a protective effect of transfusion in pts with nadir Hb ≤8 g/dL (adjusted HR 0.13, $P=0.013$; Figure). By contrast, transfusion was associated with increased mortality in pts with nadir Hb >8 g/dL (adjusted HR 2.2, $P<0.0001$). Similar results were obtained for the composite endpoint of death/MI/heart failure (P for interaction=0.04; Figure).
Conclusion: RBC transfusion in pts with acute MI and Hb ≤8 g/dL may be appropriate. The increased mortality observed in transfused pts with nadir Hb above 8 g/dL underscores the clinical difficulty of balancing risks and benefits of RBC transfusion in the setting of ACS.



Is the Increased Use of Coronary Angiography in Acute Coronary Syndromes Accompanied by a Survival Benefit?

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Objectives: Although the common practice of treatment of Acute Coronary Syndromes (ACS) includes coronary angiography (CA) with the intention to perform coronary revascularization, it is not clear whether such strategy is accompanied by a survival benefit in all age groups.

Methods: The study cohort comprised 5,398 patients with ACS derived from 3 prospective national surveys performed in 2000, 2002 and 2004 in all 25 CCU's operating in Israel. Baseline characteristics, hospital course, management and 1-year mortality were analyzed by 3 age groups: < 50 years old, 50-75 y.o. and > 75 y.o. and by the year of the index event of ACS. CA was used as a surrogate for mechanical revascularization enabling an intention to treat analysis. The association between in-hospital CA and 1-year mortality was assessed by the Cox regression analysis, adjusting for multiple factors known to influence the decision of performing CA as well as mortality.

Results: Baseline characteristics differed significantly between the 3 age groups as well as the rate of CA which significantly increased in each age group along the study period: the rate of CA in patients < 50 y.o. was 70%, 83.2% and 82.3% in 2000, 2002 and 2004, respectively. In the 50-75 y.o. patients these rates were 63.4%, 73.4% and 81.9%, respectively and 39.6%, 48.5% and 57.1% in the older group. The performance of CA was accompanied by a 1-year survival benefit within each age group; mortality was significantly lower in patients who underwent CA in comparison to counterparts who did not: HR=0.31 (95% CI 0.1-0.94, p=0.04) in the younger group, HR=0.5 (95% CI 0.38-0.65, p<0.0001) in the intermediate group and HR=0.54 (95% CI 0.42-0.71, p=0.0001) in the older group, reflecting the enormous differences between patients who underwent CA and those who did not. The increased use of CA was accompanied by a survival benefit only in the intermediate age group (mortality of 10.4%, 7.6% and 6.6%, in 2000, 2002 and 2004, respectively). However, no survival benefit was observed in the younger and the older groups. The over all 1-year crude cumulative mortality in 2000, 2002 and 2004 was 2.2%, 1.1% and 2.7% , respectively in the younger group and 27.8%, 24.5% and 26.2% respectively, in the older group (p=0.5, p for trend=0.6).

Conclusion: Patients with ACS who undergo CA during hospitalization have a better prognosis at 1-year. However, the increased use of CA in the treatment of ACS along the years was not accompanied by a change in 1-year survival in all age groups.

Acute Myocardial Infarction (AMI) and Pregnancy: Changes in Clinical Profile, Treatment, and Outcome

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Background: The published clinical profiles, treatments and outcomes of patients with AMI during pregnancy and the postpartum period were outdated.
Methods: Chart review of patients with documented pregnancy-related AMI before 1995 and between 1995-2006.
Results:

Variable	Before 1995 (*n*=125)	1995-2006 (*n*=103)
Mean age ±SD, *y*, range	33±6 (16–45)	33±5 (19–44
Anterior MI location, *n/n* (%)	89/122 (73)	73/94 (78)
Multiparous, *n/n* (%)	93/111 (84)	53/80 (66)
Hypertension, %	19	15
Diabetes mellitus, %	5	11
Smoking	26	45
Family history of MI, %	8	22
Hyperlipidemia	2	24
Preeclampsia, %	11	6
Elective cesarean section, %	14	19
Semielective/emergency cesarean section, %	12	19
Heart failure/cardiogenic shock after MI, *n* (%)	25 (19)	9
Coronary anatomy available, *n* (%)	68 (54)	96 (93)
Stenosis	29 (43)	41 (43)
Thrombus	14 (21)	8
Dissection	11 (16)	28 (29)
Spasm	1	2
Embolus	-	2
Normal	20 (29)	13
Intracoronary/systemic thrombolytic drug treatment for coronary thrombosis, *n* (%)	1 (1)	10 (9)
Percutaneous coronary angioplasty with or without stenting, *n/n*	1/58 (2%)	38/90 (42%)
Death, *n* (%)		
Mothers	26 (21)	11 (11)
Infants	16 (13)	6

Conclusions: Pregnancy-related AMI occurs mostly in multiparous women. AMI is anterior in >70% cases. Coronary dissection is responsible in ~30% cases. Patients diagnosed between 1995-2006 had a higher incidence of diagnostic cardiac catheterization and treatment (coronary reperfusion by either thrombolytic therapy or percutaneous intervention) and significantly better outcome (lower rate of cardiogenic shock and less maternal and fetal mortality) than those diagnosed before 1995.

Incidence, Predictors and Outcome of Upper Gastrointestinal Bleeding in Patients with Acute Coronary Syndromes

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Background: The broad utilization of revascularization and antithrombotic drugs has led to improved outcome of patients with acute coronary syndromes (ACS). Nevertheless, these strategies are associated with a substantial risk of bleeding, which is associated in turn with increased mortality. Most bleeding episodes are related to arterial punctures. The characteristics and outcome of patients who develop upper gastrointestinal (UGI) bleeding in this setting have received little attention.

Methods: Using computerized databases we identified all patients admitted to our center between 5/97 and 11/07 for an ACS who developed UGI bleeding during their hospital stay. For each case we randomly selected 3 control cases that were matched for age, gender, ACS subtype and the use of lytics. Multiple relevant baseline characteristics, as well as antithrombotic agents, revascularization strategy, endoscopy reports and 30-day mortality were recorded.

Results: 7690 patients were hospitalized in our ICCU during the study period, of whom 64 (0.8%) developed UGI bleeding, with a majority of male gender (72%). Endoscopy was performed in 35 of them. Patients with an upper GI bleeding tended to be older (67±12 vs. 64±11, $p=0.06$). There were no significant differences between groups in diabetes and other risk factors, revascularization strategy, the use of anti platelet agents and the type of ACS. Patients who bled were more frequently treated with unfractionated heparin, either alone (20% vs. 3%, $p<0.001$) or combined with LMWH during the same hospital stay (36% vs. 15%, $p<0.001$). Conversely, enoxaparin was used much less frequently in patients who bled (23% vs. 58%, $p<0.001$). Patients who developed UGI bleeding had a substantially higher 30-day mortality rate (34% vs. 5%, $p<0.001$). Among patients for whom endoscopy was available the source of bleeding was similarly distributed between the esophagus, stomach and duodenum. Gastritis and duodenitis were the most common findings.

Conclusions: Upper GI bleeding occurring in patients with ACS carries a very high risk of mortality. The use of unfractionated heparin rather than enoxaparin was associated with a substantial risk for this morbid complication.

Clinical Characteristics and Mortality Outcome of ACS Patients Treated with Bare Metal vs. Drug Eluting Stents: Insights from the National ACSIS-2004 and ACSIS-2006 Registries

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Background: The use of drug eluted stents (DES) in patients with acute coronary syndrome (ACS) which is primarily due to coronary atherothrombosis remains a topic for ongoing clinical investigation and mortality data are still awaited.

Methods: We investigated the pattern of DES vs. bare metal stents (BMS) utilization during the course of ACS in the ACSIS (Acute Coronary Syndrome Israeli Survey) 2004 and 2006 registries. We compared the baseline characteristics and short-term outcomes among the two surveys in patients who underwent PCI using either DES or BMS during or soon following the course of ACS (e.g. unstable angina, non-STEMI and STEMI). Major clinical characteristics and mortality outcomes up to 30 days were analyzed.

Results: DES utilization during the course of ACS approximately *doubled* between 2004 (16.7%) and 2006 (36.1%). The main demographic and short-term mortality results are shown in the **Table** as follow:

	ACSIS 2004		ACSIS 2006	
	DES (n=163)	**BMS (n=812)**	**DES (n=431)**	**BMS (n=763)**
Men	77	78	82	81
Age (yrs)	63.6±12*	61.3±12	61.5±12	61.8±12
Diabetes (%)	31	27	34*	26
STEMI (%)	39*	64	32*	68
Non-STEMI (%)	61*	36	68*	32
Killip Class ≥2 (%)	16	16	14	13
PCI as Primary mode of reperfusion	21*	56	30*	75
Mortality data @30 day (%)	1.2	3.5	2.8	3.2

** Statistical significant difference comparing DES to BMS groups ($p \leq 0.05$)*

Using a logistic regression analysis model, the patient's age (by 10 years increment) was the most powerful independent predictor for one month morality (OR=1.96 in ACSIS-2006 and OR=1.77 in ACSIS-2006, $p<0.05$ for both) while STEMI presentation emerged as an independent predictor for short-term mortality in ACSIS-2006 (OR=1.80, $p<0.05$) and regardless of the stent category being utilized (i.e. DES vs. BMS).

Conclusion: In Israel, the prevalence of DES utilization during the course of ACS is increasing (from 2004 to 2006) mainly among the non-STEMI patients. The short-term mortality is primarily afflicted by patients' age and STEMI clinical presentation rather by the stent type (i.e. DES vs. BMS) being utilized and long-term data are still awaited.

Coronary Computed Tomography Angiography: Evaluation of Patients in the Chest Pain Unit

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Background: 64-slice coronary CT angiography (CCTA) is established as a reliable tool in diagnosing coronary artery disease (CAD). Data regarding its utilization in the chest pain unit (CPU) are scarce.

Methods: 618 patients were admitted to the CPU during 5/2006-5/2007. 52 pts were hospitalized before performing any non-invasive test for evidence of myocardial ischemia. Of the remaining 566 patients, 232 underwent CCTA, 68 underwent stress echocardiography, and 266 underwent SPECT imaging. Exclusion criteria for CCTA: creatinine >1.4mmol/l, weight >130kg and known history of CAD. CCTA scans were performed using a 64 slice scanner (Brilliance, Philips) using beta blockers for heart rate control.

Results: CCTA findings were: normal in 142 (61%); non-obstructive CAD in 56 (24%) and technically suboptimal in 19 (8%) Coronary bridging was demonstrated in 110 patients and coronary anomalies in 3. 22 patients were referred to catheter coronary angiography (CCA) for coronary stenosis ≥70% (16/22) or for suspected stenosis, but with suboptimal imaging (6/22). Significant stenosis necessitating intervention was confirmed in 11/22 patients with >70% stenosis at CCTA and in none of the 6 patients with suspected stenosis, but with suboptimal imaging. 198 patients with normal or non-obstructive CAD were discharged without further investigation. A four-month follow-up was completed in 132 (56%) patients. During this period, none of the patients had acute coronary syndrome, did not undergo coronary intervention and/or die.

Conclusions: CCTA is a powerful tool for the exclusion of CAD in fast-track evaluation of chest pain patients. CCTA may be employed for non-invasive triage of patients with chest pain.

Modulated AC Current Defibrillation–A New, Equally Effective Method to DC Defibrillation

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Background. Defibrillation is the only clinically effective treatment of ventricular fibrillation. Early defibrillation improves the outcome and increases the chance of survival with full recovery. Immediate availability of a home-based defibrillator using mains-derived AC current will drastically improve outcome.

Aim. To develop a defibrillator based on modulated AC current, resembling biphasic configuration and compare its efficacy, in a pig model to a standard DC defibrillator.

Methods: A Computer controlled, modulated AC defibrillation system was developed using a High Voltage Switch and a High Voltage Transformer. The efficacy and safety was evaluated in 5 pigs (30-40 Kg), under general anesthesia with ketamin and isoflouran. A single quadripolar-pacing catheter was inserted percutaneously, VF was induced with rapid ventricular burst pacing and stable VF was defibrillated after 15 seconds.

DFT was determined in each animal with AC and standard DC shock using step-down protocol.

Results: The DFT with AC was 70.83±24.81 Joules and with DC was 65.83±12.41 Joules (p=0.49, Fisher Exact Test). The shock configuration is shown in the figure. No damage was observed after AC or DC defibrillation.

Conclusions: Modulated AC defibrillation is safe and effective as the commercially available DC defibrillation. The defibrillator is built from inexpensive High Voltage Transformer, without need for capacitor, batteries or routine maintenance, delivers repeated shock without any delay and provide pacing as well. It may be an ideal platform for automatic home defibrillator.

Excellent Long-Term Reproducibility of the Electrophysiologic Efficacy of Quinidine in Patients with Idiopathic Ventricular Fibrillation or Brugada Syndrome.

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Background. For almost 3 decades, our group has shown the extraordinary efficacy of quinidine in preventing the re-induction of sustained ventricular tachyarrhythmias during electrophysiologic study (EPS) in patients with idiopathic VF or Brugada syndrome. However, there are no data on the long-term reproducibility of this efficacy.

Methods. From 1979 to 2007, 76 patients with no obvious heart disease and inducible sustained VF at baseline underwent EPS on quinidine sulfate (Quiniduran*). In 71 (93.4%) of these patients, quinidine prevented re-induction of sustained ventricular tachyarrhythmias. Nine of these 71 patients underwent another EPS after 1.7 to 23.6 (9.8+6.8) years of quinidine therapy (> 5years in 8/9 patients). In 1 of 9 patients, this EPS was performed on hydrochloride quinidine (Serecor*). In 7 of the 8 patients who underwent initial and repeat EPS on the same quinidine salt, identical drug dosages were tested. Two patients underwent two late EPS on quinidine; one pt 5 years and 8 years and the other 5 years and 8 years after the initial drug study. The goal of repeat EPS on quinidine was to ensure persistent long-term drug efficacy (n=6 patients) or to elucidate the reason of syncopal episodes during therapy (n=3 patients). The protocol of programmed ventricular stimulation significantly evolved over the years as it became more aggressive (more pacing sites and/or more ventricular extrastimuli).

Results. There were 7 males and 2 females, aged 21-72 (40+16.5) years at initial EPS. Eight patients had cardiac arrest with documented VF and 1 had recurrent syncope of unknown cause. Five patients had idiopathic VF and 4 had Brugada syndrome. All 9 patients well tolerated the medication during long-term therapy and had no recurrent documented arrhythmic events during follow-up. No sustained ventricular tachyarrhythmias could be induced in any patient during repeat late EPS. In 3 patients, more aggressive extrastimulation (triple) could be tested at repeat EPS while only double extrastimulation was applied at the initial EPS.

Conclusion. Our results showed an excellent long-term reproducibility of the EP efficacy of quinidine in patients with idiopathic VF or Brugada syndrome and inducible VF. This suggests that EP-guided quinidine therapy represents a valuable long-term alternative to ICD therapy for these unique types of malignant idiopathic ventricular tachyarrhythmias.

Survival of Defibrillators the "Real World"

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Background: Defibrillator (ICD) usage is expanding rapidly, especially the use of ICD's for primary prevention. The use of this advanced and costly technology is based on assumptions of cost versus survival benefit. Most of the analysis estimate 5-7 year battery life as a base for calculations of cost benefit. The purpose of this study was to evaluate the actual survival of implanted ICD's.

Methods: The study group included 298 patients who underwent ICD implantation between 1993 and November 2007 at our hospital. We evaluated all devices replaced and also looked at patients surviving for 5 years (60 month) after implant.

Results: There were 256 men (86 %) and 42 women, mean follow up 41±26 month (6 were excluded). 203 were implanted for secondary indications (68%). 69 Devices were replaced in 61 patients 1-3 devices replaced per patient. In patients who underwent replacement the average time to replacement was 53±13 month (13-97 month). Most of the devices were replaced due to battery depletion, need for upgrade or replacement at time of procedure due to lead failure. No device was replaced due to company alert (as the only indication). Altogether 81 patients had a follow-up of more than 60 months, 31 (38%) of them without replacement.

Conclusions: The longevity of ICD's may not be as expected. The rate of ICD replacement within 5 years is higher than assumed (in the cost-effective calculations) even with a very conservative policy regarding replacement due to company alerts. Cost benefit estimations should probably be based on actual clinical data. Evaluations relying mainly on expected device longevity estimations may be inaccurate.

Is There Really No Role for EPS Testing in Risk-Stratification of the ICD-Eligible Patient Population?

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The role of EPS testing in risk-stratification of CAD patients with decreased LVEF has been questioned based on poor predictability of a negative EPS in MUSTT and MADIT-II sub-studies. However "positive EPS" in these studies excluded ventricular flutter (Vfl) or polymorphic VT (PMVT) with 3 extra-stimuli, which may be inappropriate. The recently completed Alternans (MTWA) Before Cardioverter-Defibrillator (ABCD) study included mandatory EPS -- thus providing a unique opportunity to re-assess the appropriate definition of a "positive EPS" not only based on events but also as a marker of a MTWA+ (and thus high-risk) patient. We compared on a patient-to-patient basis EPS and MTWA in the 46 patients enrolled in the 2 Israeli centers of the ABCD study. Of the 17 MTWA+ patients, 7 patients had "only" inducible Vfl or PMVT with 3 extra-stimuli ("pseudo-negative" EPS); 9 had a traditionally-defined positive EPS; and only 1 EPS was completely negative; whereas 8 of the 25 MTWA- patients had completely negative EPS. All 10 EPS- patients were free of arrhythmic events during follow-up, whereas 4 of the 7 patients with "pseudo-negative" EPS and MTWA+ had arrhythmic events. In conclusion, the definition of a +EPS test for risk-stratification needs to be broadened to include inducible PMVT or Vfl with 3 extra-stimuli, the negative predictive value of a completely negative EPS warrants a second look as a marker of a low risk patient, and most importantly no patient should be denied an ICD based on a "pseudo-negative" EPS of Vfl or PMVT with 3 extra-stimuli!

Outcome after Implantation of ICD in Patients with Brugada Syndrome: a Multicenter Israeli Study (ISRABRU)

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Background: Many electrophysiologists recommend the implantation of a cardioverter-defibrillator (ICD) in patients with Brugada syndrome who are cardiac arrest survivors or presumed to be at high-risk of sudden death (patients with syncope, familial history of sudden cardiac death or inducible VF at EPS). This multicenter study analyzes the outcome of the patients implanted in Israel.

Methods and results: All patients with Brugada syndrome who underwent ICD implantation in 11 Israeli centers between 1994 and 2007 were analyzed. There were 58 patients (52 males, 89.6%) with a mean age of 43.4 years. The indications for ICD implantation were a history of sudden cardiac arrest (10 patients, 17.2%), syncope [30 patients (51.7%) including 19 of 21 (90.4%) with inducible VF], inducible VF in asymptomatic patients (12 patients, 20.6%), history of familial sudden cardiac death (3 patients, 0.5%) and various reasons in 3 patients (0.5%). VF was induced in 4 of 5 (80%) patients who presented with cardiac arrest (n=10) and in 35 of 38 (92.1%) patients without documented cardiac arrest (n=48). During a follow up of 1-156 months (mean 42 + 35) months no patient died, 4 patients (7%) had an appropriate device therapy that was limited to those patients with a previous history of cardiac arrest. Indeed, the appropriate device therapy rate in these patients was 40%. Conversely, none of the other "high-risk" patients implanted with an ICD had an appropriate device therapy during a mean 36 + 30 months follow up period. The overall complication rate was 31.5% during follow-up, including an inappropriate shock in 16 (27.1%) patients caused by lead failure/ dislodgment (5 patients), T wave oversensing (2 patients), device failure (1 patient), sinus tachycardia (4 patients) and supraventricular tachycardia (4 patients). One patient suffered a pneumothorax and another brachial plexus injury during the implant procedure. One patient suffered a late (2 months) perforation of the right ventricle by the implanted lead that manifested with chest pain and hypotension without signs of cardiac tamponade. Eleven (18.9%) patients required a re-intervention either for infection (1 patient) or lead problems (10 patients). Eight patients (13.7%) required psychiatric assistance during follow-up due to complications related to the ICD (mostly inappropriate shocks in 7 patients).

Conclusions: In this Israeli patient population with the Brugada syndrome implanted with an ICD and followed during a mean 42-month period: 1) Appropriate device therapy was limited to cardiac arrest survivors while none of the other "high-risk" patients including those with a positive electrophysiologic study suffered an arrhythmic event; 2) The overall complication rate was particularly high, especially inappropriate device therapy, need for re-intervention and severe psychiatric disorders.

What Makes Patients with Implantable Cardioverter Defibrillator (ICD) Miserable? A Prospective Quality of Life Assessment

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The quality of life (QOL) in patients (pts) with Implantable Cardioverter Defibrillator (ICD) may be compromised by many facets of their illness and therapy

Aim of the study: To assess impact of socio-economical and clinical characteristics of ICD pts on their QOL and on their attitude toward arrhythmia symptoms and ICD therapy.

Methods: A prospective study on ICD pts, hospitalized in the Ha'Emek Cardiology Department. Demographic and clinical data was collected. A structured questioner on educational, social-economic background, experience with ICD therapy, attitude toward arrhythmia recurrences, death, and disability was administered by ICCU nurses to the pts. QOL was assessed by the Minnesota living with heart failure questioner (A high score signifies a low QOL).

Results: Thirty five pts, (5 female), mean age 68+/-10 (53-89). Time from the first ICD implantation was 2-12 years. Six pts were Israeli-Arab, 29 Israeli-Jews (5 new immigrant). Only 7 pts (21%) were employed. Seventeen pts (48%) received symptomatic ICD shocks. Eight pts (23%) had syncopal ventricular arrhythmia documented by the ICD. There was no significant difference in clinical baseline characteristics between pts who had ICD therapy or syncope and those who did not. Twenty one pts (60%) expressed fear of receiving ICD shock in public place and 14 pts (40%) expressed fear of dying from cardiac arrest. Nevertheless, 26 pts (74%) would recommend ICD to others. The mean QOL score was 21.2+/-16.7. The QOL in man was 19+/-16 versus 34+/-14 in women ($p=0.063$). QOL in pts who had ICD shock was 26+/-18 versus 16+/-14 ($p=0.069$). In pts with syncopal arrhythmia QOL was 33+/-19 versus 17+/-14 ($p<0.015$). No other clinical or socio-economical factor predicted QOL score.

Conclusion: In pts with ICD, the QOL is significantly lower following syncopal arrhythmia. Patient who had ICD shock and women tend to have a lower QOL.

Native Coronary Artery Plaque Composition of Intermediate Lesions as Assessed by Virtual Histology Intra-Vascular Ultrasound - Potential Implications for Interventional Strategy

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Background – One of the main morphologic characteristics of vulnerable plaque is a large necrotic core (NC). As most of acute rupture plaque events occur at lesion with mild stenosis we sought to investigate, using IVUS radiofrequency data analysis (virtual histology, VH), the NC distribution in coronary segments containing intermediate lesions

Methods - We have analyzed 42 native coronary segments with denovo lesions obtained from 26 non-ST elevation myocardial infraction patients (81% men, mean age 63±10.6 years, diabetes 50%, and unstable angina 50%). IVUS was performed using automatic pullback and ~2400 slices were analyzed for VH. Maximal necrotic core was defined by absolute NC area.

Results – Investigated segment location included LM 2, LAD/Diagonal 22, LCX/OM 15, Ramus 1 and RCA 2. The mean segment and lesion length were 31±20mm 12±7mm, respectively. Maximal NC area was present at MLD site in 35%, proximal to MLD site in 51% and distal to it in 14% of segments. The mean distance between MLD site and non-MLD Max NC site was 8.5±7 mm. Maximal NC area had less plaque burden, ~50% larger NC area and calcification and significantly less fibrous and fibrofatty tissues, compared to MLD site (Table). Max NC area was inversely related to plaque burden (r= -0.1147, p=0.0001) and to %FF (r= -0.684, p=0.0001), was proportional to %Ca (r=0.68, p=0.001).

IVUS/VH	MLD site	Non-MLD Max NC site
CSA	4.44±1.62	7.76+3.95
Plaque burden (%)	67±11	57.68±9.18
NC area (mm^2)	0.97±0.77	1.46±0.87
NC (%)	16.44±10	22.4±10.14
Calcium (%)	8.14±8.18	13.4±9.56
Fibrous (%)	73.63±43.94	53.28±14.73
Fibrofatty (%)	17.88±13.55	10.88±7.42

* P<0.0001 for all comparisons

Conclusions – In segments containing intermediate lesion, plaque containing maximal NC area is often located in angiographycally segments adjacent to the MLD site. This preliminary observation may carry implications for designing optimal interventional strategies and should be evaluated in larger patient's population.

Computerized Gradual Angioplasty Improves Outcome of Coronary Stenting – Final Results of a Randomized Controlled Trial

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Background: Mechanical trauma caused by PCI is a major reason for restenosis and subsequent target lesion revascularization (TLR). Drug-eluting stents (DES) reduce this problem as compared to bare-metal stents (BMS) with an increased risk of late thrombosis. To minimize this trauma we developed an automated computerized device with slow and gradual inflation (CAPSID). In a previous study in patients undergoing POBA or stenting we demonstrated improved outcomes particularly in the stented patients. The objective of this prospective study was to examine whether use of CAPSID reduced MACE and TLR in patients undergoing stenting.

Methods: Patients undergoing stenting were eligible for the study and randomized to CAPSID or standard manual inflation. Exclusion criteria were acute MI, total occlusions, bifurcation lesions, or vein grafts. Clinical follow-up for MACE was performed up to 12 months, with repeat coronary angiography performed for clinical symptoms or positive stress testing with TLR as needed.

Results: 310 patients have been randomized and have completed 12 month follow-up. Baseline clinical characteristics were similar, including age, sex, risk factors, the number of patients with unstable coronary syndromes, QCA data in both the CAPSID and control groups. 90% of the patients in each group received BMS. There was a significant reduction in MACE (death, MI, TLR) in the CAPSID group - 8% vs. 18% in the control group based on significant reductions in MI (1% vs. 7%) and TLR (5% vs. 12%) in the CAPSID group, $p<0.05$.

Conclusions: Gradual computerized balloon inflation using the CAPSID device results in a reduction in MACE and TLR in patients undergoing stenting. This method may be a valuable adjunct to BMS implantation which may provide results comparable to DES without the risk of late thrombosis.

Coronary Optical Coherence Tomography (OCT) – A Single Center Experience

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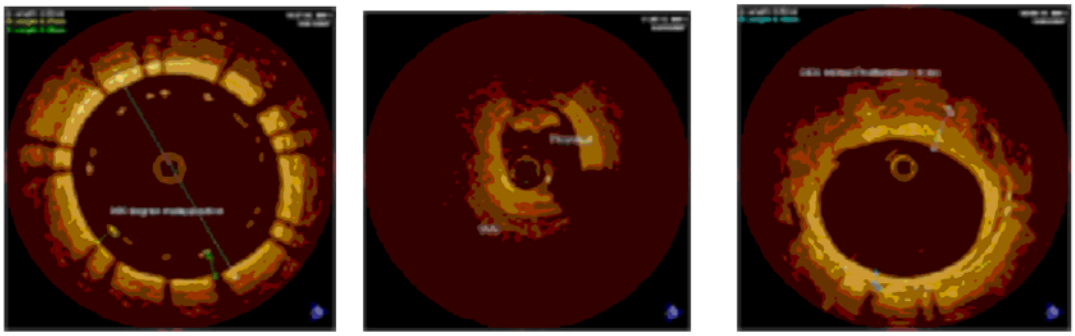
Background: OCT is a new high-resolution light-base infrared imaging modality for visualization of intra-coronary microstructures during the course of PCI.
Objective: To evaluate the use of intra-coronary OCT among patients undergoing coronary angiography and angioplasty for feasibility, safety and imaged findings.
Methods and Results: OCT was employed in 6 patients. Two patients with occlusive balloon technique while in four patients imaging was obtained with non occlusive technique. The mean age was 63±7 yrs, the majority had unstable angina at presentation (67%), four patients had pre and post stent deployment imaging for optimal stent deployment. In every case imaged, an unexpected finding has been revealed. For example (Figure): case #1 (left panel) showed severe DES mal-apposition of 360° that was well corrected with post dilatation; case #2 (middle panel) demonstrated thrombus containing lesion with tissue prolapse following angioplasty of a totally occluded graft; Case #3 (right panel) showed intimal proliferation @4 months after DES implantation. All OCT procedures went uneventfully.



Conclusions- Intra-coronary OCT imaging is feasible and seems to be safe. It provides high resolution imaged insights into intimal tissue, fibrous cap, stent apposition, tissue prolapse and the presence of thrombus in atherosclerotic lesions.

Bifurcation Lesions in the Coronary Arteries: Association between Geometric Changes after Intervention and Clinical Results

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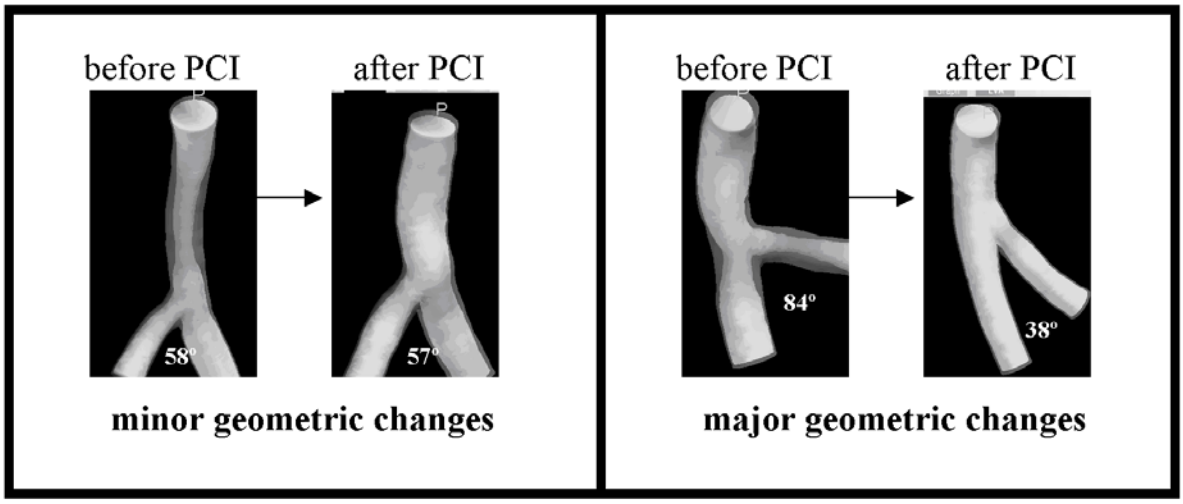
Background: Recent studies show that after bifurcation percutaneous coronary interventions (PCIs) severe morphological changes might occur. These changes appear especially at the angle between the distal main-branch and the side-branch (DMB-SB), with clinical impact that is not known yet.
Objectives: To evaluate clinical outcome of bifurcation PCIs according to the severity of angulation changes between bifurcation branches after the procedure
Methods: We used the CardiOp (Paieon Medical) system for 3-dimensional reconstruction of the coronary vessels. We conducted evaluation of 118 images from 23 patients (78% men, age 60±14 years) with bifurcation lesions in the coronary arteries undergoing angioplasty procedures. We included only interventions performed in both the main vessel and the side-branch (non-provisional) and only cases where no drug-eluting stents were used. Angles between bifurcation branches were measured, before and after stenting. For each patient a follow-up clinical evaluation was performed for up to 1 year with documentation of adverse-events such as death, myocardial infarction or need for repeat revascularization.
Results: Of the 23 patients studied, 10 patients (43%) needed target-vessel revascularization in 1-year follow-up (the TVR group). In the TVR group a non-significant trend towards a decrease in DMB-SB angle appeared (67±20 degrees vs. 54±18, p=0.13) whereas in the non-TVR group there was almost no change in the mean angle after PCI (60±14 vs. 63±18), this difference between the TVR group and the non-TVR group is statistically significant ($p<0.05$). Significant decrease in DMB-SB angle (more than 15 degrees) appeared in 40% of cases in the TVR group whereas in no patients of the non-TVR group ($p<0.05$).
Conclusion: Interventions at coronary bifurcations could result in significant geometrical changes. After intervention, a severe decrease in the angle between the distal-main branch and the side-branch could be associated with increased restenosis.



Atherosclerotic Coronary Plaque Characteristics in Diabetic Compared to Non-Diabetic Patients - Insights from Comprehensive Virtual Histology Analysis

Shmuel Fuchs [1], Ifat Lavi [2], Omer Tzang [2], David Brosh [1], Tamir Bental [1], Abid Assali [1], Hagit Dafni [1], Shmuel Einav [2], Ran Kornowski [1]

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Background – Diabetic patients known to have more diffuse coronary artery disease. Preliminary IVUS radiofrequency data analysis (virtual histology, VH) also suggest larger necrotic core (NC) in culprit lesions of patient with diabetes. However, the relation between diabetics and NC distribution in non-severe coronary obstruction was not fully elucidated. Accordingly, we sought to investigate plaque characteristics of whole coronary segments containing intermediate lesions in patients with and without diabetes.

Methods - We have analyzed 39 native coronary segments with denovo lesions obtained from 23 non-ST elevation myocardial infraction patients (83% men, mean age 64±11, unstable angina 56%, hypercholesterolemia 82%). IVUS was performed using automatic pullback and ~2100 slices were analyzed for VH. Comparison between groups was performed for most severe obstruction [minimal luminal diameter, (MLD)] and for maximal necrotic core sites.

Results – In diabetic patients, plaque composition at MLD site contained less fibrous tissue but other wise was similar to non-diabetic patients. Maximal NC area sites also differed between groups (Table). Strong correlation was noted between NC% and calcium deposition ($r=0.79$ and 0.61 for diabetics and non diabetics, respectively, $p<0.0001$ for both), whereas inverse correlation was noted between NC% and fibrous tissue in both groups ($r= -0.58$ and -0.68, respectively, $p<0.001$).

	Diabetes		Non-Diabetes	
IVUS/VH	MLD site	Non-MLD Max NC	MLD site	Non-MLD Max NC
CSA	4.5±1.8	6.2±2.1	4.8±1.6	7.1±3.1
Plaque burden (%)	69±12	63±8	66±1	59±11
NC area (mm2)	1.08±0.97	1.68±1	0.88±0.58	1.35±0.81
NC (%)	16.5±11.48	24.5±10.3	16.1±9.2	22.4±9.4
Calcium (%)	9.9±10.6	15.5±10.7*	5.7±5.0	9.8±5.7*
Fibrous (%)	53.0±12.05¶	49.9±14.7**	63.5±9.1¶	58.0±12.0**
Fibrofatty (%)	20.5±15.2	10.1±7.6	14.6±8.4	9.8±5.8

*, **, ¶: p value <0.05 between compared parameters.

Conclusions – Plaque composition of atherosclerotic coronary segments containing intermediate lesions in diabetics and non-diabetics differ in the amount of fibrous and calcified tissues. Similar relations between NC and other plaque components may suggest similar pathophysiological process. Further studies are needed to explore these early observations.

"Normal Coronary Artery" with Slow Flow Improved by Adenosine Injection, Not so Normal for the Myocytes

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Background: Some patients with chest pain and ischemia by objective criteria, undergoing coronary angiography, show no significant coronary narrowing (CN) but slow flow. For these cases we challenge the entity "normal coronary arteries".

Methods: 35 patients with chest pain and evidence of ischemia (dynamic ECG changes, ischemia at exercise test, radioisotope scan or stress echo), underwent coronary angiography. No significant CN (>50% minimal lumen diameter stenosis) was found but there was a slow coronary flow phenomena defined by angiography frames count (FC) for each coronary artery. Intra coronary (IC) adenosine was given (40-80 micrograms) followed by repeat dye injection with FC (at the same projections) and LV pressure recording.

Results:

	LAD FC	LCX FC	RCA FC
Pre Adenosine IC injection	45±12	26±8	26±7
Post Adenosine IC injection	18±3	14±4	15±6
Post/Pre	0.40	0.53	0.57

Mean LV diastolic pressure and trans-myocardial gradient where 11.5±4 and 82±12 mmHg respectively.

Conclusions: Slow coronary flow with no epicardial artery narrowing, indicates failure to deliver sufficient blood to meet the myocytes metabolic demand due to small intramyocardial blood vessel malfunction. The good but short term response to adenosine injection calls for specific oral medication (Dipyridamole? Calcium channel blocker?) to get a similar long term effect in addition to the general recommendation of risk factors modifications.

Comorbidities Convey Important Prognostic Information for Post MI Risk Stratification

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BACKGROUND: Scores, based on conventional cardiovascular parameters are available for predicting mortality after myocardial infarction (MI). There is no validated risk model to predict post MI mortality integrating non cardiovascular comorbidities.

OBJECTIVE: To create a new prognostic index for post-MI patients incorporating comorbidities based on simple available data.

METHOD: We retrospectively analyzed 2773 consecutive MI patients (age: 66±13 years, 70% males) who were discharged during 2002-2004 and had one year of follow up. Post discharge annual mortality was 12.6%. Patient data included demographics, cardiovascular, laboratory and non cardiac discharge diagnosis. Two thirds of the patients were used as the study population and a third was used to validate the model. All cause mortality was the primary end point. Multifactorial logistic regression analysis was used to identify independent predictors.

RESULTS: Out of 39 parameters that were introduced into multivariable mortality model, 18 were identified as independent predictors. Each parameter adds points (in brakes) to the model according to its independent relative risk: age 65-75y (1),>75 (3), hyponatremia (1), hyperkalemia (1), absence of echocardiography (1), severe Lt ventricular dysfunction (2), significant Lt ventricular hypertrophy (2), moderate or severe mitral regurgitation (3), moderate or severe pulmonary hypertension (2), CABG (-4), other reperfusion therapy (-2), old MI (1), renal failure (1), obesity (-1), gastro-intestinal hemorrhage (3), anemia (1), COPD (2), malignant neoplasm (3), alcohol or drug addiction (3), neurological disorders (3), schizophrenia or psychosis (3). Mean score was 2.36 (-4-+15). For each rise of one point the one year mortality increased by 1.55 (CI: 1.47-1.64; $p<0.001$). There was no significance difference between the study and validation cohorts. A One year mortality for$\leq$ 0 point was 0.3% and for patients with $\geq$7 points was 45%

CONCLUSION: Comorbidities convey important prognostic information and should be included in post MI risk models. The additional use of a simple available prognostic indicator provides a practical tool to identify patients who are at high risk of death.

Income, Education and Long-Term Survival after First Acute Myocardial Infarction

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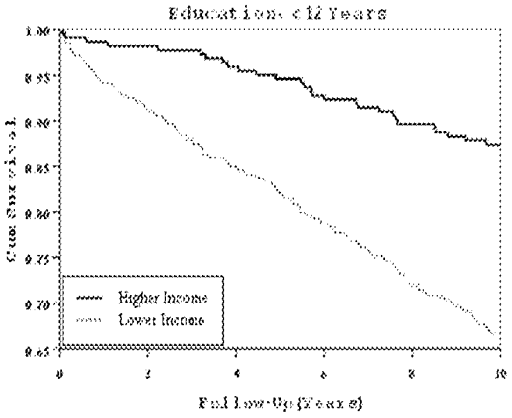
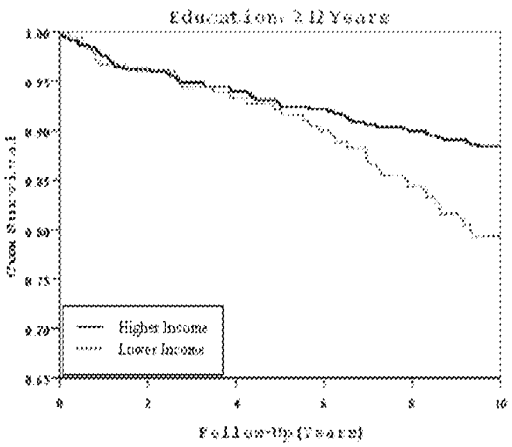
Background: Population-based data on the impact of socioeconomic status (SES) on long-term survival after myocardial infarction (MI) are lacking. We evaluated the association of income and education with all-cause mortality and cardiac mortality after MI and assessed the income-education-mortality interaction.

Methods: Between February 1992 and February, 1993, 1,521 consecutive patients aged ≤65 years discharged from 8 hospitals in central Israel after first acute MI were enrolled and followed. Data on SES indicators, cardiovascular risk factors, MI characteristics, comorbidities, and treatment variables were assessed at baseline.

Results: Low SES, as defined by income and education, was associated with older age, female sex, and higher prevalence of risk factors and comorbidities. Further, low SES patients presented with more severe disease and received fewer cardiac procedures and medications. During follow-up (mean, 12 years), 427 patients died. Income and education were independently associated with mortality. However, both factors strongly interacted (P=0.008). The hazard ratio (HR) for death associated with income (below-average vs. average/above-average) was considerably higher for less educated (<12 years) patients (2.64, 95% CI: 1.92-3.63) than for more educated (≥12 years) patients (1.53, 95% CI: 1.02-2.29) (Figure). Adjustment for various post-MI prognostic indicators attenuated these estimates, yet excess risk persisted for the less educated group (HR=1.78, 95% CI: 1.27-2.51). Similar patterns were noted for cardiac mortality.

Conclusion: Among community patients with MI, low SES is related to higher risk profile and poorer treatment. Low income is associated with a large increase in mortality risk when accompanied by low education, suggesting a double jeopardy phenomenon.





Influence of the Socio-Economic Level on the Characteristics and Outcomes of Patients Treated with Percutaneous Coronary Interventions

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Cardiology, Cardiology, Soroka Medical Center, Beer Sheva, Israel

Background: Income and educational level have been associated with compliance to treatments and outcome of cardiovascular diseases. The relation between socio-economic level and prognosis after percutaneous coronary intervention (PCI) has not been studied in Israel

Aim: To investigate the influence of the socio-economic status on clinical aspects and prognosis of residents of cities in the south of Israel who undergo PCI

Methods. Retrospective analysis of 1418 pts treated with PCI between 4/04 and 10/06. The analysis was limited to patients who were clients of Clalit Health Service and lived in cities in the south of Israel . Patients were classified according to the socio-economic index defined according to the city of residence and provided by the Central Bureau of Statistics of Israel. This index includes 10 levels and is based on 14 variables based on demography, education, occupation, income and level of life .

Patients were divided in three categories of socio – economic status: low (index=1), mid (index 3 to 5) and high (index 9-10). Groups were compared in terms of their clinical characteristics and mortality during a median follow up period of 672 days.

Results: We identified 101, 1172 and 145 patients in the groups with low, mid and high socio economic status, respectively. Patients in group "low" were younger (59±12 vs.65±12 vs.63±12, $p<0.01$); more often diabetic (45% vs. 32% vs.30%, $p=0.04$) and smokers (68% vs. 53% vs. 47%,$p=0.05$).The use of drug eluting stents was similar in the three groups (32%, 30%, 33%).The duration of clopidogrel treatment after PCI was shorter in the low group (94 ±81 days vs.132±146 vs.224±172, $p<0.01$) as was the case with aspirin (453±551 days vs. 551±347 vs.547±346 days). Higher rate of myocardial infarction was seen in the low group (9% vs.5% vs.3%,$p=0.05$). No differences were seen in mortality (10% vs.11% vs.11%) or revascularization (28% vs.17% vs 16%). Independent predictors of mortality were diabetes mellitus [OR:2.2(1.2-41)], age [OR:1.06(1.03-1.09)], duration of aspirin treatment (OR:0.99) and duration of clopidogrel treatment (OR:0.99). An independent association between socio-economic level and mortality was not found.

Conclusion: A low socio-economic index is associated with younger age at the time of PCI, more risk factors for coronary artery disease and decreased compliance with clopidogrel and aspirin therapy. We could not confirm an independent role for socio economic status on prognosis in this population.

Higher Rate of Participation in Cardiac Rehabilitation Programs among CABG Patients following an Educational Intervention

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Objectives: To evaluate an intervention designed to increase rate of Cardiac Rehabilitation (CR) attendance among patients following coronary artery bypass grafting (CABG) surgery and examine associated socio-demographic factors.

Patients and methodology: A controlled prospective study of 808 CABG patients (427 – control; 381 -intervention) recruited from 5 medical centers across Israel. The intervention included oral and written information given to patients and medical staff on patients' eligibility and benefits associated with CR participation under the Medical Insurance Basket. At baseline hospitalized patients were interviewed before surgery and again at 1-year follow up at home, for sociodemographics and clinical data.

Results: The sample consisted of 77.6% males (mean age 64.7 $\pm$10.1 years). Females were 5 years older on average. The majority (74.8%) were Jewish-Israelis followed by 21.9% Russian immigrants, and 3.3% Arab-Israelis. CR participation rate was *35.2%* in the intervention group compared to *19.4%* in the control group. A logistic regression model revealed that the following were associated with non-attendance to CR: older age (OR=1.03; 95% CI, 1.01-1.05, p=.002), being a Russian immigrant (OR=6.48; 95% CI, 3.05-13.77, p<.0001), lower income (OR=1.32; 95% CI, 1.1-1.59, p=.003), being less educated (OR=1.08; 95% CI, 1.03-1.14, p=.003).The likelihood of participating in CR was independently significantly higher in the intervention, compared to the control group (OR=1.002; 95% CI, 1.001-1.002, p<.0001).

Conclusion: The intervention almost doubled the rate of attendance at CRs and can be implemented throughout the country. Sociodemographic factors, however, should be addressed and educational material should be tailored towards specific patient-groups.

Rate of Perceived Exertion (RPE) 13 for Monitoring Cardiac Rehabilitation: A Validation Study

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Background: Supervised exercise training is an important modality in preventing recurrent cardiac events. Today many patients come to cardiac rehabilitation after successful angioplasty, with good functional capacity, and with low risk on exercise testing. These individuals can initiate exercise outside of a rehabilitation center but the need exists for follow up and monitoring. RPE 13 has been advocated as a useful and validated surrogate for monitoring individuals during exercise yet the number of studies in cardiac patients is limited. Documenting improvement over time using RPE 13 facilitates patients' self evaluation.
Methods: All patients were assessed on entry and at follow up to our cardiac rehabilitation center using a branching, symptom limited stress test. Borg ratings were recorded and blood pressure, heart rate responses, and mets at both RPE 13 and RPE 19 were entered into our database. Rates of improvement were calculated using both max mets (RPE 19) and mets at RPE 13. Data was assessed on 2785 patients for whom valid data was available.
Results:

	Pearson Correlation	Sig. (2-tailed)	N
Initial Max Met Initial RPE13 Met	**.869**	**<.0001**	**2785**
3month Max Met 3month RPE13 Met	**.882**	**<.0001**	**1788**
6month Max Met 6month RPE13 Met	**.875**	**<.0001**	**1106**
Difference initial-3month Max Met Difference initial-3month RPE13	**.550**	**<.0001**	**1676**
Difference initial-6month Max Met Difference initial-6month RPE13	**.644**	**<.0001**	**1045**

These significant correlations were maintained regardless of age, gender and original exercise capacity.

Conclusions: Our data shows significant correlations in documented improvement in exercise capacity in patients utilizing both maximum mets and RPE 13 mets independent of age, gender, and initial exercise capacity. Mets at RPE 13 may be useful as a measure for monitoring improvement in functional capacity after a cardiac event.

Low Cardiac Rehabilitation Rates among Russian Immigrants following CABG Operation and an Effective Way to Increase These Rates

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Background: Despite the wealth of evidence illustrating the benefits of Cardiac Rehabilitation Program (CRP) following CABG surgery, referral and attendance rates in Israel remain low. Since almost one third of CABG-operated patients are USSR-born, special attention should be given to the specific needs of this population.

Objectives: To assess attendance rate in CRP of USSR-born patients and to characterize their functional capacity, physical fitness and quality of life 1-year following CABG surgery as compared to Israel-born patients.

Methodology: 1110 CABG patients operated on in 5 cardiothoracic units in Israel participated in a controlled intervention trial of language-specific patient-education regarding benefits and eligibility of cardiac rehabilitation. All participants took part in two interviews: *(1) Baseline* – before surgery *(2) Follow*-up – 12 months thereafter.

Findings: USSR-born patients constitute 27% of the entire sample. In comparison to Israel-born cardiac patients, USSR-born group had a greater female proportion (31% vs. 21% respectively, p=0.017), larger rate of participants above 70 years old (39% vs. 36% respectively, p=0.04) and widowers (20% vs. 10% respectively, p=0.03). Following the intervention the attendance rate in CRP among Israeli-born patients increased from 24% to 44%, while USSR-born patients' attendance rate increased from 2% to 10%.

Conclusion: USSR-born cardiac patients underutilize cardiac rehabilitation treatment even more than Israeli born patients. A culture and language specific referral program to CRP, targeted towards USSR-born patients should be implemented throughout the country.

The Right Atrium of Patients with Various Heart Diseases Retain Progenitor Cells with Regenerative Capacity

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BACKGROUND: The notion that the adult human heart contains a pool of cardiac progenitor cells (hCPC) can be translated into an attractive approach to repair damaged hearts. However, significant amount of data regarding the characterization and function of hCPC are lacking, and no efficient, reproducible method exists to isolate CPC from human hearts.

OBJECTIVE: To determine whether the hearts of patients with ischemic and non-ischemic heart disease contain cardiac progenitor cells with regenerative capacity.

METHODS AND RESULTS: We developed an efficient and reproducible method to isolate hCPCs from the myocardium of patients with ischemic and non-ischemic heart disease, heart failure and diabetes. Following patients' consent tissue samples were donated during all kinds of open heart surgery and percutaneous RV septum biopsies. Isolated cells created typical clones, possessed self-renewal capacity and expressed stem cell markers including C-Kit, CD133, MDR1, and GATA 4.

Following *in-vitro* manipulation, hCPC successfully differentiated into the osteogenic, adipogenic and myogenic lineages.

Cell cultures from the right atrium were found to have larger amounts of C-Kit^{+} cells (17%) compared with the left atrium (5.7%) or septum (7.9%). Correspondingly, right atrium cells had better *in-vitro* differentiation capabilities.

hCPC were injected into nude rat myocardium to examine myogenic differentiation. After one week, some cells still expressed stem cell markers while others expressed specific human cardiac markers, such as human cardiac troponin I and human fetal cardiac α-actin with early sarcomere formation, indicating that some of the implanted human cells developed into cardiomyocytes *in vivo*.

CONCLUSIONS: Our preliminary findings suggest that adult human heart, especially the right atrium, retains a unique cell population with stem cell markers and multi-lineage differentiation capability. These cells, which can be isolated, expanded and stored, could be used to treat patients with heart disease.

The Impact of the NT-proBNP Assay in the Emergency Department on the Diagnosis of Heart Failure and on Outcomes in Patients Admitted for Dyspnea: A Prospective Randomized Placebo-controlled Double-center Trial (BNP4EVER)

Simcha Meisel [1], Margarita Medvedovski [2], Moshe Sharist [3], Jalal Ashkar [2], Pavel Pschianski [2], Michael Glikson [4], Shmuel Bar Haim [3], Michael Shochat [1], David Blondheim [1], Avraham Shotan [1]

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We have evaluated prospectively the impact of the NT-proBNP assay on the diagnosis of HF in patients presenting to the ER with dyspnea. NT-proBNP assay was performed in all patients randomized in 2 hospitals to open or blinded NT-proBNP. A preliminary diagnosis was made in the ER prior to obtaining result. Throughout the 17-month study, 485 recruited patients (72.5±14 years, 236 males and 249 females) presented 517 times to the ER. Validated NT-proBNP cutpoints determined the HF-unlikely (17% of patients), HF-less likely (24%), and HF-likely (59%) groups. Corresponding NT-proBNP levels were 115±94, 809±391, and 8318±8243 pg/ml. Diagnosis of HF in the ER was made in 18%, 54.5%, and 75% of patients in the 3 groups. Admission rates were 80%, 87%, and 96% ($p<0.01$), with HF as discharge diagnosis in 11%, 24%, and 66% in the 3 groups, respectively. Assay availability did not affect admission within group. 60% of blinded and 74% of unblinded patients among admitted HF-likely patients were diagnosed as HF patients ($p<0.007$). The assay did not confer a survival benefit at 21 months
in the HF-likely patients. However, if this group was divided by median NT-proBNP level (5000 pg/ml) there was a survival difference between subgroups ($p=0.0003$) and the lower than median subgroup benefited if NT-proBNP level was known ($p=0.05$). These preliminary results show that appropriate diagnosis of HF was missed in 40% of patients when NT-proBNP level was unknown. In general, survival in the HF likely patients was not altered by assay unless NT-proBNP level was less than median, in which case HF patients could be salvaged if correctly diagnosed and treated. These findings suggest underdiagnosis of HF in dyspneic patients and improved diagnostic accuracy by NT-proBNP assay.

Echocardiographic and Plasma N-Terminal Pro-B Type Natriuretic Peptide Evaluation During Pregnancy in Patients with Preexisting Dilated Cardiomyopathy

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Background: There is little experience in pregnant patientis with previously diagnosed dilated cardiomyopathy (DCM). These patients are usually advised firmly against further pregnancies.
Study aim: To exam the ussfulness of serial echocardiographic follow-up and plasma N-Terminal Pro-B-type natruiretic peptide (NT-ProBNP)evels in the management of pregnant women with preexisting DCM.
***Methods*:** We prospectevlly enrolled pregnant women with known DCM or diagnosed in the first trimester of pregnancy. Demographic, clinical caractheristics, serial echocardiographic studies and plasma ProBNP levels at base line, 30 weeks pregnancy, one and 90 day post-partum were prospectively collected.
Results: Between June 2004 to March 2007 we enrolled 7 women fulfilling the study criteria. The mean age was 33.5±3.3 years, (24 to 41), 6 caucasian, four (57%) primagravidas, two of them became pregnant after assited reproduction technique and multiple past abortions. There was a high prevalence of hypothyroidism (57%) and only one cases of diabetes mellitus, chronic hypertension, and rheumatic arthritis.
The delivery and post-partum were complicated in three patients (42%): acute heart failure resolved conservatively in two, and one with major pulmonary embolism.
The left ventricular ejection fraction (LVEF) was stable throughout the pregnancy (baseline 35% ±2.8,
30 weeks 33% ±2.9) and post-partum (1 day 35% ±2.8, 90 days 34% ±3.1). Similar stable behavior was observed regarding left ventricular dimensions, LVESD - 43.3 ±2.7 and LVEDD - 57.3±3.3 at baseline compared with 44.1±3.1 and 58.7±3.1 respectively. Two patients had demostrated good myocardial contraction reserve in pre-gestational dobutamine stress echocardiography.
The NT-ProBNP levels rised significantly in the early post-partum in all 3 patients with complications. In one additional patient the NT-ProBNP showed similar behaivor but without clinical event. In the remaining 3 patients the NT-ProBNP levels were in the upper limit range and increased only slightly one day post-partum and decreased 90 days later.
Conclusion: Serial Pro NT-BNP levels, as opposed to echocardiography, may be a better clinical tool in monitoring and management of pregnant women with preexisting DCM. An early rise in NT-ProBNP level appears to predict the occurrence of adverse events.

Early and Late Outcome of Atrial Fibrillation in Hospitalized Patients with Heart Failure

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Background: Atrial fibrillation (AF) and heart failure (HF) commonly coexist, and each adversely affects the other condition, and the interrelations between them may consititute a viscious cycle. However, the mortality, the impact of medications especially on AF subgroups have not fully investigated.

Objectives: To prospectively evaluate the impact of AF and its subtypes on management, hospital long-term mortality in hospitalized HF patients, and to identify predictors of mortality in HF-AF in comparison to HF-no AF patients.

Methods: we prospectively collected and analyzed the data of 4,102 hospitalized HF patients in a national survey conducted in all public hospitals in Israel (HFSIS 2003). AF patients were subgrouped to paroxysmal AF (PAF) (first-onset, paroxysmal or persistent) and chronic (permanent).

Results: During March-April 2003 we recorded 4,102 HF patients, 1,360 patients (33.2%) had AF: 600 patients (44.1%) PAF, 562 patients (41.3%) had chronic AF, and 198 patients (14.6%) undefined AF

Table (%):

	PAF	Chronic AF	AF-all	No AF	P (AF vs. No AF)
Male	52	52	52	60	0.0001
Age (yrs)	77	77	77	72	0.0001
Mortality					
Hospital	5.5	5.3	5.9	4.1	0.02
30-day	8.3	8.2	8.9	6.9	0.02
1-year	29.0	36.7	32.9	25.8	0.0001

Predictors of increased 1-year mortality in HF-AF versus HF-no AF patients: NYHA III-IV, renal failure, Killip class II, and III-IV, LVEF <30%, stroke/TIA anemia chronic AF COPD, age and use of furosemide and spironolactone. Hypertension, primary HF diagnosis and the use of non-dihydropyridines CCBs, anticoagulants, beta blockers and statins were associated with decreased 1-year mortality.

Conclusions: In hospitalized HF patients AF is associated with increased mortality. After adjustment to clinical variables and medications, chronic AF, Severe forms of HF, comorbidities and use of diuretics were associated with higher mortality in HF-AF patients, while PAF is tended towards lower mortality.

Correlation of Abnormal Liver Function Tests in Patients with Severe Heart Failure to Outcomes.

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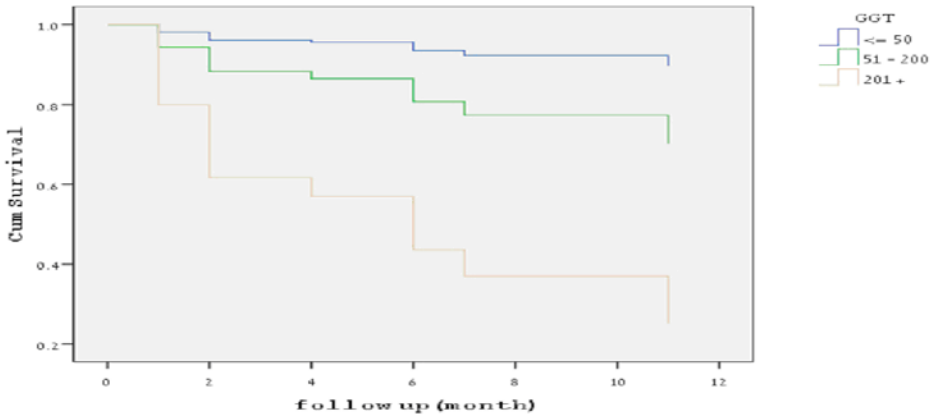
Background- Patient selection is crucial for the success of heart transplantation.
The relation of abnormal liver function tests (LFT) to outcomes of pts with severe heart failure waiting for heart transplantation is unclear yet.
Aim- To assess the relation of LFT to mortality or heart transplantation in pts with severe heart failure.
Methods and results: We analyzed all clinical, hemodynamic and laboratory data of pts with severe heart failure on the Rabin Medical Center waiting list for heart transplantation from 1/2006 -05/2007. There were 69 pts (86% males) at a mean age of 53.7± 10.0 years. The etiology was coronary artery disease in 44 (64%) pts. Mean time on the list was 4.8± 3.2 years. Mean left ventricular ejection fraction was 24%±7. 24 pts (35%) had significant pulmonary hypertension, 30 pts (43%) right ventricular dysfunction and 17 pts (25%) had significant tricuspid regurgitation. Clinical signs of right heart failure were present in nearly quarter of the pts. During the study period 12 pts (17%) underwent heart transplantation, and 5 pts (7%) died. We assessed the relation of different LFT (taken at: 1. entrance to waiting list; 2.peak results during follow-up; 3. last results) to mortality and heart transplantation. Only peak GGT, (304± 265 u/l for pts who died/transplanted vs. 136± 165 u/l for all other pts, p=0.04) was significantly related to survival or heart transplantation
Figure 1 demonstrates the relation of GGT tertials to combined outcomes:



Conclusions: In pts with severe heart failure, even mildly elevation in GGT is significantly related to mortality or heart transplantation, and thus can be used as a simple surrogate of high-risk pts, who need closer surveillance, and perhaps more aggressive interventions.

Major Adverse Events in Patients with Peripartum Cardiomyopathy: Clinical Profile and Risk Predictors

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Background: Clinical profile and predictors of major adverse events (MAE) associated with Peripartum Cardiomyopathy (PPCM) have not been characterized

Methods: A review and analysis of clinical data of 182 patients with PPCM.

Results: Forty-six patients had ≥ 1 MAE, including death (13), heart transplantation (11), temporary circulatory support (4), cardiopulmonary arrest or fulminant pulmonary edema (23), thromboembolic complications (4) and defibrillator or pacemaker implantation (10). Diagnosis of PPCM was delayed ≥ 1 week in 60% of patients and MAE preceded the diagnosis in 50% of patients. Seven (32%) of the surviving patients had residual brain damage. Patients with MAE were younger (27±8 vs. 30±7, p=0.03); more often non-Caucasians (61% vs 37%, p=0.005), had lower left ventricular ejection fraction (LVEF) (24±10% vs. 31±11%, p<0.001) and higher incidence of LVEF ≤ 25% (63% vs 31%, p=0.001) at time of diagnosis. Significant predictors of MAE were: LVEF ≤ 25% (HR = 4.20, CI: 2.04 – 8.64) and non-Caucasian background (HR = 2.16, CI: 1.17 – 3.97). These predictors in addition to diagnosis delay (HR = 5.51, CI: 1.21 – 25.04) were also associated with death or heart transplantation.

Conclusion: 1. PPCM may be associated with mortality or severe and lasting morbidity. 2. Incidence of MAE is higher in non-Caucasians and in women with LVEF ≤25%. 3. Diagnosis of PPCM is often delayed and preceded by MAE. 4. Increased awareness of PPCM is required for early diagnosis and aggressive therapy in order to improve outcome.

	No MAE n=136	**MAE n=46**	**P-value**
Age (years)	30±6	27±8	0.03
Age > 30 years	53%	42%	0.3
Non-Caucasian	37%	61%	0.005
Multipara	53%	41%	0.3
Twin Pregnancy	19%	4%	0.02
Gestation Hypertension	46%	32%	0.2
Tocolytic Therapy	18%	17%	1.0
Caesarian delivery	21%	15%	0.7
Diagnosis delay (weeks)	1.7±3.0	3.8±6.1	0.02
LVEF (%) baseline	31±11	24±10	<0.001
LVEF ≤ 25%	31%	63%	0.001
LVDD (mm) baseline	57±6	61±9	0.01
LVEF (%) at ≥ 6month	47±13	32±14	<0.0001
LVDD (mm) at ≥ 6 month	52±10	64±5	0.004
LV Recovery (LVEF ≥ 50%)	45%	18%	<0.001

Bolus Injection of Acetylcholine Terminates Atrial Fibrillation in Rats

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Background. The usefulness of the currently existing approaches to treat atrial fibrillation (AF) is limited because of their relatively low effectiveness and/or potential for adverse effects. We tested the hypothesis that uniform, transient activation of muscarinic K^+ channels throughout the atria could destabilize and terminate the arrhythmia thereby turning the heart into the sinus rhythm.

Aim. To explore the effectiveness of rapidly hydrolysable cholinergic agonists for AF termination.

Methods. Sustained AF episodes were elicited in anesthetized Wistar rats by programmed electrical stimulation via transesophageal catheter. Rats were randomly and blindly assigned with a model drug, acetylcholine (ACh, n=17), or saline injection (n=15) either via the tail vein or into the right ventricular cavity, three minutes after the AF initiation.

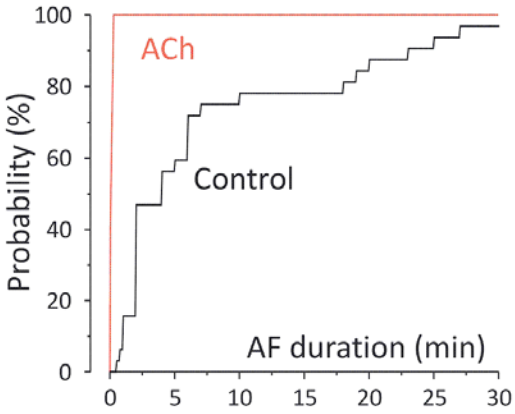

Figure 1. Probability density plot of AF episode duration in control (black) and following intravenous ACh administration (red).

Results. In all rats tested, AF was successfully converted into sinus rhythms by intravenous ACh injection, while injections of the same quantities of saline had no effect whatsoever. AF episodes were terminated almost immediately (within 8.4 ± 1.9 seconds, Fig. 1, red) following ACh administration, while the episodes in untreated AF were significantly longer (average 516 ± 132 seconds, $p < 0.0001$). The termination of AF episode was always accompanied with transient bradycardia; the sinus rhythm gradually accelerated and reached its pre-AF values within 10-20 seconds following the injection. Similar results, but with shorter recovery of sinus rhythm, were obtained with intracardiac ACh delivery (n=7).

Conclusions. These experiments provide first evidence that bolus administration of rapidly hydrolysable muscarinic agonist could be an effective way to pharmacologically terminate atrial fibrillation and restore sinus rhythm.

ZnT-1, a Novel Modulator of Cardiac L-type Calcium Channels; Insights into the Molecular Mechanism

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BACKGROUND: L-type calcium channels (LTCC), the main route of calcium entry into cardiomyocytes, are involved in various aspects of cardiac function. Modulations of LTCC activity are observed in various cardiac pathologies such as ischemia\reperfusion, cardiac hypertrophy and atrial fibrillation. We recently demonstrated that ZnT-1, a membrane protein that inhibits the LTCC without altering its expression, exists in the heart and is increased in the rat atria following acute rapid pacing as well as in the atria of AF patients. In this study we explored the molecular mechanism of ZnT-1 activity, especially in regard to possible interactions with the regulatory β-subunit of the LTCC. **METHODS AND RESULTS**: ZnT-1 induced inhibition of the LTCC was tested in HEK 293 cells and *Xenopus* oocytes. In the absent of the β-subunit ZnT-1 did not inhibit the LTCC current in *Xenopus* oocytes. Direct interaction between ZnT-1 and the LTCC β- subunit was demonstrated by co-immunoprecipitation of ZnT-1-myc and β-subunit using anti- β-subunit and anti- myc antibodies. Furthermore, Fluorescent Resonance Energy Transfer (FRET) was demonstrated in cells co-expressing β_{2a}:CFP and ZnT-1:YFP indicating molecular-range proximity between these proteins *in-situ*. In addition, changes in the cellular distribution of the ZnT-1 in cells co-expressing the β-subunit with ZnT-1:YFP were demonstrated by Total Internal Reflection Fluorescence measurements. **CONCLUTION**: The interaction between the LTCC β-subunit and ZnT-1 is an essential component in the mechanism underlying the ZnT-1 induced inhibition of the LTCC. This mechanism can serve as an important drug target for modulation of LTCC function in the diseased myocardium.

CRP Accelerates Thrombosis by Suppressing COX-2 expression and Activity

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Background: C-reactive protein (CRP) is a mediator of increased thrombogenicity and thus an increased risk of vascular disease. The prostanoids, thromboxane (TXA2) and prostacyclin (PGI2) play key, yet opposing, roles in vascular homeostasis; hence, alterations or imbalances of these two prostanoids levels, are implicated as mediators of various CV diseases. The present study examined the effects of CRP on the cyclooxygenase (COX) mediated pathways in transgenic mice that express human CRP (CRPtg).

Methods: CRPtg and littermate C57/BL mice were subjected to femoral artery wire injury. The expression of key genes in the prostanoid pathway was measured by real time PCR and Western Blot in injured arteries and in lung tissue, at baseline, 6hr, and 24hr after injury (n=5-7/group).

Results: COX-2, prostacyclin synthase and prostacyclin receptor after vascular injury were significantly reduced in CRPtg while thromboxane synthase and thromboxane receptor were significantly augmented. Immunohistochemcial staining confirmed the reduced expression of COX-2 and the elevated thromboxane receptor expression in the injured arteries of CRPtg. Urinary prostacyclin metabolites were significantly reduced in CRPtg as compared with wildtypes. Aspirin therapy (30 mg/kg/day) reversed the prothrombotic effect of CRP as measured by reduced carotid thrombosis following photochemical injury and prostanoid pathway gene expression after femoral wire injury.

Conclusions: In mice transgenic for human CRP, arachidonic-acid cyclooxygenase pathways are modulated towards suppressed prostacyclin expression and increased thromboxane activity. These effects may promote thrombosis in response to injury and may provide rationalization for the increased incidence of vascular events that is associated with high CRP levels.

In Vivo Engraftment of Tissue-Engineered Human Vascularized Cardiac Muscle

Manhal Habib [1], Ayelet Lesman [2], Oren Caspi [1], Yaara Basevitch [2], Amira Gepstein [1], Gil Arbel [1], Irit Huber [1], Shulamit Levenberg [2], Lior Gepstein [1]

[1] Sohnis Family Research Laboratory, Bruce Rappaport Faculty of Medicine, [2] The Department of Biomedical Engineering, Technion- Israel Institute of Technology, Haifa, Israel

Myocardial cell-replacement and tissue-engineering strategies are hampered by the lack of sources for human cardiomyocytes and by significant donor cell loss following transplantation. As a possible solution to these obstacles, we assessed the ability of 3D tissue-engineered human, vascularized, cardiac-muscle to engraft in the *in-vivo* rat heart and to promote functional vascularization.

Human embryonic stem cell-derived cardiomyocytes, alone(C), or in combination with human vascular precursor cells and embryonic fibroblasts (CHM), were seeded on degradable biopolymer-scaffolds. Synchronously contracting cardiac tissue-constructs were formed *in-vitro* that contained a dense vessel-network (CHM group). Grafting of the engineered tissue in the rat heart resulted in the formation of long-term stable grafts, showing cardiomyocyte structural maturation. Electromechanical integration between donor and host tissues was suggested by Cx43 immunostaining and electrical recordings. The formation of human and rat-derived vasculature within the scaffold was confirmed by immunostaining for SMA and human-specific-CD31. Intraventricular injection of fluorescent microspheres and lectin resulted in their incorporation by blood vessels within the scaffolds, confirming their functional perfusion capabilities. Finally, the number of vessel lumens per mm^2 was significantly greater in the CHM-containing scaffolds (57 ± 7, $p<0.05$) when compared to those containing cardiomyocytes alone (37 ± 5).

Conclusions: (1) Tissue-engineered human cardiac muscle, containing a dense vascular network, can be established *ex-vivo* and grafted *in-vivo* to form stable, integrated, cell-grafts. (2) The transplanted tissue-constructs showed significant vascularization, consisting of both pre-existing human- and newly-formed rat vessels. (3) The pre-existing human vessels increased scaffold vascularity and also became functional by integrating with host rat vascular network.

Isl1 Gene Therapy – Triggering Endothelial Cells' Angiogenic Properties in a Direct and Paracrine Manner

Aya Barzelay [1], Jeremy Ben-Shoshan [1], Sophia Maysel-Auslender [1], Michal Entin-Meer [1], Iris Barshack [1], Eldad Tzahor [2], Gad Keren [1], Jacob George [1]

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The LIM-homeobox transcription factor islet-1 (isl1) plays a key role in the specification of myocardial, pacemaker, endothelial, and smooth muscle cells, which are derived from the secondary heart field during heart embryogenesis. Moreover, Isl1+ precursors have the potential of self renewal and differentiation into endothelial, cardiomyocyte and smooth muscle lineages.

We investigated whether retroviral gene delivery of isl1 to endothelial cells (ECs), could promote angiogenic properties of transduced and wild type (WT) ECs.

Murine ECs were transduced to express isl1. transduced Cells' Proliferative capacity was assessed by thymidine incorporation assay and propidium iodide staining. Adhesion to fibronectin, and to monocytes was also examined. Cell based-ELISA was established to evaluate VCAM-1 and ICAM-1 expression. Angiogenesis–related cytokine secretion of transduced cells was detected using cytokine arrays. Paracrine effect on WT ECs migration and vasculogenic activity was evaluated using a Boyden chamber and tube formation on Matrigel, respectively. Eventually, the contribution of Isl1 to ECs-induced vessel formation was studied by a Matrigel plug *in vivo* assay in mice.

Isl1 expression resulted in enhanced proliferation, adhesion to fibronectin and monocytes. In addition, increased IL-1β and VEGF secretion was evident, which translated to a promoting paracrine effect on WT ECs migration and tube formation. Finally, Isl1 expressing ECs induced enhanced *in vivo* vascularization in mice, evident by immunohistochemistry.

These data suggest that isl1 cell based gene therapy approach may have a considerable therapeutic potential in promoting angiogenesis by triggering EC intrinsic proangiogenic functional properties, as well as by endowing paracrine amplification on angiogenesis.

Percutaneous Anterior Leaflet Augmentation - a Novel Approach to Mitral Valve Repair in Ischemic Mitral Regurgitation

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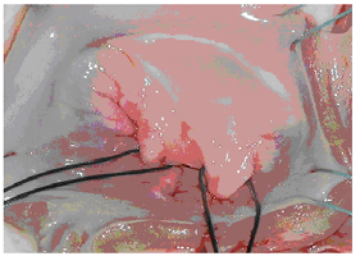
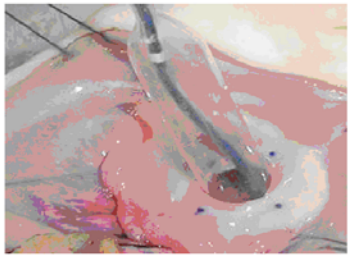
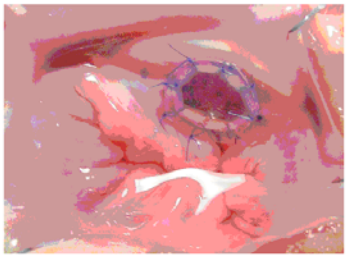
BACKGROUND: Ischemic mitral regurgitation (IMR) is a common complex and poorly understood clinical entity, associated with poor long-term survival. Numerous surgical techniques have been developed for IMR, but none has resulted in clearly improved patient outcome. Additionally co-morbidities often associated with ageing and age itself is independent risk factors for adverse outcome after surgery. Percutaneous techniques to treat MR can reduce surgical risk and can be categorized to a) mitral annulus reshaping techniques, and b) leaflet edge-to-edge repair. We report a novel percutaneous technique and initial preclinical experience of mitral valve repair with anterior leaflet augmentation.

METHODS AND RESULTS: the novel percutaneous approach is based on the understanding that anterior leaflet augmentation allows relief of leaflet tethering and excellent leaflet coaptation. The procedure was tested ex vivo in three pig hearts. Mitral valve incompetence was achieved by posterior leaflet chordal shortening. The central portion of the anterior leaflet was augmented using balloon inflation and implantation of a 0.9 cm balloon-deliverable disc in the area created by balloon inflation. A flow system was used to test the presence of mitral regurgitation. In all three experiments, morphological augmentation was achieved and no signs of mitral valve incompetence (leak) were present. The concept soon will be tested in-vivo in a sheep model of Ischemic Mitral Regurgitation.

CONCLUSIONS: Novel percutaneous anterior leaflet augmentation for ischemic MR was feasible and resolved mitral regurgitation in ex vivo model. This novel method may be a viable option for patients with ischemic MR.

Prognostic Importance of Body Mass Index in patients Undergoing Primary Coronary Angioplasty for Acute Myocardial Infarction

Igal Teplitsky, Abed Assali, Eli Lev, David Brosh, Hana Vaknin-Assa, Itsik Ben-Dor, Fuchs Shmuel, Nurit Shor, Alexander Battler, Ran Kornowski

Cardiology, Rabin Medical Center,and the Sackler Faculty of Medicine,Tel-Aviv University, Petach Tikva, Israel

Background: Recent studies have shown a lower mortality in obese patients (pts) with coronary artery disease as well as in specific group of pts after elective percutaneous coronary intervention (PCI). There is paucity of data regarding outcomes of obese pts with acute myocardial infarction (AMI). Thus, our study aimed at evaluating clinical outcomes of obese pts treated by primary PCI for STEMI.

Methods and results: we used our clinical database consisting of all patients treated by primary PCI (≤ 12 hours) for AMI between 1/2001 and 7/2007 excluding pts with cardiogenic shock. The clinical and angiographic results of pts was determined according to body mass index (BMI) as follow: normal BMI (< 25); overweight (BMI=25-29.9) and obesity (BMI ≥ 30).

Results: are shown in **Table**:

	BMI<25 (N=310)	**BMI=25-29.9 (N=380)**	**BMI ≥30 (N=199)**	**P value**
Age	61±13	60± 13	58±10	0.007
Male	79%	85%	83%	0.1
Diabetes mellitus	20%	21%	36%	0.001
Hyperlipidemia	37%	48%	48%	0.005
Hypertension	37%	45%	59%	0.0001
Killip Class≥2	15%	15%	18%	NS
LVEF≤40%	47%	41%	37%	0.05
Ref. diameter (mm)	3.0±0.5	3.0±0.5	3.2±0.5	0.002
Pre-TIMI grade 0-1	61%	62%	68%	NS
Post TIMI 3	97%	94%	96%	NS
1-month / 6-months				
Death (%)	3.9/5.7	2.4/3.9	2.0/4.2	NS
Re-MI (%)	2.6/4.7	2.6/5.5	2.0/4.2	NS
Stent Thrombosis (%)	1.6/2.7	1.8/3.3	1.5/2.6	NS
TVR (%)	0/8.3	0/9.1	0/6.8	NS
CABG (%)	1.9/4.3	3.4//4.7	1.5%/5.3	NS
MACE (%)	7.4/16	8.4/16	6.5/15	NS

Conclusion: 1) Despite increased incidence of diabetes mellitus, hypertension and hyperlipidemia and worse LV function at STEMI presentation, obese patients have the same mortality and MACE outcomes for compared to counterparts with normal BMI, 2) These findings could be explained in part by increased vessel diameter and/or yet undefined cardio-protective BMI-related mechanisms.

A Method for Reducing Amount of Contrast in Patients at Risk for Contrast Nephropathy

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Cardiology Department, Catheterization Laboratory, Meir Hospital, Kfar-Saba, Israel

Background: Hydration, reno-protective medications and low osmolality contrast are used to reduce the incidence of contrast nephropathy (CN).
We describe a method that permits coronary angiography and PCI with minimal amount of contrast .
Methods: The essence of our method is using high rate (e.g. 6 ml/sec) ACIST injections which allows very small volume (<2 ml) to opacify the coronaries. Reviewing injections may need frame by frame rather than loop inspection. We meticulously adhered to the following 10 rules: 1. Plan the procedure to use the smallest amount of contrast (e.g. review previous catheterizations). 2. Avoid contrast for catheter intubation at the coronary ostium. 3. Do not use side holes catheters. 4. Use "friendly" catheters to enter the ostium with minimal manipulation. 5. Use ACIST for volume controlled injections and avoid manual injections. 6. Train your finger to inject very small test injections. 7. Avoid reflex administration of contrast. 8. After each injection sum on the total amount of contrast used. 9. Avoid contrast if possible while introducing guidewires. 10. Use markers (calcification, previous stent) for road mapping and positioning of balloon/stent.
Results: Ten patients at high risk for CN were catheterized using this method. The average age was 66.5±9.5 years. Seventy percent had DM. The average amount of contrast was 14.06±4.6 ml for diagnostic coronary angiography and 15.7±6.6 ml for angioplasty. No angiographic effect was noted at the site of coronary injection. Serum creatinine was 2.26±0.66 mg% before and 2.15±0.58mg% (1 and 3-5 days) after the procedure.
Conclusions: Diagnostic coronary angiography and PCI can be completed with use of tiny amount of contrast. This method avoids contrast nephropathy even in patients at high risk.

Metabolic Syndrome is Associated with Worse 6-month Outcomes of Patients Undergoing Primary Percutaneous Coronary Intervention for Acute Myocardial Infarction

David Brosh, Abid Assali, Igal Teplitsky, Hana Vaknin-Assa, Shmuel Fuchs, Eli Lev, Avital Porter, David Hasdai, Eldad Rechavia, Alexander Battler, Ran Kornowski

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Background: Metabolic syndrome is associated with increased risk of cardiovascular events. Recent studies have shown that it is highly prevalent among young patients with acute myocardial infarction (AMI), and it is not associated with increased risk of restenosis in patients undergoing elective percutaneuos coronary intervention (PCI). However, only limited data are available on the effect of metabolic syndrome on long-term outcomes of unselected patients undergoing primary PCI for AMI.

Method and Results: We used our database of all pts (n=1336) undergoing primary PCI for AMI between 1/2001 and 7/2007, excluding those with cardiogenic shock and late arrivals (>12hrs from symptoms onset to 1st balloon inflation). Metabolic syndrome was defined according the WHO clinical criteria as: diabetes type-II or impaired fasting glucose (≥110mg/dL) plus any 2 of the following criteria: HTN (on medical treatment) or systolic BP≥140mmHg or diastolic BP≥90mmHg; Trig≥150mg/dL; HDL<35mg/dL in men or HDL<39mg/dL in women; BMI>30kg/m2. Patients (n=833) were allocated into 2 groups: 1st Group (n=674 pts) included those without metabolic syndrome and 2nd Group (n=159 pts) included those with metabolic syndrome. Patients' clinical and angiographic characteristics as well as 6-month outcomes are shown in **Table:**

	No Metabolic Syndrome	**Metabolic Syndrome**	P Value
N	674	159	
Age	60±13	61±11	0.6
Male (%)	83	75	**0.02**
Anterior AMI (%)	49	43	0.4
2-3 Vessel CAD (%)	54	68	**0.001**
Renal failure(GFR<60) (%)	12	20	**0.005**
CADILLAC score	4.3±3.6	4.1±3.4	0.6
Initial TIMI Flow 0-1 (%)	1.3	1.3	0.99
Anti GP 2B/3A (%)	78	76	0.8
Final TIMI Flow 3 (%)	96	96	0.7
No/Slow Reflow incl. transient (%)	5.6	7	0.6
Six Months			
Death (%)	4.4	6.9	0.3
Re-MI (%)	5.9	8.9	0.2
Stent thrombosis (%)	2.8	6.3	**0.03**
TLR / CABG (%)	8.2 / 4.3	11.3 / 6.9	0.1 / 0.2
MACE (%)	15.3	23.3	**0.007**

Conclusion: Metabolic syndrome in patients undergoing primary PCI for AMI was associated with increased risk of stent thrombosis, resulted in worse 6-momth outcomes.

Timing of Percutaneous Coronary Intervention of the Non-Culprit Artery in Patients with Multivessel Disease and Acute Myocardial Infarction

Itsik Ben-Dor, Ran Kornowski, Paz Kedem, Shmuel Fuchs, Hana Vaknin-Assa, Eldad Rechavia, David Brosh, Eli Lev, Tamir Bental, Alexander Battler, Abid Assali

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Background: The role and timing of complete revascularization of non-infarct related artery [n-IRA] after STEMI is controversial

Objective: To compare n-IRA outcomes between different PCI timing strategies of n-IRA

Methods: We used our clinical Database consisting 145 consecutive patients with multi-vessel disease (≥70% stenosis of ≥2 coronary arteries) treated by primary PCI within 12 hours of chest pain for AMI. Patients with cardiogenic shock were excluded. Patients were subdivided in 3 groups: 1) patients undergoing PCI of the non-IRA during initial procedure 2) patients undergoing PCI of the non-IRA in hospitalization 3) patients undergoing PCI of the non-IRA during 6-months [operator's discretion: clinical, anatomic, or stress testing].

Results: The study included 145 patients with multivessel disease who underwent PCI of the non-IRA during the first 6 month. Clinical characteristic and 6 months are summarized:

	Group I (Initial) **N=38**	**Group II** (Hospitalization) **N=36**	**Group III** (within 6-moths) **N=71**	**P-value**
Age (years)	66±15	68±12	62±10	0.06
Males (%)	76	81	82	0.8
GFR (<60 mL/min/1.73 m^2) (%)	26	22	14	0.6
Killip class >1 (%)	27	29	16	0.2
Anterior MI (%)	55	33	45	0.3
Diabetes (%)	34	48	37	0.4
No reflow-culprit (%)	5	15	7	0.3
Successful PCI-culprit (%)$^{\tau}$	97	91	92	0.7
Ejection fraction <40% (%)	55	43	49	0.6
CADILAC risk score	6.1±3.9	6.4±4	5.5±3.5	0.4
6-monhs outcome				
Death (%)	10.5	14	3	0.08
Re-AMI (%)	10.5	11	13	0.9

$^{\tau}$ TIMI 3 and residual stenosis <30%,

Conclusions: Our preliminary data suggest that deferring PCI of n-IRA in AMI patients with multivessel is preferred in suitable cases based on clinical and anatomic consideration.

The Effect of Baseline Platelet Count on Outcomes in Patients with Acute Myocardial Infarction Undergoing Primary PCI

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Background: Platelets may impact the thrombosis outcomes in the acute myocardial infarction (AMI). There are few data regarding the impact of platelet count (PC) on clinical outcomes of patients undergoing emergent PCI during STEMI. This study aimed at evaluating the impact of baseline (PC) on clinical outcomes among patients treated by primary PCI for AMI.

Methods and Results: we used our data consisting of all patients treated by primary PCI (≤ 12 hours) for AMI between excluding pts with cardiogenic shock. The clinical results of treated pts studied, distinguished according to quartiles of baseline PC are shown in the accompanied **Table**:

Platelet Count 10^9	**<210 (N=232)**	**≥210-<246 (N=232)**	**≥246-<298 (N=233)**	**PC≥298 (N=234)**	**P**
Age (yes)	61±12	62± 13	59±13	60±12	0.1
Male	87%	82%	83%	77%	0.04
Diabetes mellitus	20%	28%	28%	25%	0.2
Hyperlipidemia	49%	53%	45%	43%	0.2
Hypertension	45%	41%	48%	49%	0.3
MV disease	59%	60%	58%	55%	0.9
Killip Class>1	13%	16%	16%	19	0.7
Anti GP 2B/3A	79%	77%	77%	75%	0.8
6-months events					
Death	3.2%	5.8%	5.8. %	7.9%	0.1
Re-MI	6.3%	6.7%	3.5%	7.9%	0.8
Stent Thrombosis	2.7%	2.2%	2.2%	6.6%	*0.04*
TVR	10.9%	8.5%	6.6%	13.6%	*0.07*
CABG	6.3%	6.3%	3.1%	3.5%	0.2
MACE	18.6%	17.9%	15.9%	21%	0.5

Conclusion: Patients with higher baseline PC who were treated on emergent basis using primary PCI for STEMI had higher 6 months rates of stent thrombosis and also tended to have higher TVR. It remains to be determined the exact platelet-derived mechanism which may be responsible for this observed phenomenon.

Human Plasma Corin Level as a Predictor of Major Cardiovascular Events Post PCI

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Background: Corin is a Type II transmembrane protease responsible for the cleavage of Pro-ANP to ANP and Pro-BNP to BNP.
ANP and BNP have vasodilatory and antiproliferative functions , and may confer protective effect against atherosclerosis.
In a previous study we found that plasma corin level is significantly higher in atherosclerotic patients compared to healthy volunteers (Abstract 3741:Human serum corin levels in healthy and atherosclerosis .Circulation 2007;116:II_850-II _851).
The assay of plasma corin level in the human was developed in our institution.

Hypothesis: Plasma corin level measured pre-PCI can predict major adverse cardiovascular events in long term follow up .

Methods and results: 98 atherosclerotic patients in whom plasma corin levels was measured pre-PCI were followed between two to three years for MACE .Forty six patients suffered from MACE (mortality ,re-infarction ,angina pectoris ,recurrent revascularization , CVA/TIA). Plasma corin level was significantly lower in the MACE group compared to the non-MACE group (729 pg/ml ,Std error 39 vs 849 pg/ml ,Std error 45 ,P=0.05 by unpaired t test). By multivariate analysis corin was an independent predictor of MACE

Conclusion: Plasma corin level can predict long term MACE in coronary artery disease patients post-PCI.

Outcome of Emergency Percutaneous Coronary Intervention for Acute ST-Elevation Myocardial Infarction Complicated by Cardiac Arrest

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Background: The poor prognosis of primary percutaneous coronary intervention (PCI) in patients resuscitated from cardiac arrest complicating acute ST-elevation myocardial infarction (STEMI) may be at least partly explained by the common presence of cardiogenic shock. We examined the effect of emergency primary PCI on outcome in patients without cardiogenic shock who were resuscitated from cardiac arrest before the procedure.

Methods: The study group included 948 consecutive patients who underwent emergency primary PCI at our medical center from 2001 to 2006 for STEMI not complicated by cardiogenic shock. Twenty-one were resuscitated from cardiac arrest before the intervention. Data on background, clinical characteristics, and outcome were prospectively collected in all the patients.

Results: There were no differences between resuscitated and non-resuscitated patients in age, sex, infarct location, or left ventricular function. The total one-month mortality rate was higher in the resuscitated patients (14.3% vs 3.4%, p=0.033), but noncardiac mortality accounted for the entire difference (14.3% vs 1.2%, p=0.001), whereas cardiac mortality was similarly low in the two groups (0% vs 2.0%, p=NS). Predictors of poor outcome in the resuscitated patients were older age (r=0.47, p=0.032), unwitnessed sudden death (r=0.44, p=0.04), longer interval from cardiac arrest to arrival of a mobile unit (r=0.67, p=0.001) or to spontaneous circulation (r=0.65, p=0.001), low glomerular filtration rate (r=-0.50, p=0.02), and the initial Thrombolysis in Myocardial Infarction grade of flow (r=-0.51, p=0.017).

Conclusions: In patients with STEMI not complicated by cardiogenic shock, emergency PCI exerts a similar beneficial effect on cardiac mortality in those who were resuscitated from cardiac arrest and in those without this complication. The higher mortality rate in among resuscitated patients is explained by noncardiac complications.

Twenty Years of Out-of-Hospital Resuscitations
The SHL Experience in Israel

Edo Birati [1], Nomi Malov [2], Yevgeni Kogan [3], Yigal Yanay [2], Mira Tamari [2], Mayera Elizur [2], David Steinberg [4], Michal Golovner [2], Arie Roth [2,3,5]

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Background: The Magen David Adom 1988 report on resuscitation outcome of out-of-hospital cardiac arrest victims in Israel revealed that 17% of them were admitted to hospital of whom 7% were discharged alive from hospital. The most common heart rate recorded upon arrival of the Mobile Intensive Care Unit (MICU) at the scene was asystole or severe bradycardia.

Objective: To report the 1987-2007 experience of resuscitation of out-of-hospital cardiac arrest victims, who were 'SHL' subscribers, by SHL-Telemedicine MICU teams.

Methods: The medical records, including MICU reports and reports by MICU physicians containing specifics of CPR maneuvers and outcome of patients who underwent resuscitation, were analyzed. In addition, each patient who had been resuscitated and transported to hospital was followed by telephone calls and report of hospital discharge or expiration in the hospital.

Results: A total of 1810 patients (67% males) with a mean age of 76±12 years (16-104) were resuscitated. One-third (597, 33%) were admitted to hospital and 279 (15.4%) were discharged alive. Factors associated with successful resuscitation included witnessed collapse and ventricular defibrillation. A history of heart failure, diabetes, hyperlipidemia, stroke or advanced age adversely affected results. Noteworthy, transtelephonic instructions for basic CPR were given to and performed by laymen on 121 patients of whom 13 (10%) survived to hospital discharge.

Conclusions: The knowledge of the availability of the SHL-Telemedicine call center for prompt response in the setting of out-of-hospital sudden collapse enabled witnesses to summon rapid medical assistance for victims by directly contacting the SHL call center.

The Relationship of Plasminogen Activator Inhibitor-1 Levels to the ST Deviation Pattern of Acute Myocardial Infarction

David Rott [1], David Leibowitz [1], Zvezdana Finci-Yeheskel [2], Vivian Barak [3], Tova Chajek-Shaul [1], Teddy Weiss [1], Mark Levin [2], Simcha Urieli-Shoval [2]

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Background: Myocardial infarction (MI) may be classified as ST elevation MI (STEMI) or non ST elevation MI (NSTEMI). In STEMI the culprit artery is usually completely occluded by a thrombus, whereas in NSTEMI it is usually patent with a non-occlusive thrombus. Pro-coagulants such as Plasminogen activator inhibitor-1 (PAI-1) as well as markers of inflammation such as C-reactive protein (CRP), serum amyloid A (SAA) and interleukin-6 (IL-6) are elevated in acute coronary syndromes however, no study has examined whether levels of these markers differ in patients with STEMI as opposed to NSTEMI.

Objective: To determine whether there are differences in plasma levels of PAI-1, CRP, SAA or IL-6 in patients with STEMI as compared to patients with NSTEMI.

Methods: Consecutive 76 patients presenting with an acute MI (37 with STEMI and 39 with NSTEMI) were prospectively enrolled. Blood samples were obtained from patients within 6 hours from presentation and plasma PAI-1, CRP, IL-6 and SAA concentrations were measured.

Results: Plasma levels of PAI-1 were significantly higher in patients with STEMI as compared to NSTEMI: 85.7±5 vs 61.3±5 ng/ml ($p<0.001$), while CRP, SAA and IL-6 levels were not significantly different in STEMI as compared to NSTEMI.

Conclusions: Higher plasma PAI-1 levels in STEMI patients may contribute to the predilection of these patients to occlusive thrombi and STEMI.

Serum Anti CRP Antibodies,CRP and Coronary Atherosclerosis in Patients with Acute Coronary Syndromes

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Background: Serum **CRP** concentrations levels are correlated with the presence and severity of **CHD**. Anti **CRP** antibodies were first described in 1985 in the sera of patients with different rheumatic conditions, including 23% of **SLE** patients.
A positive correlation was demonstrated between anti CRP antibodies and SLE activity, yet the relation between anti **CRP** antibodies and **CHD** have not been established
We tested the presence and potential association of anti-**CRP** antibodies with **CRP** and with the incidence and extent of coronary atherosclerosis in patients with acute coronary syndromes (**ACS**)
Methods: between September 2004 and December 2005 we collected the sera of 324 patients admitted to the hospital due to **ACS** and underwent cardiac catheterization, and tested the levels of **CRP** and anti- **CRP** antibodies. The extent of coronary vessel disease was assayed from admission cardiac catheterization.
We also prospectively evaluated major cardiac events in this population 24 months post admission
Results : We observed a direct association between **hsCRP** levels and the extent of coronary atherosclerosis. Interestingly, we have found a negative correlation between antibodies to **CRP** and vessel affliction. There was also an inverse correlation between circulating anti **CRP** levels and **hsCRP** levels. Neither **hsCRP** nor antibodies to **CRP** predicted MACE in the **ACS** patients over a two year follow up period.
Conclusions: This is the first description of antibodies to **CRP** in patients with **ACS**. It appears that anti **CRP** antibodies are inversely correlated with **hsCRP** levels and with coronary atherosclerosis. The significance of this finding remains to be elucidated.

Shortcuts:
CRP- C Reactive Protein
hsCRP- High Sensitive CRP
CHD- Coronary Heart Dissease
SLE – Systemic Lupus Erythematosus
ACS- Acute Coronary Syndrome

Pre Hospital Anti Platelet Regimen and Angiographic Predictors of Spontaneous ST Resolution in Acute ST Elevation Myocardial Infarction

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Background:

The favorable outcome of Spontaneous ST segment resolution (STR) during acute ST elevation myocardial infarction (STEMI) is well known. However the predictors of this phenomenon are not well established.

Objectives:

To evaluate the role of pre hospital anti platelet treatment and angiogrphic predictors of STR in patients with acute STEMI prior to primary PCI.

Methods:

We conducted a retrospective chart review of all patients admitted with STEMI between January 2002 to June 2006. Pre hospital anti platelet therapy and angiographic data were collected.

Results:

Among 227 patients studied, 37 patients (16%) showed spontaneous STR. 12/227 (5%) deaths were reported, non of them belong to the STR group.

Pre hospital clopidogrel treatment was found to be an independent predictor for STR (p=0.0488, OR 2.10, 95% CI 1.00 to 4.40),however, GP IIb/IIIa inhibitors and aspirin were not found to be independent predictors of this phenomenon. Stepwise logistic regression analyses identified the following angiographic independent predictors of STR: single vessel disease (p=0.0157, OR 2.85, 95% CI 1.22 to 6.7), collaterals (p=0.0020, OR 4.28, 95% CI 1.70 to 10.80), circumflex culprit vessel (p=0.0080, 95% CI 1.49 to 14.97)and thrombus (p=0.0065, OR 5.76, 95% CI 1.63 to 20.39).

Conclusion:

Early clopidogrel treatment was found to be an independent predictor for STR. Patients with single vessel disease , collateral flow, thrombus and circumflex as the culprit vessel were more likely to have STR.

Primary Coronary Intervention Reduces the Incidence of Significant Mitral Regurgitation in Patients with Acute Inferior Myocardial Infarction

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Ischemic mitral regurgitation (MR) is associated with worse outcome and increased mortality. Thrombolysis reduces the incidence of significant MR after first myocardial infarction. **Aim**: To test the hypothesis that primary percutaneous coronary intervention (PPCI) reduces the incidence of MR. **Methods**: Prospective study of **225** patients with first inferior myocardial infarction. PPCI was performed in **82** (**36.4%**), with pain to balloon time 5.3+3.4 hrs, thrombolytic therapy was administered to **93** patients (**41.3**%), with average pain to needle time 4.5+2.8 hrs and **50** (**22.3**%) patients were managed without reperfusion therapy. Transthoracic Doppler-echocardiography was performed in all within 48 hrs, and repeated after 7-14 days in 198 patients, and at 30-45 days in 176 patients. MR grade ≥ 2 MR was considered significant. **Results**: The incidence of significant MR in all the subjects within 24 hours, 36 of 225 (16%) was similar to that at 7-14 days, 35 of 198 (18%), p=ns, but decreased after 30-45 days and at 21 of 176 subjects (12%), $p<0.05$. In patients with PPCI the incidence of significant MR at 24 hrs evaluation 2.7% was less than in those without PPCI, 13.3%, $p<0.002$. Evaluation at 7-14 days revealed lower incidence of MR in PPCI patients 2.5% vs 15.2% in those without, $p<0.001$. After 30-45 days MR incidence was 1.7% in PPCI patients compared to 13% without, $p<0.0001$. PPCI reduced the incidence of significant MR compared with thrombolysis, at 24 hrs, 2.7% vs. 5.3%, $p<0.012$, at 7-14 days 2.5% vs. 6.6%, $p<0.01$, and after 30-45 days 1.7% vs. 5.7%, $p<0.01$. In PPCI patients, MR grade 3 developed only in 2 compared to 11 patients in those without. **Conclusions**: PPCI reduces the incidence of significant MR in patients with first inferior myocardial infarction and was superior to thrombolysis.

SERCA2A Gene Delivery Prevents Deterioration of Global Function and Retards Remodeling in a Sheep Model of Ischemic Mitral Regurgitation

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Mitral regurgitation (MR) doubles post-myocardial infarction (MI) mortality. We have shown that moderate MR augments remodeling in an apical MI model (no intrinsic MR) with independent LV-to-LA MR-type flow, and that repair of MR after 1 month induces reverse remodeling. In particular, sarcoplasmic reticulum calcium ATPase 2 (SERCA2) levels were depressed in correlation with the degree of hypertrophy. We hypothesized that up-regulating SERCA2A levels using a gene therapy approach will prevent ischemic MR-induced ventricular remodeling in our model.

Methods: Antero-apical MIs were created, and an LV-to-LA shunt was implanted in 12 sheep (regurgitant fraction=30%). One week before MR and MI creation, all the sheep underwent percutaneous transcoronary delivery of adeno-associated virus serotype 5 encoding either for βgal as a control (AAV5. βgal- 6 sheep) or SERCA2a (AAV5.SERCA2a- 6 sheep).

Results: Sheep in the AAV5.SERCA2a group had a significantly smaller increase in **LV end-systolic volume** at 1 and 3 months (88.1 ml vs 69 ml at one month, and 99.4 ml vs 82.6 ml at 3 months, P=0.05 and P=0.03 respectively). **LV end-diastolic volumes** did not differ significantly between the groups, reflecting persistent MR-induced volume overload. **Maximal systolic dP/dT** increased significantly at 1 and 3 months in the AAV5.SERCA2a group, while decreasing in the control sheep (807.5 mmHg/sec vs 1165 mmHg/sec, P=0.002 at 1 month, and 607.8 mmHg/sec vs 877.8 mmHg/sec, P=0.006, at 3 months) . **Preload recruitable stroke work**, reflecting global systolic function, was significantly higher in the AAV5.SERCA2a sheep at 3 months (32.2 vs 48.3 ml*mmHg, P=0.003). Pro-hypertrophic and anti-apoptotic **STAT3 and pAkt** decreased significantly more in the control group (P=0.001 and P=0.007 respectively).

Conclusion: Upregulating myocardial SERCA2a using virally mediated gene delivery in an established controlled model of ischemic MR increases global systolic function and reduces end-systolic volumes, reflecting improved contractile function of the muscle. The decrease in intracellular pathways involved in compensated remodeling was smaller in the genetically modified animals. Thus, upregulating SERCA2a in ischemic MR may retard the appearance of decompensated remodeling and failure.

Platelet Responsiveness to Aspirin Loading in Patients with ST-Elevation Myocardial Infarction Undergoing Primary Percutaneous Intervention is Associated with Myocardial Reperfusion and Clinical Outcome

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Background: In patients with stable coronary artery disease, and patients undergoing elective percutaneous coronary intervention (PCI), laboratory resistance to aspirin is associated with a higher incidence of adverse events. Nevertheless, the responsiveness to aspirin in acute myocardial infarction (AMI) and its implications have not yet been investigated.
Methods: The study comprised 76 aspirin naïve patients who underwent primary PCI (PPCI) for ST-elevation MI (STEMI). Platelet reactivity was assessed 30-60 mins after a loading dose of 300mg chewable aspirin, by conventional aggregometry and Impact R, where platelet reactivity to arachidonic acid (AA) was expressed by platelet deposition under flow conditions.
Results: Patients were stratified using the median value of AA-induced platelet aggregation (PA) (49%) to good responders to aspirin (n=38), who had a median AA-induced PA of 33% (25-41), and poor responders to aspirin (n=38), who had a median AA-induced PA of 77% (70-84). Similarly, good compared with poor responders had higher surface coverage by Impact R (3.9±2.6 vs. 2.2±1.3, p=0.003). Good versus poor responders were similar regarding baseline demographic, clinical and angiographic characteristics. However, good responders were more likely to demonstrate early ST-segment resolution ≥70% after PPCI (84% vs 54%, p <0.01), suggestive of better myocardial reperfusion. Good compared to poor responders had a lower incidence of adverse cardiovascular events (re-infarction, need for re-intervention, congestive heart failure and/or death) throughout a 6-month follow-up (11% vs 24%, respectively; p<0.05).
Conclusions: Ex vivo poor platelet responsiveness to aspirin loading in STEMI patients is associated with a worse prognosis in patients undergoing PPCI.

Incidence of Early Left Ventricular Thrombus after Acute Anterior Wall Myocardial Infarction in the Primary Coronary Intervention Era

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BACKGROUND: Rapid reperfusion has been shown to decrease mortality and improve LV function recovery. Previous studies have reported that left ventricular thrombus (LVT) is a major complication of ST-segment elevation acute anterior wall myocardial infarctions (AMI). This thrombus may dislodge and emboli to brain or other tissues. There is no data on LVT in the current primary PCI (PPCI) era. We sought to demonstrate the incidence of LVT after AMI in patients (pts) treated with PPCI compared to thrombolysis or conservative treatment.

METHODS: We conducted a retrospective, single center study in 642 pts with anterior wall AMI who were treated with PPCI (n=297), Thrombolysis (n=128) or conservative treatment (n=217) between January 2000 and December 2006. A LVT was defined as an echodense mass adjacent to an abnormally contracting myocardial segment.

RESULTS: No statistical difference was found in LVT rate among the groups: 21/297 pts (7.1%) in PPCI, 10/128 (7.8%) in thrombolytics and, 9/217 (4.1%) in the conservative. This is an almost identical incidence (P=0.28) as reported in the pre-PPCI era. Those in the thrombolytics group were characterized by shorter duration from symptom start and were generally treated with heparin/LMWH.

CONCLUSIONS: This is the largest report to evaluate the incidence of LVT formation after AMI. In the current era of rapid reperfusion by PPCI, the rate of thrombus formation is similar to that reported in the past and not different than for patients treated conservatively or with thrombolysis. This may be also as a result of pts selection for PPCI.

A Comprehensive Evaluation of Drug Eluting Stents Compared with Bare Metal Stents for Patients with Acute ST Elevation Myocardial Infarction

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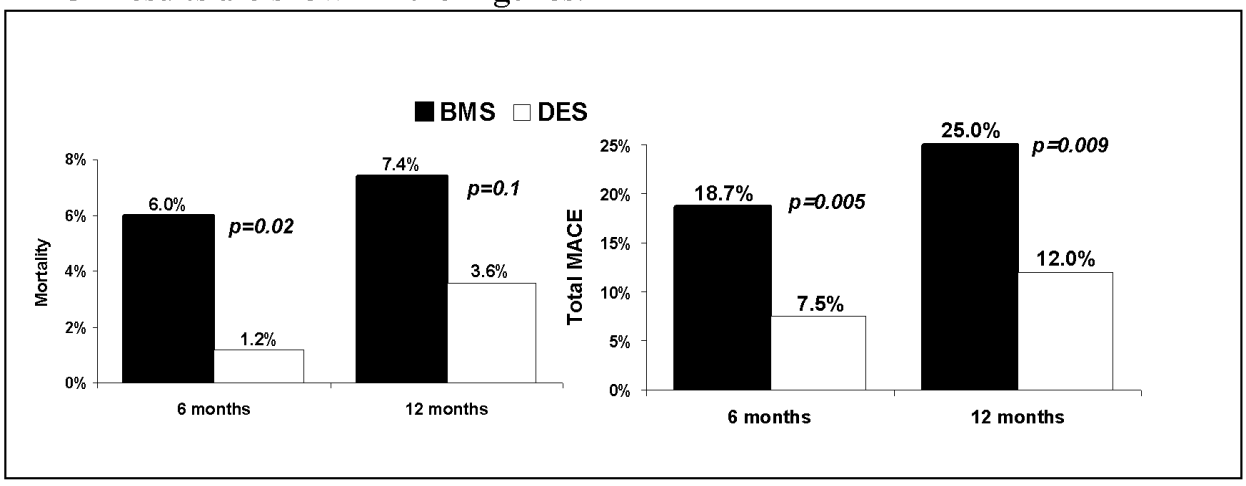
Background: The present study investigates the clinical outcomes in consecutive group of patients with ST elevation MI (STEMI) treated with either dug eluting stents (DES) or bare metal stents (BMS) at our institution.

Methods: This prospective registry included 162 patients with STEMI undergoing primary PCI within 12 hours of symptoms onset and using DES implantation (e.g. 51% Cypher, 42% Taxus, 7% Endeavor stents). The control group consisted of 897 patients implanted with BMS. Patients with cardiogenic shock were excluded from analysis. The incidences of major adverse cardiac events (MACE) including recurrent MI, angiographically proven (i.e. definite) stent thrombosis, target vessel revascularization (TVR) and target lesion revascularization (TLR) were assessed at six months and one year.

Results: STEMI patients treated using DES were somewhat younger (59±12 vs. 61±13, p=0.07) but had more anterior MI location (64% vs. 45%, p=0.0001). The prevalence of diabetes mellitus was 25% in both groups. Angiographic success was achieved in 97% of patients in both groups. At one year, the rate of definite stent thrombosis was 4.1% in the BMS group vs. 0.7% in the DES counterparts (p=0.04). TVR was remarkably lower among DES vs. BMS treated patients by one year (5.7% vs. 15.4%, p=0.002). Overall mortality and MACE results are shown in the **Figures**.



Conclusion: According to our clinical experiences, the use of DES in STEMI is safe and effective as compared to BMS. DES was not associated with an increased risk of coronary thrombosis and was effective in reducing the incidence of adverse events up to one year in patients with STEMI referred for emergent primary PCI.

The Impact of Right Ventricular Dysfunction on Long Term Mortality in Patients with Acute Myocardial Infarction

Robert Dragu [1], Michael Kapeliovich [1], Yoram Agmon [2], Diab Mutlak [2], Yonatan Lesick [2], Doron Aronson [2], Salim Dabah [2], Shimon Reisner [2], Haim Hammerman [1]

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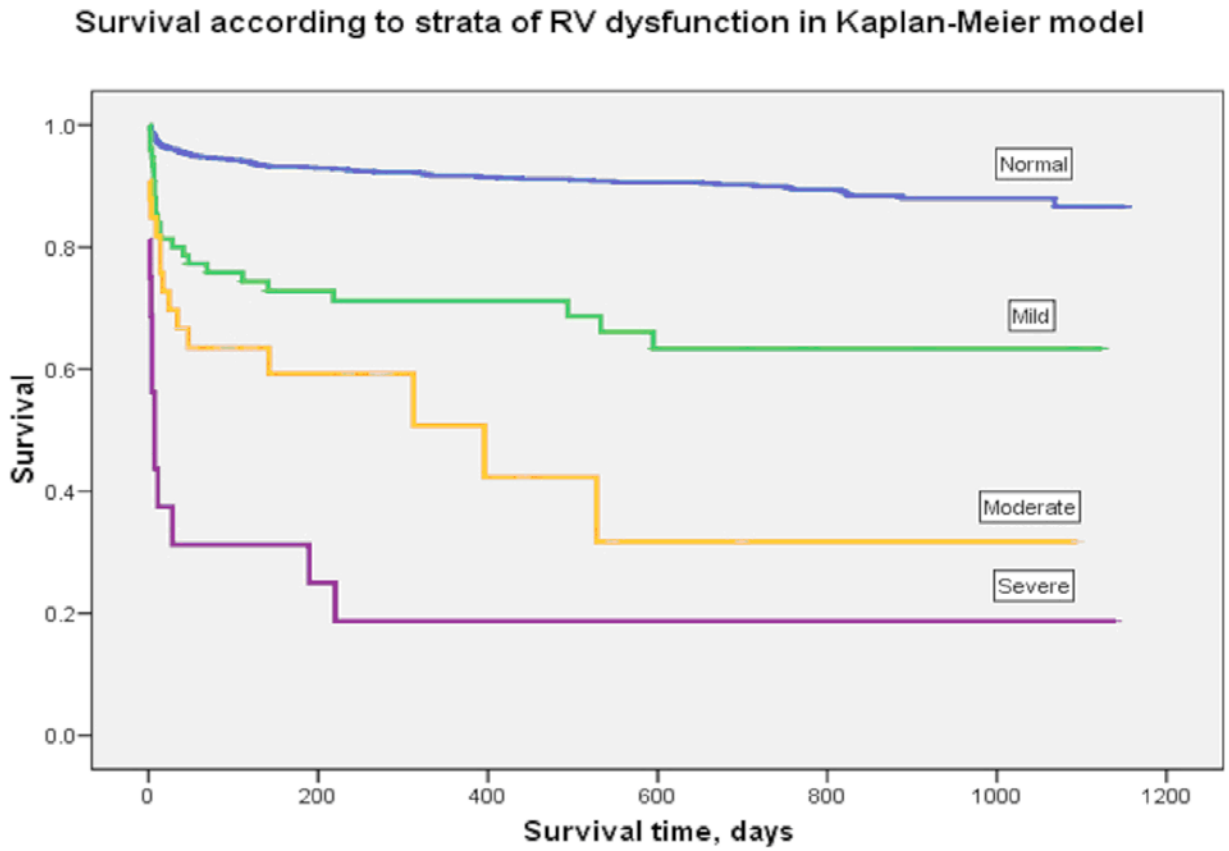
Aim: To assess the impact of right ventricular (RV) dysfunction on long-term mortality in patients with acute myocardial infarction.

Methods: We prospectively studied 1217 consecutive patients with AMI and RV function assessed by echocardiography in the first 24 hours from admission. They were followed-up for a mean of 17 months.

Results: Mild RV dysfunction was detected in 6.2%, moderate in 2.7% and severe in 1.3% of the patients. The overall mortality was 32.0%, 45.2% and 81.3% respectively, and only 9.3% in the normal RV function group ($p<0.0001$). After adjusting for age, gender, Killip class, on-admission blood pressure, diabetes mellitus, inferior wall involvement, ST-elevation AMI, creatinine clearance and left ventricular systolic function, the odds ratio for mortality were 3.07 (95% confidence interval [CI], 1.25-7.53, $p<0.01$), 3.89 (95%CI, 1.22-12.34, $p<0.02$) and 21.66 (95%CI, 3.12-150.0, $p<0.002$) for mild, moderate and severe RV dysfunction respectively, as compared to normal RV function group.

Figure 1 depicts the Kaplan-Meier cumulative survival for each group.

Conclusion: There is a graded independent association between the severity of RV dysfunction after AMI and long-term mortality. Even a mild dysfunction is associated with an increase in risk of death.



Comparison of the Predictive Value of Four Different Risk Scores for Outcomes of Patients with ST-Elevation Acute Myocardial Infarction

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Background: Accurate risk stratification has an important role in the management of patients with acute coronary syndromes (ACS). Even among patients with ST-elevation acute myocardial infarction (STEMI) for whom early therapeutic options are well-defined, risk stratification has an impact on early and late therapeutic decision-making. We aimed to compare the prognostic value of four risk scores used to evaluate patients with STEMI.
Methods: We studied 855 consecutive patients with STEMI treated with primary percutaneous coronary intervention (PCI), who were included in our primary PCI registry between 01/2001-06/2006 (age = 60.5±13 years, 19% females, 28% diabetes, 48% anterior MI). Excluded were patients with cardiogenic shock. For each patient the TIMI, CADILLAC, GRACE and PAMI risk scores were calculated using clinical variables, and for the CADILLAC score also angiographic characteristics. Thirty day and one year outcomes, including death, MI, target vessel revascularization and major adverse cardiac events (MACE) – composed of the previous three components – were assessed. The predictive value of the four risk scores was evaluated by the area under the curve (AUC) or C-statistic method.
Results: Predictive accuracy of the four risk scores for the various clinical outcomes is presented in the Table.

Risk Score	**TIMI** AUC (P trend)	**CADILLAC** AUC (P trend)	**GRACE** AUC (P trend)	**PAMI** AUC (P trend)
30 day death	0.724 (<0.0001)	0.824 (<0.0001)	0.471 (0.5)	0.742 (<0.0001)
30 day MI	0.61 (0.05)	0.685 (0.001)	0.533 (0.5)	0.64 (0.005)
30 day MACE	0.635 (<0.0001)	0.714 (<0.0001)	0.544 (0.1)	0.65 (<0.0001)
1 year death	0.747 (<0.0001)	0.813 (<0.0001)	0.475 (0.5)	0.752 (<0.0001)

Conclusions: The CADILLAC, TIMI and PAMI risk scores all demonstrated a high predictive value for mortality in patients with STEMI undergoing primary PCI. The GRACE score, which was developed from a registry of patients with a wide spectrum of ACS, had a lower predictive value. Therefore, the CADILLAC, TIMI and PAMI scores can be used effectively to risk stratify patients with STEMI.

The Impact of Glycoprotein 2b/3a Antagonist Therapy on Early and Late Clinical Outcomes in AMI Patients Undergoing Primary PCI

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Background: Glycoprotein (GP) 2b/3a inhibitors have been shown to improve clinical outcome in ACS pts undergoing PCI. Data are scarce and controversial concerning the use of GP 2b/3a in AMI pts undergoing primary PCI.

Aims: To assess the outcome of AMI pts undergoing primary PCI and stenting with or without an adjunctive therapy of Eptifibatide [Epi] as a bolus plus infusion for 8-18 hrs.

Methods: We analyzed our clinical results among pts undergoing primary PCI within 12 hours of symptoms onset of AMI. Patients with cardiogenic shock were excluded

	Epi- therapy	Control	P value
No.	**705**	**232**	
Age (yr)	59±12	65±14	<0.001
Male (%)	85	72	<0.001
Anterior MI (%)	48	47	NS
DM (%)	21	33	0.002
HTN(%)	41	53	<0.001
Smoking (%)	49	34	<0.001
Dislipidemia (%)	45	44	NS
MV CAD (%)	56	56	NS
DES (%)	15	11	NS
No Reflow (%)	5	7	NS
EF (%)	42	44	NS
CADILLAC Score	3.9±3.4	5.1±4.0	<0.001
ACT (sec)	252±53	257±57	NS
One month adverse events			
Stent thrombosis (%)	1.8	2.2	NS
Death (%)	1.7	8.6	<0.001
Six months adverse events			
Death (%)	3.7	12	<0/001
Re-MI (%)	5.2	7.5	NS
TVR (%)	8.2	11.2	NS
CABG (%)	4.0	4.4	NS
Stent thrombosis (%)	2.8	3.1	NS

Using multivariate analysis, CADILLAC Score and adjunctive GP 2b/3a therapy emerged as independent correlates with adverse clinical outcome at one month (O.R. 1.4 (1.2-1.5); p<0/001; O.R. 0.3 (0.1-0.6); p=0.001, respectively) and 6 months (O.R 1.4 (1.3-1.5); p<0.001; O.R. 0.4 (0.2-0.9); p=0.02, respectively) in pts undergoing primary PCI for AMI.

Conclusion: Our analysis shows that adjunctive therapy of eptifibatide in AMI pts undergoing primary PCI might be associated with improved clinical outcomes

Natural History of Experimental Arterial Chronic Total Occlusions

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Background: Arterial chronic total occlusions (CTO) are common and associated with adverse clinical outcomes. To date, no studies have systematically assessed structural and perfusion changes occurring during CTO maturation, which may adversely affect angioplasty outcome. Methods and Results: Occlusions were created in 63 rabbit femoral arteries (38 rabbits) by thrombin injection. Histology, contrast (clariscan) enhanced MRI blood volume index and micro-CT imaging were analyzed at 2, 6, 12 and 18-24 weeks (n= 12-20 arteries/time point). Average T1-weighted MRI signal within the CTO was used to calculate relative blood volume (RBV). Collagen and proteoglycan content were assessed by picrosirius red and alcian blue staining, respectively. Early changes were characterized by an acute inflammatory response and negative arterial remodeling, with >70% reduction of arterial cross-section area (CSA) from 2 to 6 weeks. Intraluminal neovascularization occurred with a 2-fold increase in total microvessel CSA from 2 to 6 weeks (0.014±0.002 to 0.023±0.005 mm^2, $p<0.001$) and a 3-fold increase in RBV (5.1±1.9% to 16.9±2.7%, $p<0.001$). However at later time periods, there was significant reductions in both RBV (3.5±1.1%, $p<0.0001$), and total microvessel CSA (0.017 ± 0.002 mm^2, $p<0.02$). Micro-CT imaging at 6 weeks demonstrated a corkscrew-like recanalization channel at the proximal end that regressed at later time points. Vascular changes were accompanied by marked decrease in proteoglycans and accumulation of a collagen-enriched extracellular matrix, particularly at the entrance. Conclusions: Vascular and matrix changes within CTO followed a specific time sequence. Regression of intraluminal neovascularization, together with collagen accumulation may underlie the high angioplasty failure rate in CTO, and could represent targets for novel therapeutic interventions.

Commissural Opening after Percutaneous Mitral Commissurotomy: Impact on Long-term Outcome

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Objectives: We sought to evaluate the prognostic value of the degree commissural opening (CO) on outcome.

Background: CO is the main mechanism by which the mitral valve area (MVA) increases after percutaneous mitral commissurotomy (PMC) but its impact on long-term outcome has never been evaluated.

Methods: 875 patients with mitral stenosis (MS) and good immediate results of PMC (MVA≥1.5 cm^2 and no regurgitation >2/4) were prospectively evaluated and divided into three groups: Group 1 (N=189; both commissures partially opened or not split), Group 2 (N=459; one commissure completely split) and Group 3 (N=227; both commissures completely split).

Results: Immediately after PMC, there were significant differences between Groups as regards to mean gradient (Group 1: 5.1±2.1mmHg, Group 2: 4.5±1.7mmHg, Group 3: 4.0±1.6mmHg, $p<0.0001$) and MVA (Group 1: 1.8±0.2cm^2, Group 2: 1.9±0.2cm^2, Group 3: 2.1±0.3cm^2; $p<0.0001$). Ten-year rate of good functional results (survival without need for mitral surgery or repeat dilatation and NYHA functional class I or II at last follow-up) was significantly higher in Group 3 (76±5%) than in Group 1 and 2 (39±8% and 57±11% respectively; $p<0.0001$). In multivariate analysis, degree of CO did not emerge statistically but when MVA was excluded from the model, complete bi-commissural opening was an independent predictor of good late functional results ($p<0.05$).

Conclusions: Complete CO is associated with larger MVA, smaller gradients and functional improvement. Degree of CO provides important prognostic information and can be considered as a complementary measure of procedural success in addition to the MVA not always easy to assess.

Percutaneous Carotid Artery Stenting with Distal Protection Device in High- risk Patients

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Recent studies have shown conflicting results regarding the safety of percutaneous carotid artery angioplasty and stenting (CAS) as compared to surgical carotid endarterectomy (CEA). **Aim:** We evaluated the safety and feasibility of contemporary carotid artery angioplasty and stenting, with routine use of distal protection device in patients at high-risk for surgical endarterectomy. **Methods:** Between October 1999 and September 2007, a total of 190 consecutive patients with severe carotid stenosis underwent CAS with distal protection device. Of them, 90 (47%) pts had restenosis after a prior CEA and 66 (35%) were symptomatic. Patients who had high risk features, including restenosis after CEA, multivessel coronary artery disease, NYHA class III/IV heart failure or EF<30%, need for cardiac or vascular surgery within 30 days, COPD, occlusion of the contralateral carotid artery or hostile neck anatomy, were considered to be at high surgical risk, and were referred to CAS by both, the vascular surgeons and the interventional cardiologist. **Results:** The baseline clinical characteristics, outcomes up to 1-year follow-up, are presented in the table.

Clinical characteristics (N=190)		**Clinical outcomes**		
Age	70.2±9		**at 30-days**	**From 30-days to 1-year**
Male (%)	122 (64%)	**Composite death/any stroke (%)**	6 (3.1%)	13 (6.8%)
Diabetes mellitus (%)	70 (37%)	**Death- all cause (%)**	2 (1%)	10 (5.2%)
Smoking (%)	71 (37%)	**TIA (%)**	9 (4.7%)	
Ischemic heart disease (%)	108 (57%)	**Minor stroke (%)**	3 (1.5%)	2 (1%)
Hypertension (%)	160 (84%)	**Major stroke (%)**	1 (0.5%)	1 (0.5%)

At 1-year follow-up, the rate of restenosis (>70%) was 2.6%.

Conclusions: In correctly selected patients, with a multi-disciplinary approach, CAS is safe and durable. These results support the use of carotid artery angioplasty and stenting with a routine use of distal protection device in high surgical risk patients with significant primary or secondary carotid artery stenosis.

Percutaneous Renal Artery Angioplasty for Renal Artery Stenosis Reduces the Incidences of Flash Pulmonary Edema and Hospitalization Rate for Acute Heart Failure

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Background: Renal artery stenosis may cause uncontrolled hypertension, renal azotemia, episodes of acute heart failure and flash pulmonary edema.
Aim: to evaluate the clinical benefit of renal artery angioplasty with stenting for the control of recurrent, refractory congestive heart failure.
Methods:Renal artery angiography was performed in 470 patients having coronary angiography according to pre-selected criteria, 98 patients from these cohort (21%) had a recurrent episodes of flash pulmonary edema requiring hospitalization and treatment.
Results: Significant renal artery stenosis (luminal narrowing > 70%) was found in 46 patients, 21 patients (46%) of them had recurrent episodes of flash pulmonary edema before performing the procedure. The rate of hospitalizations for acute heart failure after performing renal artery angioplasty was reduced significantly from 2.31+ 1.25 hospitalizations per year to 0.5+0.5 per year after the procedure,(p=0.002), a reduction that was not observed in the remaining group of patients not having a significant renal artery stenosis. The reduction of hospitalizations was observed not only among those with preserved left ventricular ejection fraction (LVEF), but also among patients with moderate and moderate to severe reduced LVEF.
Conclusions and implications: Renal artery angioplasty for significant renal artery stenosis reduces hospitalizations for flash pulmonary edema and events of congestive heart failure exacerbation independently of the LVEF rate. Screening, diagnosis and treatment of significant renal artery stenosis is an important factor for reduction of morbidity and mortality among patients suffering from recurrent episodes of heart failure.

Impact of Percutaneous Closure of Inter-atrial Shunts on Future Pregnancies: Successful Single Center 10-year Experience

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Introduction

Over the last decade percutaneous closure of inter-atrial shunts has become the standard of care. Closure of most secundum atrial septal defects, whenever amenable to percutaneous treatment, is no longer performed surgically. Moreover, in young patients who underwent cryptogenic strokes believed to be secondary to paradoxical embolism, percutaneous closure of patent foramen ovale in order to prevent recurrent neurological events is also rapidly gaining popularity. Since young girls and women constitute the majority in these two target populations one of the most important measures of long term success would be normal future fertility and uncomplicated pregnancies.

Patients and Methods

124 and 78, out of 218 ASD and 130 PFO consecutive percutaneous closures, respectively, were girls or women. In the ASD group: 64 girls were younger than 18 years old (7.5 ± 4.2), 29 women were younger than 45 years (33.6 ± 6.2); In the PFO group: 33 women (36.6 ± 6.9) were in childbearing age.

Results

All inter-atrial shunts were closed successfully on first attempt by Amplatzer ASD or PFO occluding devices. The size of the implanted devices was 15.8 ± 4.9, 24.6 ± 7.4 and 29 ± 6.2 cm for the young ASD, older ASD and PFO, respectively. Only two negligible residual shunts were recorded over a long follow-up period (70 ± 20 months). None of the PFO cases had a recurrent stroke. During follow-up 16 healthy babies were borne altogether. In the PFO group two women gave birth to two children each and two more gave birth to a single child. In the young ASD group two girls got married and gave birth to a single baby. In the older ASD group two women gave birth to two children, two had a single baby and one had a triplet following IVF. All pregnancies were normal and uneventful. Three cesarean sections were performed due to previous sections.

Conclusions

Percutaneous ASD closure yields comparable results to surgical intervention and does not hamper future fertility prospects. Normal pregnancies and deliveries are similarly possible following percutaneous PFO closure. Cardiologists, gynecologists and obstetricians should get familiar with this novel therapy and its favorable ramifications.

"Solysafe" Atrial Septal Occluder Device - The First Israeli Experience

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Introduction

We report our early experience with the Solysafe® atrial septal occluder device (Carag AG, Baar, Switzerland). The device is self-centering flat-profile device with two foldable patches which are attached to eight metal wires. It fits into a 10 F introducer. Once placed in the defect, the two wire-holders are moved towards each other until the wires snap into a stable position and form a flower-like shape. By snapping like this, the wires stretch the patches that are attached to them and the defect gets covered therewith. A clicking mechanism keeps the wire-holders together. It is the only guidewire based septal occluder which is deployed without the necessity of a long transseptal sheath.

Patients and Methods

Eight patients, average age 48.5 ± 13.5 (29-61) years old, underwent percutaneous closure of PFO due to recurrent CVA. The average unstretched diameter of the PFO was 4.5 (2-10) mm, the average stretched diameter measured in 5 patients was 9 (8-18.5) mm. The largest defect was encountered in a patient who had two distinct 5 mm holes that merged into one when stretched by a balloon. The size of the implanted devices was 18 ± 4.6 (15-25) mm.

Results

All PFOs were closed successfully on first attempt. Procedure length and x-ray exposure were comparable to other devices. There were no immediate or late complications during 3-months follow up. Device visibility on TEE and user-friendliness were acceptable. There were no residual shunts except for a negligible one recorded soon after closing the fenestrated inter-atrial septum. That small shunt resolved spontaneously on TTE after a month. All patients will undergo TCD 6-months after the procedure.

Conclusions

PFO closure utilizing Solysafe is safe, feasible and effective. Solysafe has several theoretical advantages that make it a good alternative to other devices. More patients and long-term follow up data are obviously still required.

Novel Injectable Alginate Scaffold and Fetal Cardiomyocyte Transplantation as a Staged Procedure Improve Cardiac Remodeling and Function after Myocardial Infarction in Rat

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Objective: To determine and compare the therapeutic effect of injectable alginate scaffold with staged cardiomyocyte transplantation, injectable collagen scaffold, and saline on left ventricular (LV) remodeling and function after MI in rat.

Background*:* Adverse cardiac remodeling and progression of heart failure after myocardial infarction (MI) are associated with excessive and continuous damage to the extracellular matrix (ECM). We hypothesized that injection of i*n-situ* forming alginate hydrogel into the infarct provide a temporary scaffold, and attenuate adverse cardiac remodeling and dysfunction.

Methods and Results: We developed a novel absorbable biomaterial composed of a calcium cross-linked alginate solution, which displays low viscosity and after injection into the infarct and undergoes phase transition into hydrogel after injection into the infarct. Rats (n=48) were subjected to extensive anterior MI and immediately after coronary artery occlusion, injectable resorbable alginate biomaterial (n=24), collagen (n=12), or saline (n=12) were injected into the infarct. One week later, 12 of 24 alginate-treated rats received rat fetal cardiomyocytes transplantation ($1x10^{6}$ cells) into scar (staged procedure). Echocardiography study was performed at 3 days (baseline), 1 and 2 months after MI and showed that both collagen and saline -treated animals developed significant LV dilatation accompanied by progressive deterioration in LV contractility ($p<0.01$). On the other hand, injectable alginate scaffold with and without staged transplantation of cardiomyocytes attenuated LV dysfunction. Invasive hemodynamic studies, performed with pressure-volume (PV) system (Millar instruments) two months after MI, showed that LV end-diastolic and systolic volumes were significantly smaller in animals treated with injectable alginate scaffold, with and to lesser extent without staged cell transplantation, compared with animals treated with collagen scaffold and saline. (426 ±14 and 549±42 vs 661±40 and 623±53 uL, p=0.02; and 349±2 and 448±42 vs 607±49 and 552±60 uL, p=0.01).

Conclusions: The present study shows, for the first time, that injectable alginate scaffold with staged transplantation of fetal cardiomyocytes can improve the favorable effects of injectable alginate biomaterial on cardiac remodeling and function after MI.

Baseline LDL-cholesterol Levels and Outcome in Patients with Severe Heart Failure

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Background: The prevalence of HF increases constantly in the US and Europe. Treatment by statins is well established for primary and secondary prevention of coronary events. There are controversial reports concerning low cholesterol as a negative prognostic predictor for patients with advanced HF. However there is no sufficient data to show whether low cholesterol is associated future HF admissions mortality in patients with HF. We evaluated the impact of baseline LDL-cholesterol levels on the clinical outcome in patients with HF

Methods and Results: We evaluated 297 CHF patients with an average NYHA of 2.8. Mean follow up was 3.7 years. One hundred and seven (37%) of the patients died during follow up and the mean time till first hospital admission due to HF was 25 ±17 months.
Patient cohort was divided into 3 groups (Tertiles) according to LDL levels: Group1- LDL<89 mg/dl values, group 2- 89 mg/dl<LDL<115 mg/dl group3- LDL >115mg/dl. The prevalence of diabetes mellitus, HTN, IHD was lower in latter tertile, yet there were more patients with advanced NYHA class (3-4). The best overall outcome was evident in group 3 with the highest LDL (>115 mg/dl). The same trend was observed in groups of patients with only IHD sentence to vague
Conclusion: Very low LDL cholesterol levels are associated with a reduced survival in patients with clinically controlled severe HF.

Are Statins Protective in Heart Failure Patients?

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Aim: This study aimed to investigate the impact of statin therapy before the admission to the hospital on one-year survival of patients hospitalized due to decompensated heart failure (HF).

Methods: We performed a retrospective cohort analysis of 949 consecutive patients older than 18 years hospitalized in Soroka University Medical Center with a principal discharge diagnosis of HF (acute myocardial infarction excluded) between 11/2001 and 06/2005. Two groups of patients were compared: those who received statins within 3 months before the admission (S) and those who did not (NS). The primary outcome was one-year all cause mortality. To adjust for a potential misbalance between S and NS groups in baseline characteristics, propensity score for statin therapy was incorporated into the survival model.

Results: 297 patients (31.3%) had received statins prior to admission. Patients with ischemic heart disease (IHD) (686/949 subjects, 72.3%) had higher rate of S therapy as compared to the rest 36.2% vs. 18.6%, $p<0.001$. Overall one year mortality rate in S group was 21.9% vs. 32.7% in NS group, $p<0.001$. In the subgroup of patients with IHD statins were protective after adjustment for comorbidities and propensity score (hazard ratio [HR], 0.63; 95%CI 0.44-0.91). However, in patients with non-ischemic HF statins had a neutral effect (HR 0.79; 95%CI 0.43-1.48).

Conclusions: Statins' protective effect on one year survival in HF patients is restricted to patients of IHD etiology. As for other etiologies, statin use may be a marker of better health care, but does not improve outcome *per se*.

Mitral Valve Annulus Diameter and Mitral Valve Leaflets Lengths: Contributors of Mitral Regurgitation in Patients with Hypertrophic Obstructive Cardiomyopathy

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Introduction: The mechanism of obstruction of the left ventricular outflow tract (LVOT) in hypertrophic obstructive cardiomyopathy (HOCM) is mainly due to dynamic systolic anterior motion (SAM) of the mitral valve. Mitral regurgitation (MR) is associated with complicated abnormalities of the mitral apparatus which contributed to a high pressure gradient through the LVOT. The aim of the study to evaluate the contribution of mitral valve annulus diameter (MVAd) and leaflets length on MR.

Methods: A retrospective analysis of our hospital database (12,500 electronic transthoracic echocardiograms between11/2003 -11/2006) was performed to search for patients with combined HOCM and MR. All studies reviewed for MR grading, LVOT gradient, Left Ventricle (LV) dimensions, Ascending Aorta and Aortic Root diameters and MVAd.

Results: MR was found in 48 pts with HOCM (M/F= 9/39, aged 73.6± 15y). MR grading from1-5 (Average 2.3±1.2), MVAd = 27±4cm, MV Anterior leaflet length (MVALL) = 22±2.42 mm, MV Posterior leaflet length (MVPLL) = 17±2.17 mm, LV septum=15.6±2cm, Posterior wall thickness (PWT) =11.3± 0.7cm, LVOT gradient=60.3±23mmHg. In regression analysis the major contributors for MR were: LVOT Gradient r = 0.86, MVALL r = 0.85, MVAd r= 0.83, LV septum r = 0.64, MVPLL r = 0.63, all $P<0.05$. PWT, ascending aorta diameter, aortic root diameter, age and gender did not contribute to the MR (p = ns).

Conclusions: For patients with HOCM and MR not due to independent mitral valve disease, mitral valve annulus diameter and mainly anterior MV leaflet length are strongly related to the magnitude of the LVOT gradient and the severity of MR and thus should be considered during evaluation and management.

In vitro Model Assessment and in Vivo Safety of a New Device-Based Approach for Treating Diastolic Heart Failure

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Introduction: Diastolic heart failure (DHF) accounts for over 40% of heart failure cases, and leads to significant mortality and morbidity. Treatment of DHF patients is empirical, limited, and disappointing. We used in vitro and in vivo studies to evaluate the efficacy and safety of a new approach for treating DHF, directed towards enhancing left ventricular (LV) relaxation and filling, utilizing a passive mechanical device which stores energy during systole and releases it in a recoiling force during diastole.

Methods: The device was evaluated in vitro, utilizing a fatigue machine and ventricular model. The device was implanted on the beating heart of 12 healthy sheep, Echocardiography, Angiography and pressures measurements were conducted to evaluate long term safety, and the effects of tachycardia and acute volume overload.

Results: In vitro studies showed device durability for over 450 million cycles and a reduction in modeled end diastolic pressure. In vivo studies exhibited good clinical recuperation in all animals, Ejection Fraction was preserved up to 170 day follow-up and angiography demonstrated normal coronary flow. Average device energy transfer to the LV remained constant during follow-up.

The device was not restrictive during tachycardia and volume overload 170 days post implantation. Histopathological evaluation 6 months post implantation demonstrated mild to moderate fibrosis limited to the myocardium around device attachment.

Conclusion:

This study demonstrates that a passive mechanical device, which transfers energy to LV during diastole, reduces filling pressures in an in vitro model, is durable for cycles simulating 10 functional years and can be safely implanted.

Routine Laboratory Results and One-Year Mortality Risk Following Hospitalization with Acute Heart Failure

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Aim: The study aim was to evaluate the relationship between admission routine laboratory tests results, patient characteristics and one year mortality of patients admitted for heart failure.

Methods: All heart failure admissions to the seven major general hospitals of the Clalit Sick Fund during years 2002-2005 throughout Israel were screened. Patients with a principal diagnosis of heart failure were enrolled. Patients with acute heart failure due to myocardial infarction were excluded. Data on diagnoses, co-morbid conditions, medications, laboratory findings, in-hospital management and mortality were assessed.

Results: 8,246 patients were included into the study cohort. Hospital mortality rate was 5.7%. One year mortality rate 28.7% and was associated with patients' age, co-morbid conditions and routine admission laboratory results in Cox regression survival analysis. Three dichotomized abnormal laboratory results with highest hazard ratio for one year mortality were: hypoalbuminaemia in 36.3% (HR 1.76, 95%CI 1.60-1.97), hyponatremia in 22.0% (HR 1.65, 95%CI 1.48-1.85) and hyperuricaemia in 70.3% (HR 1.51, 95%CI 1.32-1.73) of patients. A simple prediction tool with one point assigned for each abnormal result was capable of discrimination within 0.7% to 13.9% in hospital mortality rate range, and within 11.6% to 55.6% one-year mortality rate between patients with score of 0 (1,477 patients) and score of 3 (544 patients).

Conclusions: Age, dementia and increased Charlson score are all predictive of one year mortality from HF. A small panel of easily obtainable laboratory tests can risk-stratify patients admitted to the hospital due to the heart failure.

Guidelines of Heart Failure Medications; the Gap between "Real World" Practice and Official Recommendations

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Background: Current heart failure (HF) guidelines advocate the need to maximize the doses of anti-renin angiotensin system medications; beta blockers (BB), angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB) and aldactone. However, "real life" HF pts are usually older and sicker than pts who participate in the clinical trials. Consequently, there is a gap between the "official" medications' doses recommendations and daily practice.

Accordingly, we examined medical records of 154 consecutive pts who are followed at our HF center. We compared the doses of BB, ACEI, ARB and aldactone between the first clinic visit and 1 year later. We also analyzed the clinical implications of the intolerance to the different regimes.

Results: Our pts mean age was 67±13 years, 110 were males. Mean ejection fraction (EF) was 32%±14% and 98(64%) pts had EF less than 30%. Ischemic etiology was present in 90(58%) pts. Anemia (hemoglobin<12 gm %) was present in 88(57%) pts, diabetes mellitus was present in 65(42%) pts and chronic renal failure (baseline Creatinine>1.5 mg/dl) was present in 51(33%) pts.

Beta blockers doses were reduced after 1 year in 33(21%) pts and were discontinued in 9(6%) pts.

The dose of ACEI/ARB was reduced after 1 year in 24 (16%) pts and in 8 (5%) pts ACEI/ARB were discontinued.

Aldactone was given in 46(30%) pts and in 20 (43%) pts was discontinued one year later. Of note, all decrease doses changes and/or discontinuation in the BB, ACEI, ARB and aldactone regimens were done due to either hemodynamic and/or renal deterioration causes.

A total of 17(11%) pts died, in 4(24%) pts, the BB regimen was stopped prior to their death. Of all the medical regimens changes, only the BB intolerance had a significant clinical implication, as it was associated with high mortality (p=0.03).

Conclusion: In almost 1/4 of our HF pts, at least one of the"official" recommended HF regimens doses had to be either reduced or discontinued as the patients did not tolerate the guidelines target recommended doses. In addition, it is important to note that intolerance for BB carries the highest risk for future mortality in HF pts and may serve as a prognostic marker for mortality.

Clearance of the Haptoglobin 2-2-Hemoglobin Complex is Impaired in Diabetes Mellitus Resulting in a Modification of HDL Structure and Defective Reverse Cholesterol Transport

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Background. Haptoglobin (Hp) plays a key role in clearing extracorpuscular hemoglobin (Hb). Two common alleles exist at the Hp locus (1 and 2). We recently demonstrated that reverse cholesterol transport is impaired in individuals with Diabetes Mellitus (DM) and the Hp 2-2 genotype which may explain the increased incidence of CVD in this population. We sought to test the hypothesis that clearance of the Hp 2-Hb complex is slower in DM allowing more complex to bind to HDL thereby resulting in increased oxidative modification of HDL and inhibition of reverse cholesterol transport.

Methods and Results. Injection of I^{125}- Hp 1 or Hp 2-Hb complexes into non-DM mice demonstrated that the half-life of the Hp 2-Hb complex was 2-3 fold longer than the Hp 1-Hb complex (57.8±2.8 vs. 20.4±1.7 min). Moreover, in DM the half-life of the Hp 2-Hb complex was doubled while the half-life of the Hp 1-Hb complex was unchanged (103±3.9 vs. 18.6±1.8 min). Coimmunoprecipitation studies demonstrated that over 25% of the injected Hp 2-Hb complex was associated with HDL in DM mice representing a greater than 10 fold increase compared to Hp 1-Hb complex in non-DM mice. Reverse cholesterol transport was impaired by DM in Hp 2 mice but this impairment was prevented by vitamin E supplementation to these mice.

Conclusions. These data may explain why the Hp 2 genotype promotes less efficient reverse cholesterol transport in DM and suggests that strategies targeted to decrease oxidation of HDL by the Hp 2-Hb complex may improve HDL function.

Key Words: Haptoglobin, Hemoglobin, Diabetes Mellitus, Atherosclerosis, Cardiovascular Disease, HDL cholesterol, Oxidant stress.

Lifestyle Intervention in Obese Arab Women at High Risk for Diabetes and Cardiovascular Disease: Preliminary Results

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Background: Arab women in Israel are at high risk for obesity, diabetes and cardiovascular disease (CVD). Lifestyle intervention proved successful in preventing diabetes and modifying cardiovascular risk in Western populations might fail in conservative societies.
Aims: To design, implement and evaluate a culture-sensitive lifestyle intervention in obese Arab women at high risk for diabetes and CVD.
Study Design: Randomized clinical trial.
Intervention: A total of 204 women, 35-54 years old, were allocated to either the intensive or to the moderate (control) lifestyle intervention arm.

- Intensive lifestyle intervention: included dietary and physical education counseling in weekly sessions.
- Moderate lifestyle intervention: included two educational sessions at baseline, individual dietary counseling every 6 months, and provision of written educational material on lifestyle modification.

Endpoints: Weight reduction and change in risk factors associated with diabetes and CVD.
Results: Preliminary results in 178 women who completed 6 months' follow-up showed greater reduction in body weight and HOMA-IR in women allocated to the intensive lifestyle intervention arm compared to women in the moderate intervention arm (see Table). Drop-out rate at 6 months was 21%.

	Type of Lifestyle Intervention (Study Arm)		P
	Intensive *N=93*	Moderate *N=85*	
Baseline weight (kg)*	87.7 ± 9.6	86.9 ± 8.0	0.56
% weight change at 6 months*	-4.0 ± 5.5	-0.4 ± 4.8	<0.001
Change in HOMA-IR at 6 months**	-0.65 (-5.30-3.04)	-0.15 (-2.11-1.91)	<0.001

*-Mean ± SD
**-Median (range)
Summary and Conclusion: A culture-sensitive lifestyle intervention can lead to significant moderate weight reduction and improve insulin sensitivity in obese Arab women.

Tight Diabetic Glycemic Control Reduces the Risk of Cardiovascular Disease Only in Individuals with the Haptoglobin 2-2 Genotype

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Background. The Haptoglobin gene is polymorphic in man with two classes of alleles denoted 1 and 2. Several cross sectional and retrospective analysis have suggested that the Haptoglobin genotype may be a major determinant of susceptibility to diabetic CVD. We sought to examine this relationship in a prospective population based study.

Methods. We recruited 3000 individuals, age ≥55 years with DM from primary health care clinics of the Clalit Health Services and obtained Haptoglobin genotype on all individuals. The prevalence of CVD at baseline was 25%. Patients were followed for 18 months, for the primary composite outcome of the study which was incident non-fatal myocardial infarction, stroke and CV death.

Results. We found that the Haptoglobin 2-2 genotype was associated with a highly significant increase in the incidence of myocardial infarction, stroke and CV death. Moreover, after stratification of patients by baseline HbA1c to those above and below 7.0, as currently recommended by the AHA/ADA, only in Haptoglobin 2-2 individuals was poor glycemic control found to be associated with an increased risk of major cardiovascular events (2.2% vs. 4.7% respectively, p=0.027 by log-rank).

Conclusions. Optimal utilization of health care resources for risk factor modification should be focused on DM individuals with the Haptoglobin 2-2 genotype. Benefit from tight glycemic control only in a subset of the DM cohort defined by the Haptoglobin 2-2 genotype may explain the inability to show a benefit from tight glycemic control on reducing cardiovascular events in the entire DM cohort in multiple prior clinical studies.

Long-Term Association of Brachial Artery Flow-Mediated Vasodilation and Cardiovascular Events in Middle-Aged Subjects with No Apparent Heart Disease

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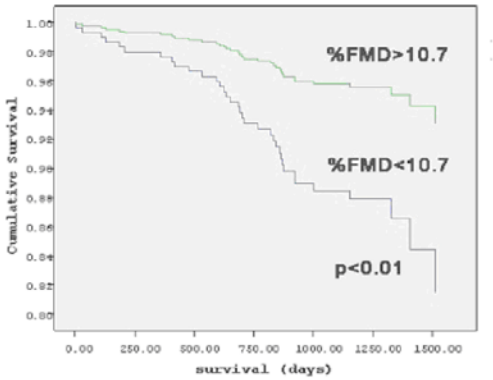
Background: Endothelial dysfunction is considered an important prognostic factor in atherosclerosis . The aim of this study was to find out the long-term association of peripheral vascular endothelial function and clinical outcome in healthy subjects with no apparent coronary artery disease (CAD).

Methods and Results: We prospectively assessed flow-mediated dilation (FMD) in 435 consecutive healthy subjects: 281 (65%) men, mean age 54±12 years and body mass index 28±4 kg/m^2. After overnight fasting and discontinuation of all medications for ≥ 12 hours, percent improvement in endothelium-dependent brachial artery FMD (%FMD) and endothelium-independent nitroglycerin (%NTG)-mediated vasodilatation were assessed using high resolution (15 MHz) linear array ultrasound. Subjects were divided into 2 groups: below (n=221) and above (n=214) the median %FMD of 10.7. The 2 groups were comparable in regard to CAD risk factors, lipoproteins, fasting glucose, hs-CRP, and concomitant medications. Subjects underwent clinical follow-up for a mean of 25±2 months. The composite cardiovascular endpoints (all-cause mortality, non-fatal myocardial infarction, hospitalization for heart failure or angina pectoris, stroke, coronary artery bypass grafting and percutaneus coronary interventions) were significantly more common in subjects with %FMD below rather than above the median of 10.7% (11.8% vs 4.7%, p=0.007, respectively). Univariate analysis demonstrated that the median %FMD significantly predicted cardiovascular events [odds ratio (OR) of 2.78 and 95% CI (1.35 to 5.71) (p=0.003)]. After multivariate analysis that included conventional CAD risk factors, median %FMD was the best independent predictor of long-term cardiovascular adverse events [OR of 2.70 and 95% CI (1.16 to 6.32) (p=0.011)] (Figure).

Conclusions: Brachial artery median %FMD independently predicts long-term adverse cardiovascular events in healthy subjects in addition to those derived from traditional risk factor assessment.



How Low Should HbA1c Levels be in Patients with Coronary Artery Disease?

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Introduction

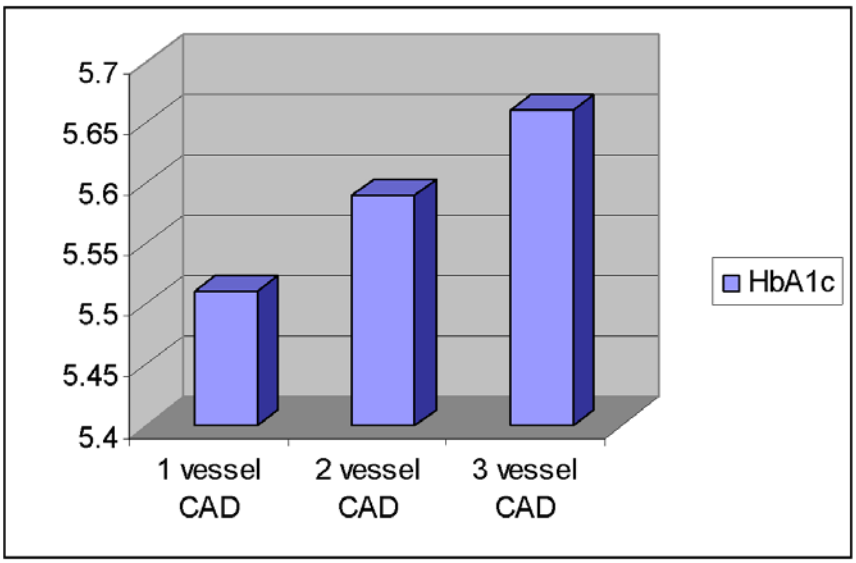
Borderline fasting glucose has been implicated as a risk factor for Coronary artery disease (CAD). HbA1c is a biomarker of glucose control. We examined the potential link between HbA1c and the number of diseased vessels in a non-diabetic cohort.

Methods

We have prospectively collected patients undergoing angiography at the Tel Aviv Sourasky medical center. We included only patients that were non diabetic according to their medical history, were not taking any anti-diabetic medication and had an HbA1c≤ 6mg%. A blood sample for HbA1c was taken during the angiography procedure. All patients gave their informed consent.

Results

We have collected 270 patients undergoing angiography. The correlation between the severity of CAD and HbA1c was 0.16 (p=0.01). We divided our population into 3 groups according to the extent of their CAD (1, 2, or 3 vessel disease). There was no difference in glucose levels between the groups. However, there was a significant difference in mean values of HbA1c between the groups (p=0.038). Patients with higher levels of HbA1c had a more extensive CAD (see below).



Conclusion

HbA1c at levels below than 6mg% may correlate to metabolic changes that result in CAD.

Cardiovascular Event Reduction in Diabetic Patients - Pharmacogenomic Application of the Haptoglobin Genotype

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Objective: Clinical trials of vitamin E have failed to demonstrate a decrease in cardiovascular events. However, these studies did not address possible benefit to subgroups with increased oxidative stress. Haptoglobin (Hp), a major anti-oxidant protein, is a determinant of cardiovascular events in patients with diabetes mellitus (DM). The Hp gene is polymorphic with two common alleles, 1 and 2. The Hp 2 allelic protein product provides inferior anti-oxidant protection compared to the Hp 1 allelic product. In retrospective analysis of HOPE DM participants with the Hp 2-2 genotype, vitamin E significantly reduced the incidence of myocardial infarction and cardiovascular death. We sought to validate this observation in a prospective trial. Additionally, a preplanned secondary analysis was to assess vitamin E influence on outcomes in those ICARE participants who were taking statins.

Methods and Results: 1434 DM individuals with the Hp 2-2 genotype were randomized to either vitamin E or placebo. The primary composite outcome was myocardial infarction, stroke and cardiovascular death. At the first evaluation of events, 18 months after initiating the study, the primary outcome was significantly reduced in individuals receiving vitamin E (2.2%) compared to individuals receiving placebo (4.7%) ($p=0.01$) and led to early termination of the study. Dual treatment with statins and vitamin E dramatically reduced the event rate compared to statin treatment alone. (1.3% (5/386) for vitamin E vs. 4.1% (17/415) for placebo

Conclusions: Vitamin E supplementation reduces cardiovascular events in individuals with DM and the Hp 2-2 genotype and augments statins reduction of cardiovascular events.

Lipid Levels among the African and Middle-Eastern Bedouin Populations

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Background: Previous studies observed higher high-density lipoprotein (HDL) levels and lower triglycerides levels among people of African ancestry. The goal of this study was to characterize lipid levels in Bedouins of African vs. Middle-Eastern ethnicity.

Methods: A cross-sectional study was conducted in a Bedouin primary care clinic in southern Israel, with 4470 listed individuals over the age of 21, of whom 402 (9%) were of African origin. A stratified random sample was included in the analysis. Associations between ethnicity, age, gender and lipid levels were assessed. Multiple linear regression and logistic regression models were used for multivariate analysis.

Results: The study included 261 African Bedouins and 406 Middle-Eastern Bedouins. (median age: 37 years, 58.6% females). The average total cholesterol and low-density lipoprotein (LDL) levels were 10 mg/dl lower among African Bedouins as compared to Middle-Eastern Bedouins (total cholesterol: 168.6 vs. 179.6 mg/dl, $p<0.001$; LDL: 99.5 vs. 109.0 mg/dl, respectively , $p<0.001$). Average triglycerides levels were 36 mg/dl lower among African Bedouins as compared to Middle-Eastern Bedouins (102.8 vs. 138.9 mg/dl, respectively, $p<0.001$). Average HDL levels were 3 mg/dl higher among African Bedouins as compared to Middle-Eastern Bedouins (48.3 vs. 44.6 mg/dl, respectively, $p<0.001$).

Conclusion: In conclusion, a lower prevalence of dyslipidemia was found in African Bedouins, as compared with Middle-Eastern Bedouins.

Chordal Cutting to Relieve Mitral Leaflet Tethering Diminishes LV Remodeling Following Chronic Inferior Myocardial Infarction

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Background. We have previously demonstrated that severing two second-order chordae to the anterior mitral leaflet (AL) in sheep does not adversely affect LV size and function acutely. **Objectives.** This study tested whether chordal cutting exacerbates long-term LV remodeling when applied to treat ischemic mitral regurgitation (MR) in a chronic myocardial infarction (MI). **Methods.** A posterolateral MI was created in 18 sheep by ligation of obtuse marginal branches. After chronic remodeling and MR development at 2 months, sheep were randomized to sham surgery versus anterior leaflet (AntL) or bileaflet (BiL) second-order chordal cutting (n=6 each), techniques in clinical application. 2D and 3D echo at baseline, chronic infarction (2 months), and follow-up at a mean of 6.5 months post-MI (sacrifice) measured LV end-diastolic and end-systolic volume (EDV and ESV), ejection fraction (EF), wall motion score index (WMSi), and posterior leaflet (PL) restriction angle relative to the annulus. **Results.** All measurements were comparable among groups at baseline and chronic MI. At sacrifice, AntL and BiL chordal cutting limited the progressive remodeling seen in controls. LVESV increased by 33±7.2% and 28±5.0% relative to chronic MI with AntL and BiL chordal cutting, versus 109±8.7% in controls ($p<0.01$) (LVESV=60.6±5.1ml vs 61.8±4.1ml vs 82.5±2.6ml in controls). LVEDV increased by 26±5.5% and 22±3.4% with AntL and BiL chordal cutting, versus 63±2.0% in controls ($p<0.01$). LVEF and WMSi were not significantly different at follow-up among chordal cutting and control groups. MR progressively increased to moderate in controls but decreased to trace-mild (vena contracta ≤2mm) in 83% of chordal cutting sheep. BiL chordal cutting provided greater PL mobility (decreased PL restriction angle to 54±5° versus 93±3° with AntL chordal cutting, $p<0.01$). **Conclusions:** Cutting secondary chordae in the chronic post-MI setting does not adversely affect long-term LV remodeling, and limits progressive increases in LV volumes.

Thrombolytic Therapy for Obstructive Prosthetic Heart Valve Thrombosis – 11 Years Perspective

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Background: Thrombolytic therapy (TT) can be an alternative to re-do surgery in patients with obstructive prosthetic valve thrombosis (OPVT). We present our immediate and long-term results.

Methods and Results: Within 11-years period, 65 patients were admitted with OPVT, involving mostly bileaflet valves (61/65, 94%). Forty-seven (age 55.6±15.3, male/female = 17/30) received TT, after excluding high-risk thrombi by TEE. Valve position was mitral (31), aortic (7) and tricuspid (9). Full response to thrombolysis was 31/47 (66%) – 65%, 57% and 78% for MVR, AVR and TVR, respectively. Five patients had partial response. There was no procedure-related mortality. Five patients (10.6%) developed neurological complications (2 hemorrhagic), only one with mild persistent residua. Major bleeding occurred in 2 patients. Fourteen patients (30%) required reoperation after unsuccessful TT. Late death occurred in 6/31 (19%) of initial responders. Repeated episodes of OPVT occurred in 10 patients (40% of 25 late survivors) – accounting for a total of 26 additional episodes. Re-thrombolysis was uniformly successful. A total of 20/47 (43%) of patients with primary thrombolytic approach eventually underwent valve re-replacement (14 after thrombolytic failure, 5 after recurrences, 1 as an adjunct to CABG). 22 initial responders were alive with their original valve after 66±38 months (range 13-121), with NYHA functional class 1.7±0.1.

Conclusions: Thrombolysis is an acceptable and relatively safe alternative to surgery in OPVT, and may offer long-term freedom from reoperation in more than half of patients. Repeated episodes are frequent, but usually respond to re-thrombolysis. Predictors of complications should be sought, especially in non-emergent cases.

Progression of Mitral Regurgitation in Patients with Mitral Valve Prolapse and Less than Moderate Regurgitation

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Background: Mitral valve prolapse (MVP) is a progressive disease. However, few data exists regarding the rate of progression and predictors for developing significant mitral regurgitation (MR).

Aim: To describe the rate and identify predictors of MR progression in patients with MVP and non significant MR.

Methods: Retrospective study of patients with < moderate MR who had echocardiographic follow up of > 1 year. Clinical and echocardiographic data of patients without progression of MR was compared to those who developed moderate to severe or severe MR over time.

Results: There were 114 patients with MVP. Grade of MR was none in 4, minimal in 3, mild in 66 and mild to moderate in 41. The mean age was 52 years (20-97) and 61 (53%) were male. Bileaflet prolapse was present in 45 (39%), posterior prolapse in 44 (38%) and anterior prolapse in 26 (23%) of patients. Over a mean follow up period of 55 ± 29 months, there were only 16 (14%) patients who developed moderate to severe (10) or severe (6) MR. This subgroup of patients was older (62.6 vs. 50.4 years;
$p < 0.001$) and most were men (69% vs. 51%; $p = 0.28$) as compared to the non progressive group. Flail leaflet occured in 8 (50%) of these patients and infective endocarditis in none. Posterior prolapse was originally present in 75% (12 pts) vs. 29% (33 pts) of patients with and without significant progression of MR, respectively ($p = 0.002$). Prolapse of the second leaflet was reported in follow up echocardiography for 20 patients (18%) without progression vs. only 1 patient (6%) with progression of regurgitation
($p = 0.3$).

Conclusion: The majority of patients with MVP and non significant MR progress slowly. Those who develop significant mitral regurgitation are more likely to be older, and have posterior leaflet prolapse. Development of prolapse of the second mitral leaflet is not uncommon in those without progression of MR.

Determinants of Pulmonary Artery Pressure in Patients with Aortic Valve Stenosis

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Background and Objectives: Severe elevation of pulmonary artery systolic pressure (PAP) is not a typical feature of aortic valve stenosis (AS), yet it is occasionally observed. The objectives of our study were: 1) to determine the distribution of PAP in patients with severe AS; 2) to determine the factors associated with elevated PAP in these patients.

Methods: The computerized database of the echocardiography laboratory at our institution was used to identify consecutive patients with severe AS (aortic valve area ≤1 cm^2). The echocardiographic reports of these patients were reviewed and the relevant echocardiographic data was collected. The distribution of PAP in these patients and the factors associated with elevated PAP were determined.

Results: Among 155 patients with severe AS identified during a 22 months period (age: 75±11 yrs; 37% men) – PAP was <35 mmHg in 42 (27%) patients, 35-49 mmHg in 65 (42%) patients, 50-69 mmHg in 36 (23%) patients, and ≥70 mmHg in 12 (8%) patients. The results of the age and sex-adjusted multivariate analysis are listed below. Adjusting for age and gender – reduced left ventricular ejection fraction (LVEF) and elevated mitral inflow E/A ratio (a marker of left ventricular diastolic function) were the only the variables that were independently associated with elevated PAP (PAP ≥50 mmHg). Reduced aortic valve area was associated with elevated PAP by univariate (but not multivariate) analysis.

	OR	**95% CI**	**P**
Age	1.2	0.7-2.0	0.56
Female gender	0.2	0.04-0.8	0.03
LVEF <45%	12.5	2.5-61.3	0.002
Mitral inflow E/A ratio >1.5	6.2	1.4-27.5	0.02

OR = odds ratio for elevated PAP (≥50 mmHg); CI = confidence interval.

Conclusions: PAP is frequently elevated (at times – severely elevated) in patients with severe AS. Reduced left ventricular function (systolic and diastolic) are associated with elevated PAP in these patients, wheras the association of AS severity with elevated PAP is questionable. Thus, it appears that the ventricular response to AS, probably not the severity of AS by itself, is the main factor underlying the pathogenesis of pulmonary hypertension in patients with AS.

The Role of ECG - gated MDCT in the Evaluation of Aortic and Mitral Mechanical Valves

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Purpose

To evaluate the role of ECG-gated multi-detector CT (MDCT) in the functional evaluation of mechanical prosthetic aortic and mitral valves.

Patients and Methods

Twenty sequential patients with 23 mechanical prosthetic valves were evaluated with a 40/64 ECG-gated MDCT scanner. Multi-Planar Reformation, Maximal Intensity Projection, Volume Rendering and Average techniques were used for the visualization of the valve leaflets in systole and diastole. Visibility of each mechanical valve was evaluated by a consensus of a radiologist and a cardiologist, using a subjective fivepoint scale. MDCT findings were correlated with fluoroscopic opening and closing angle measurements and echocardiographic pressure gradient measurements in 11 and 19 valves respectively.

Results

The series included 18 bileaflet and five single-leaflet mechanical valves. Visibility score for MDCT-based computerized reformations of bileaflet mechanical valves was excellent (4/4) in all 18 cases. However, visibility scores of single-leaflet valves were lower (mean =2.8/4, range 1-4), with 2/5 cases in which the leaflets location and angles could not be clearly identified by MDCT during systole and diastole. In four patients a stuck valve was demonstrated on MDCT and confirmed by fluoroscopy while in all remaining cases free movement of mechanical leaflets was demonstrated clearly with normal opening and closing angles. Echo-Doppler showed an increased trans-valvular pressure in one of the four patients with stuck mitral valve while an increased trans-aortic pressure was noted in three patients with normal prosthetic aortic valve motion.

Conclusion

Our preliminary results suggest that MDCT is a promising technique for functional evaluation of bileaflet mechanical valves, allowing reliable measurements of opening and closing leaflet angles. However, the role of MDCT in the evaluation of single leaflet valves might be limited.

Aortic Valvuloplasty for Symptomatic Non-Surgical Aortic Stenosis with Concomitant Regurgitation - Indication or Contra-Indication?

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BACKGROUND: Degenerative aortic stenosis (AS) is the most frequent valvular disease in western world. Due to its high incidence in elderly population with frequent co-morbidities, the risk is often too high for surgical valve replacement. Balloon aortic valvuloplasty (BAV) was introduced two decades ago as a palliative procedure for high risk patients. Aortic regurgitation (AR) is frequently associated with AS. The potential worsening of AR by BAV is considered a major complication and thus a relative contra-indication for BAV. To examine the feasibility of combined AS and AR for BAV, we retrospectively analyzed our center experience with BAV performed in patients with AR.

METHODS AND RESULTS: We retrospectively analyzed our database for severe AS patients that underwent BAV during years 2005-2007 and had also significant AR. Nine patients (age 85±2.7) were found. Aortic valve area increased from 0.5±0.15 to 0.9±0.2 cm2. Maximal and mean pressure gradients across the valve decreased from 72±19.5 to 46±13.6 and from 38±12 to 23±6.8 mmHg, respectively. Pre-BAV all patients had at least moderate AR (pressure half time 250±107 ms). Post- procedure there were no cases of hemodynamic deterioration; Echocardiographic AR worsening was noted in 3/9 (33%) cases, no change in 4/9 (45%), and AR improvement in 2/9 (22%). On the whole, AR severity did not change (pressure half time 245±99 ms).

CONCLUSIONS: Based on our series and review of the literature the risk of hemodynamically significant deterioration of pre-existent AR after BAV is very low. Thus, BAV should not be denied from patients with severe symptomatic AS that are not candidates for surgery.

Functional Mitral Regurgitation Assessed by Echocardiographic Sphincter Index

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Background: The abnormal systolic sphincter mechanism in functional mitral regurgitation (FMR) is generally due to either annular and/or left ventricular pathologies.
Aim: We tested a simple TTE index in two varieties of FMR by evaluating the mitral systolic sphincter mechanism.
Material and Methods: Adults with competent mitral valve and 2 different group with FMR; dilated cardiomyopaty (DCM) and ischemic etiology were included. Mitral regurgitation (MR) severity was determined by Colored -Doppler criteria.
In each group, minimal inter papillary muscle distance (IPMD-mm-B) by left parasternal short axis view and mitral valve annular diameter (MVAD-mm-A) by apical 4 chamber view were measured during systole in order to assess valvular sphincter function. The mitral sphicter index was calculated as B/A.
Results: Pts clinical characteristic, MR severity in each group, the measured TTE parameters including the calculated sphincter index are presented in the table.

Characteristics Number of pts	Normal 13	DCM 13	Post Ant MI 12	Post Inf. MI 11	P value
Age	42±14	42±17	58±11	63±14	0.001
Gender (male %)	46	54	92	82	0.044
STEMI (%)	Ø	Ø	83	64	ns
Mild MR	Ø	54	67	73	ns
Moderate MR (%)	Ø	23	33	9	ns
Significant MR (%)	Ø	23	0	18	ns
IPMD (mm) B	9±2	18±5	12±3	11±3	<0.001
MVAD (mm) A	30±4	38±5	32±5	31±3	<0.0001
B/A: Sphincter Index	0.29	0.49	0.37	0.37	<0.0001

Ischemia induced FMR was more prevalent in adult male whereas severe MR was not found after single Anterior wall MI. The largest IPMD and MVAD were found among pts with DCM manifested as largest abnormal sphincter index
Conclusions: The TTE derived abnormal sphincter mitral index can differentiate between the two etiologies of FMR and potentially may used as a tool for planning therapeutic approach.

Comparative Hemodynamic Effects of Transcatheter Closure of Atrial Septal Defects in Adult and Elderly Patients

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Objectives: There are controversial opinions about the effectiveness of transcatheter ASD closure in adults and especial in elderly patients. The purpose of the study was to evaluate and to compare the hemodynamic changes after transcatheter ASD closure in two age groups of patients:40 -59 years old and 60 years and older .

Methods: Retrospective analysis of the patient files.

Results: Forty six patients were evaluated (23 in the each group). Elderly patients had higher prevalence of cardiovascular risk factors and established coronary artery disease. There was no statistically significant difference between the two groups in Qp/Qs values, ASD diameter and occluder size.

The elderly patients had significantly higher baseline systolic pulmonary artery pressure level -53+16.2 vs 39+7.7 mmHg, p=0.003 (Figure 1). One year following the procedure the mean reduction of PAp values was 11.3% in Group 1 and 19 % in Group 2 (p=0.099). While significant baseline tricuspid regurgitation (TR) was more frequent in elderly patients , no significant TR was observed in both groups one year following the procedure.

Conclusion: transcather ASD closure induces a significant hemodynamic improvement which was even more beneficial in the elderly patients in comparison
with the 40-59 years old patients.

Balloon Mitral Valvotomy in Infants and Children with Severe Mitral Stenosis

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Severe mitral stenosis due to rheumatic heart disease (RDH) or congenital mitral stenosis (CMS) is rare in our population. Balloon valvotomy is the treatment of choice in rheumatic MS and is preferable in some forms of CMS. The procedure in children, especially infants, is challenging due to their size. We report our experience in children between 2004-2007.

Methods: 8 consecutive patients (7F, 1M) (3 CMS 5 RHD) median age 10y (0.2-17) with severe MS were referred for catheterization. Following general anesthesia and percutaneous femoral access, hemodynamic and TEE evaluation were performed. Trans-septal puncture was attempted in all patients. Through a balloon or coronary catheter a stiff wire was placed in the left ventricle. Balloon size was chosen according to BSA. All dilations were performed with Tyshak II balloons.

Results: Trans-septal access was successful in 8 patients. In 7 balloon dilation was successful. Baseline Doppler mean gradient across the valve was 19±3.2mmHg and post balloon dilation decreased to 6.7±2.2mmHg [$p<0.01$]. Estimated systolic RVp decreased in 6/7 patients. There were no complications. MR changed in up to +1 degree in 4 patients and no change recorded in 3 patients. In one patient with CMS we could not cross the valve safely.

Conclusion : Balloon mitral valvotomy is safe and successful in pediatric RHD mitral stenosis and can be considered for some anatomical types of severe CMS in infants.

Incidence of Congenital Heart Defects in Very Low Birth Weight and Extremely Low Birth Weight Infants

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Objective:

The incidence of congenital heart defects (CHD) in neonates has been studied thoroughly. However, there are few studies on the incidence in very low birth weight (VLBW) neonates. This study examined the incidence of congenital heart defects in VLBW infants and extremely low birth weight (BW) infants.

Methods:

A retrospective analysis of the population in the level III B, 30-bed neonatal intensive care unit (NICU) at Shaare Zedek Medical Center, Jerusalem, Israel was performed. VLBW (BW≤1500 grams) infants born between 2001 and 2006 who survived more than 48 hours were included. All the infants were examined daily by a physician, and infants with heart murmurs, or other clinical signs of heart disease, were referred for echocardiography. Findings of Patent Ductus Arteriosus and Patent Foramen Ovale were not included in the analysis. Atrial Septal Defects 5.5 mm or larger were regarded as CHD. All echocardiography examinations were performed by a senior pediatric cardiologist. Comparison of proportions was performed using Chi square test.

Results:

During the study period there were 505 VLBW live-born infants. Four hundred and thirty seven infants met the inclusion criteria. Of these, 225 (51.5%) were males and 281 (64.3 %) underwent echocardiography. CHD was detected in 19 infants (4.4%), significantly higher than the published incidence of 5-8/1000 live birth in the general population ($p<0.0001$). In the sub-group of 154 infants with BW < 1000 grams there were 10 (6.5%) with CHD. In the sub-group of 283 infants with BW 1000-1500 grams there were 9 (3.2 %, P=0.19 vs VLBW) with CHD. The most common defects were ventricular septal defects (n = 8; 42.1%), atrial septal defects (n = 4; 21.1%) and pulmonic valve stenosis (n = 2; 10.5%). There was one each of Tetralogy of Fallot, coarctation of the aorta, mitral valve prolapse, aorto-pulmonary collaterals, and atrio-ventricular canal defect.

Conclusions:

Our observation shows a seven-fold higher incidence of CHD in the VLBW infants and an eleven-fold higher incidence in the extremely-low BW infants, as compared to the reported incidence of 0.5-0.8% in the general population. As not all infants underwent echocardiography, and minor cardiac defects may have been missed in our VLBW infants, the true incidence may be even higher than reported here.

The reasons for the higher incidence of CHD in premature infants are unclear. We speculate

Schneider Children's Hospital Experience with Radio Frequency Ablation for Supra Ventricular Tachycardia in a Pediatric Population

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Objective: To present the Schneider Children's Hospital 7 years experience with catheter ablation for supra-ventricular tachycardia (SVT).

Study design: A total of 274 consecutive patients with SVT or overt accessory pathway (AP) underwent catheter ablation. One hundred eighty seven (68%) patients had WPW or concealed AP, eighty (29%) had atrio-ventricular nodal reentry tachycardia (AVNRT) and seven (3%) had ectopic atrial tachycardia (EAT)

Results: The mean age of the population was 13.4±4.2 years with a median of 14.1 and range of 0.2-25.5 years. The immediate success rate was (95%) 260/274 (175/187 (93.6%) for AVRT, (78/80 (97.5%) for AVNRT and 7/7 (100%) for EAT). During a mean follow-up of 37±26 months, 14 patients had recurrence of arrhythmia with a long term successful rate of (90%) 246/274 (163/187 (87%) for AVRT, 77/80 (96%) for AVNRT and 7/7 (100%) for EAT. The mean fluoroscopy time was 32.1±24.2 with a median of 24 and range of 5-135 minutes. The mean number of RF application was 4.1±3.3 with a median of 3 and range of 1-22. Among the 14 patients with the failed ablation, 2 had AVNRT, 2 left sided AP, 7 right sided AP, 2 para-Hisian AP and 1 Mahaim fiber. The mean fluoroscopy time was significantly higher in the failed ablation in comparison with the successful ablation (73±29.6 vs 29.5±21.6 minutes, respectively $P<0.001$). It was one major complication (TIA).

Conclusions: Our long term results demonstrate that a well organized setting for the ablation therapy in children with SVT can achieve a high rate successful with very low rate of complications.

Normal Values, Range and Upper Limits, of NT-pro B-type Natriuretic Peptide in Infants and Children Analysis of Combined Data From 4 Studies

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Background: The natriuretic peptides are biochemical markers for heart disease in adults and children. Both B-type natriuretic peptide (BNP) and the amino terminal segment of its prohormone (NT-proBNP) can be measured on commercial laboratory platforms and are widely used. The peptide levels are age and assay dependent. Normal value range and its upper limits are essential in order to facilitate the use of these markers in the pediatric population. This study is a summation of four studies that measured NT-proBNP levels in normal infants and children using electrochemiluminescent immunoassay (Roche Diagnostics, Mannheim, Germany). It is the largest published to date.

Methods: Age intervals for upper limits of normal were chosen for intervals where there was no age dependent peptide level change. Since NT-proBNP levels are not normally distributed, and log-transformation results in normal distribution, all statistics were performed on log-transformed data.

Results: There were 690 subjects, aged from birth to 18 years, 325 (47%) were males. NT-proBNP levels are shown to be very high in the first days of life with drastic decline in the first weeks. The peptide levels continued to decline gradually with age, with significant decrease between age 1 month and 18 years ($r=0.43$, $p<0.001$). Male and female levels were only different in the age group of 10 years to 14 years (medians: male 38 pg/ml, female 56.5 pg/ml, $p=0.002$). However, the upper limit of normal for males and females was not different even in this age group. The mean values and upper limits of normal of NT-proBNP levels are shown in the table

Age interval	n	mean±SD	95%tile	97.5%tile
0-2d	43	2,820±3,725	11,987	13,222
3-11d*	84	1,800±2,795	5,918	6,502
>1m to ≤1y	50	143±206	646	1,000
>1y to ≤2y**	38	123±125	413	675
>2y to ≤6y	81	73±82	289	327
>6y to ≤14y	278	46±64	157	242
>14y to ≤18y	116	36±54	158	207

* no data between 12 days and 30 days; ** a significant decrease with age in this age interval; Values are in pg/ml.

Conclusions: NT-proBNP levels are elevated in the first days of life and decrease drastically thereafter. There is a mild gradual decline with age throughout childhood. Girls have somewhat higher levels during puberty. Normal range for each age group is established.

Cryoablation of Atrioventricular Reentrant Tachycardia in Pediatric Patients

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Objectives: To describe our experience with cryoablation of accessory pathway with close proximity to the atrio-ventricular node (AVN).

Background: Radiofrequency (RF) ablation has become established therapy for tachyarrhythmias for both adult and pediatric population. However challenges remain in term of the safety and efficacy of RF ablation in specific locations. Cryo-therapy may be particularly useful for ablation of septal tachycardias.

Methods: A total of 12 patients with SVT or overt accessory pathway (AP) underwent 14 cryo-ablation procedures. Six patients had right antero-septal AP, 4 had para Hisian AP and 2 right mid-septal AP. Electrophysiology study was performed with diagnostic catheters. Cryomapping and cryoablation were performed with a 7F, 4mm tip catheter (freezer, Cryocth Technologies Inc., Canada). Cryomapping was performed at -35^0C for a maximum of 60 seconds and Cryoablation for 4 minutes at -80^0C. Acute successes was defined as noninducibility of SVT and conduction block over the AP.

Results: The mean age of the population was 17.5±6 years with a median of 17.6 and range of 8.6-35 years. All of the patients except one had previous ablation (mean of 1.5±0.9 with a median of 1 and range of 0-3. The immediate success rate was 100% (12/12). During a mean follow-up of 12±10.3 months, 3 patients experienced recurrence of arrhythmia two of them had successful second procedure with a total long successful rate of 11/12 (92%). All 12 patients had AP close to the His area. There were no permanent cryo-related complication or adverse outcome. One patient had mechanical ablation of the AP and one patient had transient complete AVB, occurred during an "insurance" cryomapping, with immediate return to normal AV conduction upon cessation of application.

Conclusions: Cryoablation is a safe and effective alternative for the treatment of SVT due to AP with close proximity to the AVN in children.

D-SPECT: A Novel Technology for High Speed Gated Myocardial Perfusion Imaging: A Comparison Between High Speed (D-SPECT) and Dual Detector Anger Camera (A-SPECT)

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Objective: Gated myocardial perfusion imaging by Anger SPECT camera (A-SPECT) has the limitation of prolonged imaging time. A novel, compact camera (D-SPECT, Spectrum-Dynamics, Haifa, Israel), was designed to increase sensitivity as well as spatial and energy resolution by employing a bank of independently controlled detector columns with large hole tungsten collimators in front of multiple cadmium zinc telluride (CZT) crystal arrays. The study compares high speed D-SPECT to conventional A-SPECT imaging for the evaluation of gated myocardial perfusion in patients with known or suspected coronary artery disease.
Methods: Thirty patients (27 men, 16 with known CAD) underwent one day Tc99m Sestamibi stress/rest SPECT. D-SPECT images were performed within 30 min after A-SPECT. Stress/rest acquisition times were 19 and 11 min respectively for A-SPECT, and 4 and 2 min respectively for D-SPECT. Images were visually analyzed using a 20-seg model to calculate summed stress (SSS) and rest (SRS) scores. Images were also scored for quality, using a 1-5 scale (1=poor, 5=excellent), and assessed for confidence of interpretation. Post stress left ventricular ejection fraction and left ventricular volumes were computed and compared in 11 patients for both A-SPECT and D-SPECT. Myocardial counts per min (cpm) were calculated for both A-SPECT and D-SPECT. **Results**: Myocardial count rate was significantly higher in D-SPECT compared with A-SPECT (384k/min ± 134k/min vs 47k/min ± 14k/min, respectively, $p<0.0001$) for stress, and (962k/min ± 426k/min vs 136k/min ± 37k/min, respectively, $p<0.001$) for rest.
Overall image quality was rated good and higher in 29 (97%) cases for D-SPECT, and 18 (93%) cases for A-SPECT (p=NS). D-SPECT SSS and SRS correlated linearly with A-SPECT respective scores ($r=0.84$, $p<0.0001$ for SSS, and $r=0.92$, $p<0.001$ for SRS). Of the 30 studies, 23 (77%) were diagnosed as definite normal or abnormal by D-SPECT, and 22 (73%) by A-SPECT (p=NS). Analysis of gated SPECT variables in 11 patients yielded that D-SPECT post-stress EF, EDV and ESV were highly correlated with the respective A-SPECT measurements (R 0.87, 0.97, 0.99, respectively, $p<0.001$), with insignificant difference from identity. **Conclusions**: D-SPECT is a novel technology, providing fast gated myocardial perfusion imaging with high image quality and improved resolution, with up to 8 times increased sensitivity. The amount of perfusion abnormality visualized by D-SPECT and computed gated SPECT variable is highly correlated to A-SPECT, with an equivalent level of diagnostic confidence. **Clinical Relevance:** The benefits related to the increased sensitivity include improved patient comfort due to rapid examinations and lowering radiopharmaceutical dose. The superior image quality should translate to more accurate and fewer ambiguous interpretations than are observed with A-SPECT.

Framingham and UKPDS Risk Scores Predict Extent and Severity of Coronary Disease as Determined by 64 Slice Coronary CT Angiography in Asymptomatic Patients with Type 2 Diabetes Mellitus

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Background and aims: Framingham and UKPDS risk scores are clinically useful for long-term primary prediction of coronary heart disease (CHD) events. The relationship of these scores to extent of sub-clinical coronary atheroma is not known. We examined the correlation of 10 year CHD risk with extent of prevalent sub-clinical coronary atheroma using 64 slice coronary CT angiography (CTA) in asymptomatic pts with type 2 diabetes mellitus (DM) enrolled in an ongoing prospective outcomes study.

Methods: Contrast enhanced 64-slice CTA was performed in 423 consecutive diabetic pts with no known coronary disease (age 63.4±5.3 yrs, 58% women, mean duration of DM 10.3±7.8 yrs, 35% receiving insulin). Framingham and UKPDS 10 year risk scores were calculated from baseline pt characteristics.

Results: Less pts were defined as low risk by Framingham (11.7%) than UKPDS (20.2%), nearly 40% were at high risk by both scores and remainder intermediate risk. Multivessel coronary plaque was present in 233 (55%) pts. Prevalence of coronary plaque increased with both level of Framingham and UKPDS risk (Table). Plaque prevalence correlated similarly with level of risk for both men and women. Amongst variables not included in risk scores (insulin treatment, ankle brachial ratio, serum CRP and serum fibrinogen) the ankle-brachial ratio predicted presence of multivessel coronary plaque independently of risk scores (Framingham p=0.018; UKPDS p=0.036).

Conclusions: In asymptomatic subjects with DM and no history of CAD undergoing 64 slice CTA 1. Multivessel plaque was common at all levels of risk. 2. Prevalence and extent of plaque increased with both Framingham and UKPDS risk. 3. The ankle-brachial ratio added independent information to that from either risk score..

Coronary plaque in relation to level of risk

Risk	Any plaque N (%) pts		Multivessel plaque N (%) pts		Stenosis (>50%) N (%) pts	
	Fram	UKPDS	Fram	UKPDS	Fram	UKPDS
Low (<10% 10yr risk)	26 (54.0)	22 (55.0)	15 (31.0)	21 (28.0)	4 (8.1)	7(9.0)
Intermediate (10%-20% 10yr risk)	148 (77.0)	126 (75.0)	105(54)	85 (50.0)	45 (24)	28 (17.3)
High (>20% 10yr risk)	131 (85.0)	134 (91.0)	96 (61.9)	111 (75.3)	39 (25.0)	56 (38.0)
p-value	<0.001	<0.001	0.001	<0.001	0.04	<0.001

Is there a Clinical Advantage of Doing Complementary Study of Stress SPECT or Stress Echo over One Image Modality ?

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One of the problems of the assessment of IHD by either stress SPECT or stress ECHO is the inconclusive clinical results , which cause the referral physician to apply for additional test. The aim of this study was to assess the yield of referral of patients for both stress SPECT and stress ECHO studies.

Methods: During 18 months we recruited 71 patients who underwent stress SPECT and stress ECHO or vice versa within 7 months in one medical center. Patients who underwent intervention or acute coronary syndrome were excluded. Clinical variables and results of stress SPECT and stress ECHO were compared.

Results: There were 28(39%) women and 43(61%) men aged 66±9. Chest pain was the referral reason for test in 39(55%) and history of CAD in 40 (56%) patients. Echo was performed prior SPECT in 50% and vice versa. Pharmacological stress was done in 32(45%) (Dipyridamole) by SPECT and 12(17%) (Dobutamine) by ECHO. The overall discrepancy between ECHO and SPECT was 52%. Normal study was significantly higher with ECHO than with SPECT (73% vs 45% $p<0.001$); the prevalence of ischemia with and without scar was significantly higher with SPECT than with ECHO (45% vs 11%, $p< 0.001$) and scar/wall motion abnormality was similar (10% vs 13%, p=NS). Of note, 5(7%) patients showed significant ischemia by SPECT, which was not detected by ECHO

Conclusions: The rate of discrepancy between SPECT and ECHO results done within 7 months was significantly high. However, only minority had substantial findings that might require further evaluation.

Left Ventricular Volumes Assessment by Rest Gated Tl-201 SPECT: Comparison with Two-dimensional Echocardiography

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Background: Myocardial imaging with thallium-201 is routinely used for perfusion assessment. Although rest gated thallium-201 (Gated-Tl) images are considered to have a low count statistics, this tracer is used for left ventricular assessment. The aim of this study was to compare left ventricular end diastolic volumes (EDV), end systolic volumes (ESV) and ejection fraction (LVEF) obtained on 4 hours rest Gated-Tl with those obtained by two-dimensional echocardiography (2-D ECHO).

Methods: The study included 32 patients who underwent a dipyridamole stress-rest gated SPECT myocardial perfusion imaging and 2-D ECHO studies the same day. EDV, ESV and LVEF were evaluated using the Cedars-Sinai Quantitative Gated SPECT (QGS) software package and by 2-D ECHO using the modified Simpson method for comparison.

Results: 21 (65.6%) of the patients were men, the mean age was 70.3± 8.2 years old, the incidences of a previous history of CAD and old myocardial infarction were 18 (56.3%) and 8 (25%), respectively. The mean EDV, ESV and LVEF were: 84 ml (range 67-109), 33 ml (range 22-52), LVEF 56±8 % by 2-D ECHO and 93 ml (range 59-113), 38 ml (range 28-56) and 57±10 % by Gated-Tl, respectively. Pearson's correlation co-efficient (r value) for EDV, ESV and LVEF between the two methods were 0.77, 0.74 and 0.62, respectively.

Conclusions: A good correlation was found between rest gated Tl-201 MPI and 2-D ECHO for the assessment of left ventricular volumes and ejection fraction. Rest gated Tl-201 provides credible values of left ventricular volumes to be used in routine clinical practice.

Fully Automatic Calculation of Cardiac Chamber Volumes can be Achieved Accurately from 4D CT Datasets

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Purpose: to evaluate the accuracy of a novel algorithm that performs fully automatic segmentation of the 4 cardiac chambers from gated computed tomography (CT) datasets.
Methods: 10 patients with acute myocardial infarction (AMI) and 10 normal controls underwent cardiac CT scans on a Philips Brilliance 64 scanner. Four phases (mid- and end-diastole, mid- and end-systole) were evaluated per patient. Immediately after loading the datasets, fully automatic segmentation of the 4 cardiac chambers was performed, using an algorithm based on an anatomical heart model which adapts a 3D mesh to new images exploiting simultaneously knowledge of organ shape and typical gray level appearance in images, learned from a training database. Segmentation of each chamber was then performed manually using volume-based region growing methods. Volumes obtained by each method were compared using Bland-Altman analysis and linear correlation.
Results: All chambers in all patients and for all phases achieved successful segmentation. Bland-Altman analysis showed minimal bias (-1.0ml, +0.4ml, -1.8ml) for the left (LV) and right (RV) ventricles, and right (RA) atria, but overestimation of LA volume (+23.6ml) due to inclusion of pulmonary veins. 95% CI were 10.2ml, 2.2ml, 6.5ml, and 10.3ml, respectively and correlation coefficients were all 0.98-0.99. Automatic LV and RV stroke volumes (SV) were also very accurate. As a test of physiological accuracy, left sided SV (89 ± 26ml) correlated highly with right sided SV (82 ± 21ml, r=0.88). Ejection fraction averaged 48 ± 12% for AMI and 58 ± 6% for normals with r=0.91 vs. manual approach.
Conclusion: Fully automatic calculation of volumes of all cardiac chambers can be achieved with a very high accuracy over multiple cardiac phases, however LA volume is overestimated.

ECG Location of Exercise Induced ST-T Shifts may Predict SPECT Perfusion Defects in Patients with Pre-existing CRBBB

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Background – Exercise myocardial perfusion scan is indicated in subjects with CRBBB and medium to high pre-test likelihood to coronary artery disease due to the uncertainty involved in the interpretation of ECG changes during a regular exercise test. Aim: To evaluate the association between ECG leads involved in the depolarization changes and the scintigraphic findings.
Methods: Among 1350 patients patients who underwent myocardial perfusion scan with Tl-201 or Sestamibi MIBI during the period 1.7.04 – 1.2.06, 59 (4.37%) were found to have a pre-existing CRBBB. The location of exercise induced $\geq$ 1mm ST-T shift was categorized as pattern (A) when leads V1-V3 were involved, (B) when II, III, aVF, &V5-V6, (C) when V1-V6, and pattern (D) when no ST-T shift occured. Association with the presence of perfusion defect, its location, age, gender, previous evidence of CAD, angina, and risk factors was assessed.
Results: Pattern A was observed in 7 patients, B in 24 patients, C in 18, and
D in 10 patients. All patients with pattern A (ST-T $\downarrow\downarrow$in V1-3) had normal perfusion scan, patients with pattern B, C, and D had fixed e/o reversible perfusion defects. Pattern A correlated well with no (or one) risk factors ($r= 0.72$, $p<0.05$) while patterns B, C, and D correlated well with ≥ 2 risk factors ($r= 0.65$, 0.75, and 0.66, respectively, $p<0.05$). Pattern A correlated well with the absence of previous infarction, CABG, or percutaneous intervention, $r = -0.88$, $p <0.01$.
Conclusions: ST-T shifts only in leads V1-V3 during exercise myocardial perfusion scan were found to be associated with normal myocardial perfusion and with absence of coronary risk factors, thus, with low likelihood of coronary artery disease.

Impact of Platelet Glycoprotein IIb/IIIa Receptor Inhibitors on Renal Function in Patients with Acute Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention

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Background: Worsening renal function in patients (pts) undergoing primary percutaneous coronary intervention (PPCI) for acute myocardial infarction (AMI) is associated with adverse clinical outcomes. Given platelet inhibition can modulate renal blood flow, we hypothesized that platelet glycoprotein IIb/IIIa inhibitors (GP IIb/IIIa) may decrease rate of renal function deterioration in pts undergoing PPCI. Methods and Results: Based on prospectively collected data, we analyzed rates of renal function deterioration in 603 consecutive pts (mean age 58±13 years, males 82%) with AMI treated with PPCI. Renal function deterioration was defined as an increase in serum creatinine (SCr) level of ≥25% or ≥0.5 mg/dl at 24 to 96 hours post-PCI compared with baseline value. Outcomes were stratified by treatment with GP IIb/IIIa. GP IIb/IIIa inhibition was associated with significantly lower rates of worsening renal function and lower 30-day mortality (Table). By multivariable analysis, adjusted for age, gender, diabetes mellitus, hypertension, baseline estimated glomerular filtration rate, anterior MI, Killip class on admission, and volume of contrast medium, treatment with GP IIb/IIIa was an independent predictor of preventing renal function deterioration after PPCI (odds ratio 0.35; 95% confidence interval 0.17 to 0.72; p=0.004). Conclusion: In this analysis, administration of GP IIb/IIIa to pts undergoing PPCI was associated with lower rates of worsening renal function and lower 30-day mortality.

Endpoints, %	GP IIb/IIIa inhibitors		P-value
	(+) N = 442 patients	(-) N = 161 patients	
SCr increase ≥25%, n (%)	101 (22.9)	51 (31.9)	0.02
SCr increase ≥0.5 mg/dl, n (%)	18 (4.1)	14 (8.8)	0.02
Maximum SCr change, mean±SD, mg/dl	0.14 ± 0.38	0.25 ± 0.45	0.005
30-day mortality, n (%)	10 (2.3)	12 (7.5)	0.005

Prognostic Value of Transient and Sustained Worsening Renal Function After Primary Angioplasty

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Background: Worsening renal function (WRF) is common in patients undergoing primary angioplasty and is associated with poor outcome. This study sought to determine the long-term prognostic implication of transient vs. persistent WRF after primary angioplasty for ST-elevation myocardial infarction (STEMI).

Methods: We used a prospective database consisting of all patients admitted with acute STEMI. A total of 572 patients were treated with primary angioplasty and survived the index hospitalization. Venous blood samples for creatinine were obtained on admission and at 24-h, 48-h, and 72-h thereafter. After the first 72-h from admission, creatinine measurements were checked only when clinically indicated. Patients were classified into 3 groups: 1) Patients without WRF during hospitalization (change in creatinine <25%); 2) Patients with an increase in creatinine of >25% that resolved by discharge (transient WRF); and 3) patients with an increase in creatinine >25% that did not resolve (persistent WRF). The primary end point was all-cause mortality after hospital discharge. The median follow-up was 15 months.

Results: During hospital course, transient and persistent WRF occurred in 62 (16.8%) and 76 (13.3%) patients, respectively. Mortality rates were higher in patient with transient or persistent WRF as compared with patients without WRF (16.1% and 11.8% vs. 4.4%, respectively; $P<0.0001$; **Figure**). In a Cox model, adjusting for multiple baseline characteristics (age, gender, baseline creatinine, hypertension, diabetes, smoking, anterior location of infarction, Killip class at admission), both transient (hazard ratio 3.0, 95% confidence interval 1.3 to 6.8; $P = 0.01$) and persistent WRF (hazard ratio 2.6, 95% confidence interval 1.1 to 6.2; $P = 0.02$) remained a significant independent predictor of post-discharge mortality.

Conclusion: Worsening of renal function after primary angioplasty is an important risk factor for long-term mortality after hospital discharge. Furthermore, even a transient creatinine elevation is associated with increased risk.

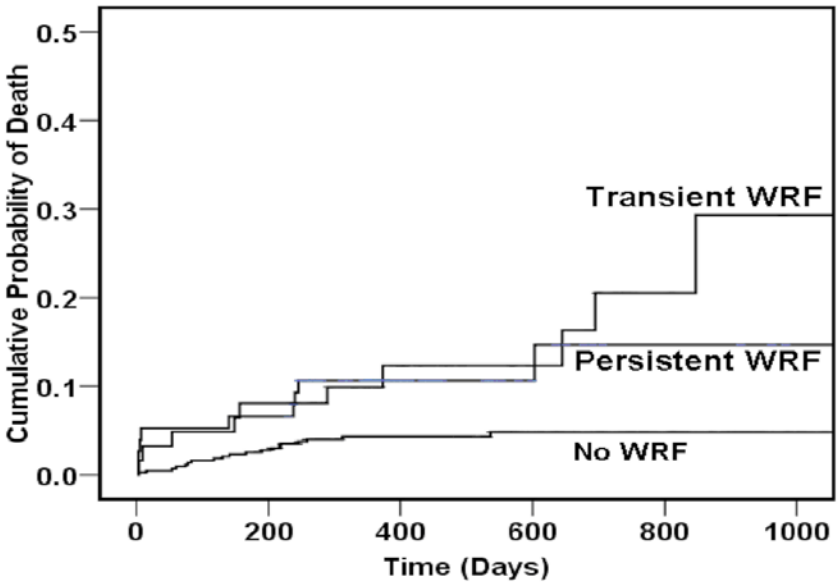

Figure: Kaplan-Meier curves of patients without WRF, patients with transient WRF, and patients with persistent WRF.

The Prevalence of Acute Myocardial Infarction Among Patients Presenting with Sustained Monomorphic Ventricular Tachycardia (SMVT)

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Sustained monomorphic ventricular tachycardia (SMVT) is a life threatening arrhythmia usually occurring in patients with structural heart disease. Since the symptoms and signs of SMVT can resemble an acute myocardial infarction (AMI), many patients presenting with SMVT on their first ECG are evaluated and treated for AMI. However, whether SMVT can be the presenting manifestation of AMI has received very little attention in the literature. Our goal was to determine the prevalence of AMI among patients presenting with SMVT.

Methods: 90 consecutive patients presenting with SMVT on their initial ECG were included in thus study. ECG tracings obtained immediately after restoration of sinus rhythm were read by "blinded" investigators. Coronary angiograms were read by a "blinded" investigator to assess for angiographic evidence of an acute coronary lesion. Among patients who satisfied the AMI criteria, we further defined a "primary" AMI as one associated with an acute coronary lesion, and a "secondary" AMI as one secondary to the arrhythmia.

Results: Patients' age was 65.2+13 years and 83% were men. 72% had previous AMI. the most prevalent presenting symptoms were palpitations and chest pain (36% EACH) Heart rate during SMVT was 183+43 and 40% were of RBBB configuration. Of the 90 patients, 54 (60%) underwent coronary angiography during the index hospitalization. Fourteen patients (15%) fulfilled the criteria of AMI, of whom only three (3%) fulfilled our definition of "primary" AMI.

During 916 +1269 days follow up of 70 patients who received an ICD, 51 (78%) had recurrent SMVT which required treatment by the device.

Conclusion: SMVT is a very rare initial presentation of AMI, , and acute coronary lesions are seldom identified during angiograpy. Thus, SMVT should be regarded as an arrhythmia secondary to a prior cardiac scar. The high rate of recurrent events among those patients strengthens this conclusion.

Primary PCI in Unconscious Patients with Acute Myocardial Infarction After Out-of-hospital Cardiac Arrest

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Background. The decision to perform primary percutaneous coronary intervention (PrPCI) in unconscious patients after out-of-hospital cardiac arrest (OHCA) is challenging due to uncertainty of prognosis of anoxic brain damage and difficulties of interpretation of ECG changes shortly after CA and CPR.

Aim. To evaluate outcome of unconscious patients with acute myocardial infarction resuscitated after OHCA who were treated with PrPCI and in whom this procedure was withheld.

Patients. Data sources: Rambam Intensive Cardiac Care (RICCa) and Primary Angioplasty Registry Rambam (PARR) databases - an ongoing registries of all consecutive patients admitted to ICCU and all consecutive patients treated according to PrPCI strategy, respectively. Study period: 01.2000-12.2006.

Results. Overall 45 patients were identified, 17(38%) were treated according to PrPCI strategy. Patient characteristics and outcomes presented in table (%).

	PCI (n=17)	No PCI (n=28)	P value
Age	59±11	68±12	0.023
Male	14 (82)	23 (82)	NS
Witnessed CA	16 (94)	26 (93)	NS
Bystander CPR	1 (6)	6 (21)	NS
Initial rhythm – asystole	2 (12)	11 (39)	0.048
Card. Shock	3 (18)	10 (36)	NS
STEMI	12 (71)	19 (68)	NS
Anterior location	7 (41)	7 (25)	NS
Severely reduced syst.LV function	4/15 (27)	10/16 (63)	0.045
Therapeutic hypothermia	2 (12)	4 (14)	NS
Survival	13 (76)	3 (11)	0.0001
Survival with good neurological outcome	9 (53)	1 (4)	0.0001

Conclusions. Patients after OHCA treated with PrPCI had better in-hospital survival and survival with good neurological outcome. These patients also had more favorable clinical characteristics which contributed to better outcome.

The Linear External-Work Pressure-Time Integral Relationship Ties the Frank and Starling Phenomena Together and Elucidates the Regulatory Roles of the Preload and Afterload

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Background: The mechanisms underlying the Frank Starling Law (FSL) of the heart are elusive and the prevalent concept suggests that the FSL is afterload independent. Isolated fiber studies suggest that the afterload determines cardiac function by modulating cross-bridge cycling and through established cross-bridge dependent cooperativity mechanisms. The study unveils the role of the afterload at the whole heart level. **Methods and Results:** The LV was exposed by left-thoracotomy in adult sheep (69.1±9.6Kg, n=8). Different afterloads were imposed by partial aortic occlusions. Transient inferior vena-cava occlusions (tIVCOs) were preformed at each steady afterload. External work (EW) and pressure time integral (PTI) were measured for each beat during the tIVCOs. A highly linear EW-PTI relationship (WPTiR) was found for each afterload (R^2=0.98±0.02) during the tIVCOs (n=54). Interestingly, the slope of the WPTiR was determined by the afterload. The slope was 34±2.8 mJ/mmHg/sec at baselines and decreased by 0.91±0.53 mJ/mmHg/sec per 1 mmHg·min/L increase in the peripheral resistance. The preload has a proportional effect on the EW and PTI. The afterload has opposing effects on the PTI and EW. Furthermore, a unique WPTiR was obtained during both occlusion and release phases of each tIVCO, while two distinct EW-preload relationships were observed, implying that the linear WPTiR is not a result of the FSL but relates directly to the underlying mechanism. **Conclusions:** A novel linear and afterload dependant WPTiR was described. This consistent WPTiR represents a basic feature of cardiac control of contraction that ties the Frank (pressure-preload) and Starling (EW-preload) phenomena together.

Sarcomere Lengthening Decreases the Rate of Cross-Bridge Cycling; Implications for the Ischemic Myocardium.

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The effects of stretch, encountered in ischemic myocardium, on force development and energy consumption, are not well understood. Prevalent theories suggest that stretch increases the force per cross-bridge (XB) but decreases the number of strong XBs (N_{XB}). We hypothesize that XB kinetics is determined by the filament sliding velocity. XB transition-rate from strong to weak state increases during shortening and decreases during stretch. Consequently, the stretch increases the force by increasing N_{XB}. The study investigates these opposing predictions under stretch conditions. **Methods:** Trabeculae were isolated from rat right ventricles. Sarcomere length was measured by laser diffraction and controlled by a fast servomotor. The number of strong XB (N_{XB}) was evaluated by fast and small oscillations. Stretches at different velocities (0-2.4μm/s) and instants were imposed on isometric twitches. **Results:** Faster stretches yielded larger forces. A tight linear correlation between force and N_{XB} was obtained, implying that the force increased due to the increase in N_{XB}. The phenomenon can not be attributed to the Force-length relationship since fast stretches (>1.6μm/sec) increased N_{XB} by >100% with only small (7.8%) sarcomere lengthening. Identical increase in force and N_{XB} was observed when similar stretches were imposed at different instants, suggesting that the phenomenon is activation level independent. **Conclusions:** stretch increases the number of strong XBs but decrease XB cycling rate and energy consumption. This yields a protective effect in the stretch ischemic myocardium by reducing energy consumption. The post-systolic shortening may results from the energy stored in the XBs that were recruited during the stretch.

Routine Upstream Use of GP IIb/IIIa Inhibitor (Eptifibatide) Preceding Primary PCI in STEMI

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Background: TIMI-3 flow rates pre primary-PCI (PPCI) for STEMI preceded by conventional therapy (aspirin and heparin) are reported in only 10-15% of patients. Adjunctive therapy with IIb/IIIa inhibitors before PPCI might increase these rates.

Methods: 144 patients (age 59 ± 13 yrs) with STEMI <12 h who underwent successful PPCI were pre-treated by protocol, with eptifibatide (in the CCU or ER) before emergency catheterization over the last 4 years (2004-2007). The primary end-point was TIMI-3 flow in the infarct-related artery on the first diagnostic angiogram pre PPCI.

Results:

Pain to Balloon (hr)	N	TIMI -0	TIMI -3	Eptifibatide to balloon (min)
<3	65	25 (38%)	25 (38%)	56 ± 22
3-6	51	17 (33%)	16 (31%)	85 ± 43
>6	28	16 (57%)	6 (13%)	100 ± 92
All	144	58 (40%)	47 (33%)	70 ± 56

The average time from pain onset to eptifibatide therapy was 100 min in pts with TIMI-3 flow, and 150 min in all other pts. TIMI 2-3 flow was more frequently observed in pts who received eptifibatide <180 min from pain onset than in those who received it >180 min from pain onset (53% vs. 30%, respectively, $p<0.01$). The average duration of eptifibatide therapy before PPCI was 70 min (range 10-270 min).

Conclusions: Routine adjunctive upstream use of eptifibatide in the ER or CCU in patients with STEMI before PPCI is associated with a 33% TIMI-3 flow in the infarct-related artery prior to intervention. This rate seems to be inversely correlated with the time from pain onset to eptifibatide therapy.

Stent Thrombosis Clinical Manifestation: Drug Eluting vs. Bare Metal Stents

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Background: Stent thrombosis has been the focus of intense interest because of high associated morbidity and mortality.

Objectives- We investigated the differences in angiographic definite stent thrombosis (ST), according to ARC definition, in patients with drug eluting stents (DES) vs. bare metal stents (BMS) implanted at out institution.

Methods: We evaluated all consecutive ST events during the period from 8/2000 and 7/2007, and recorded in details their clinical characteristics, median time to the ST event and outcomed in term of mortality at 30 days and 6 month.

Results: During the last seven years we identify 52 patients (55 vessels) who developed ST in the BMS group and 17 patients (19 vessels) that had ST in DES. Patients' demographics are described in the following **Table**.

Stent Thrombosis	**BMS**	**DES**	**P value**
Patients No	**N=52**	**N=17**	
Age (yr)	63±12	61±11	
Male	81%	71%	0.4
HTN	55%	53%	0.7
Dyslipidemia	55%	71%	0.4
Smoker	35%	18%	0.04
NIDDM	33%	29%	0.8
Previous CABG	2%	29%	0.04
renal failure	12%	24%	0.3
2/3 VD	54%	82%	0.08

The median time to stent thrombosis was 6 days (range 3 to 60d) in the BMS versus 100 days (range 14 to 450) in the DES group (p=0.03). ST in BMS was associated with mortality at 30 days of 7.7% as compare to 5.9% in the DES group (p=0.8). Following 6 month, the mortality rate in the BMS group was 19% vs. 12% in the DES group (p=NS). Recurrent ST were encountered in 4 patients in each group, with one (25%) mortality event in the BMS group, no mortality in the DES group and the need for revascularization (PCI, CABG) was 50% in both groups.

Conclusions: ST remains a severe complication for both BMS and DES although the average time interval from implantation to event is different (i.e. longer for DES vs. BMS). There was no difference in terms of mortality in both groups after six month but we noticed a worse prognosis among patients with ecurrent episodes of ST.

Prevalence and Prognostic Significance of Persistent Anemia after Acute Myocardial Infarction

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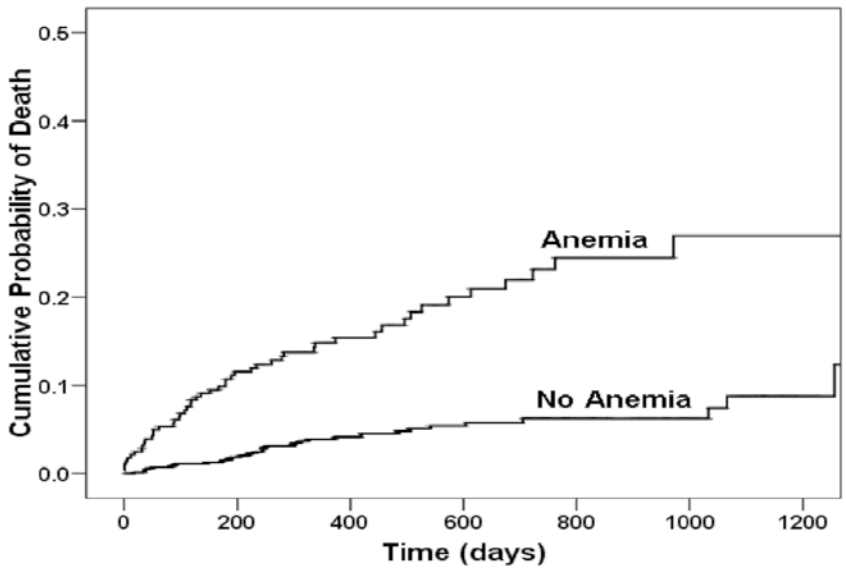
Background: Recent studies have shown that anemia occurring during an acute myocardial infarction (AMI) is an independent indicator of mortality. Anemia may be viewed as a transient phenomenon, secondary to antithrombotic agents and invasive procedures. However, anaemia might worsen or fail to improve after hospital discharge .

Methods: We studied 1110 pts with AMI who survived the acute event. Hemoglobin (Hb) levels were obtained at hospital discharge and >3 weeks after discharge (median 5.2 months). The relationship between post-discharge Hb and the primary endpoints of all-cause mortality were evaluated using Cox models, adjusting for age, gender, creatinine, previous infarction, diabetes, hypertension, smoking, anterior infarction, coronary revascularization during hospital stay, Killip class at admission, presence of known malignancy, pre-discharge Hb and pre-discharge ejection fraction .

Results: Using the WHO definition (Hb < 13 g/dL in men and < 12 g/dL in women), anemia was present in 392 pts at hospital discharge (35.3%). At follow up, anemia was present in 218 (55.6%) and 64 (8.9%) pts with and without anemia at hospital discharge, respectively. During a median follow up of 13 months after the post-discharge Hb measurements, 89 patients died (8.0%). The Kaplan-Meier curves of pts with and without anemia after hospital discharge are shown in the Figure. In a multivariable Cox regression model, the adjusted HR was 1.3 for each 1 gr/dL decrease in post discharge Hb (95% CI 1.1-1.4, P = 0.0004). In a similar model, the HR for mortality in pts with anemia after hospital discharge was 2.0 (95% CI 1.2-3.4, P = 0.008) compared with pts with increasing Hb level.

Conclusion: Pts after AMI who are discharged with anemia frequently fail to increase their Hb levels, and some Pts develop anemia after hospital discharge. Persistent or worsening anemia after AMI is associated with markedly increased risk for mortality .

Figure: Mortality of patients with and without post-discharge anemia



Relationship between Activated Clotting Time (ACT) and Ischemic and/or Hemorrhagic Complications Following Primary PCI in STEMI pts Treated with Heparin Combined with Eptifibatide

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BACKGROUND: Unfractionated heparin (UFH) is the most widely used anti-thrombin medication during percutaneous coronary intervention (PCI). Uncertainty remains about the optimal activated clotting time (ACT) for prevention of ischemic or hemorrhagic complications especially when combined with GP-IIb/IIIa receptor inhibitors.
AIM: We tested the relationship between ACT and cardiac or bleeding complications in STEMI pts undergoing primary PCI and treated using UFH in conjunction with GP-IIb/IIIa receptor inhibitors (eptifibatide [Ept] as a bolus plus infusion for 8-18 h).
METHODS: We evaluated the outcome at 30 days of 527 consecutive patients who underwent primary PCI. Patients were divided into 25-s intervals of ACTs.

RESULTS: The main results are shown in the **Table** as follow**:**

	<216 sec N=128	216-244 sec N=134	245-280 sec N=133	>280 sec N=132	P-value
Age (year)	58±12	59±11	58±12	60±12	0.5
Male	90%	87%	85%	78%	0.05
DM	22%	31%	16%	19%	0.02
Ant MI	48%	47%	43%	48%	0.9
2/3 VD	56%	65%	51%	57%	0.1
BMI (Kg/m^2)	27.5±4.2	26.9±4.3	27.3±3.6	27.6±4.2	0.6
Hemoglobin drop{mg%}	0.6±1.0	0.7±1.0	0.9±1.3	1.0±1.2	0.02
30 d Death	2.3%	2.2%	0%	0%	0.1
30 d ST	2.3%	3%	1.5%	0%	0.1
30 d Re-MI	3.1%	2.2%	1.5%	0.8%	0.5
Groin Hematoma	3.9%	1.5%	5.3%	4.6%	0.4
MACE	6.3%	7.5%	3.8%	3.8%	0.4
Hemorrhagic CVA	0%	0%	0%	0%	1.0

CONCLUSIONS: In STEMI patients undergoing primary PCI and treated using UFH+Ept, an ACT higher than >245s tended to be associated with better suppression of ischemic events but at hazards of higher hemoglobin drop due to hemorrhagic complications during the course of hospitalization.

The Significance of ST Elevation in Right Precordial Leads in Acute Anterior Myocardial Infarction

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Background: The clinical implications of ST-segment elevation in the right precordial leads in the circumstances of anterior acute myocardial infarction (AMI) are unknown.
Objectives: To asses the clinical utility of ST-segment elevation in leads V_3R and V_4R in anterior AMI.
Methods: This study comprised 120 consecutive patients admitted within 12 hours of symptom onset of anterior ST elevation AMI. All had 18-lead electrocardiograms with right precordial leads. Patients were stratified into two groups based on whether they had ST elevation $\geq$1 mV in V_3R and V_4R (group A) or not (group B).
Results: Group A included 39 patients (age mean±SD 59±11 years, males 82%) and group B included 81 patients (age 58±14 years, males 84%). Group A patients were more likely to experience primary ventricular fibrillation (VF) and comprised more patients who suffered from heart failure (HF) during hospitalization, compared with group B [for VF 8/39 (20%) vs. 2/81(2%), p=.0019, for HF 15/39 (38%) vs. 14/81(17%), p=.021]. Patients in group A compared with group B had a trend towards less spontaneous reperfusion (14% vs. 32%, p=.063), and had a higher incidence of multivessel coronary artery disease [median (interquartile range) of 2 (1-3) vs. 1 (1-2), p=.097 respectively]. There was no significant difference in the size of the infarct analyzed by peak CPK, or sum of ST-segment elevations.
Conclusions: In anterior ST-segment elevation AMI, right precordial leads could predict primary VF and HF during hospitalization, and if confirmed in large cohorts should be a routine part of the initial electrocardiogram.

Results of Drug Eluting Stents in Diabetic Versus Non-Diabetic Patients for Diffuse In-Stent Restenosis

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Background: Drug-eluting stents (DESs) are often used for the treatment of in-stent restenosis (ISR). The clinical outcome following implantation of DES for the treatment of diffuse ISR is less well defined among patients with Diabetes mellitus (DM).

Objective*:* We sought to compare the clinical outcomes using DES treatment for ISR in DM versus non DM patients.

Methods: we studied 110 patients who were treated for diffuse ISR [Mehran class >1] using DES. We identified 52 DM patients with ISR receiving DES, and compared them to 58 non DM pts treated for ISR with DES. We compared the procedural and angiographic results and clinical outcome at 6-months.

Results*:* Clinical characteristic, long-term outcome are summarized:

	No DM (N=58)	**DM (N=52)**	**P-value**
Age (years)	63±12	66±10	0.2
Males (%)	81	58	*0.007*
GFR (<60 mL/min/1.73 m^2) (%)	14%	12%	0.7
Chronic total occlusion (%)	16%	19%	0.6
Small vessel size (<2.5mm)	2.6±0.6	2.6±0.7	0.9
Mean stents length	27±7	27±7	0.99
6 months outcome			
Death (%)	3.5	1.9	0.6
Re-AMI	0	5.8	0.06
Stent thrombosis	0	7.8	*0.03*
Target vessel revascularization (%)	3.5	17.3	*0.02*
CABG	1.7	1.9	0.9
MACE$^+$	6.9	22	*0.03*

$^+$MACE= Death, re-AMI, TVR

Conclusions*:* DES implantation for diffuse ISR is associated with increase risk for stent thrombosis, re-infarction and/or need for repeat revascularization in diabetic patients compared to non-diabetic counterparts. Thus, diffuse ISR may be associated with more 'malignant' clinical course in diabetic patients.

Perfect Stent Positioning in Bifurcations: To Kiss or not to Kiss

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Background: Kissing balloons (KB) are considered essential to prevent stent distortion when treating side branches even with provisional bifurcation stenting. Current stent deployment techniques disregard the precise deployment position of the stent and its cells in relation to the sidebranch (SB) ostium. We postulated that stent deployment with precise orientation (both longitudinally and radially) followed by SB inflation would result in a patent SB in the absence of stent distortion.

Methods: Five bifurcations were treated in 3 juvenile pigs. Using a novel fixed wire based bifurcation system, stents were advanced to the bifurcation. Based on the marker system the rotational and longitudinal orientation and positioning of the stent was confirmed with relation to the main vessel and SB. The stents were deployed and in three cases the SB was dilated with balloons on the initial side branch wire. OCT was performed in two cases.

Under fluoroscopic control in a human cath lab stents were deployed silicone phantoms with a bifurcation set at 60 degrees. The stents was advanced in the main branch (MB) and deployed with the SB access cell in the proximal or distal portion of the ostium, with perfect rotational alignment. The SB was initially inflated and then followed by kissing balloon procedure, or kissing balloon (KB) was performed immediately. Phantoms were imaged with microCT and 3D reconstructions were performed at each stage of the study.

Results: In all cases the stents could be oriented as predetermined. Angiographic results were excellent with no stenoses of side branches. OCT demonstrated an unimpeded SB ostium with no stent distortion. In the phantoms, when the stent was deployed without SB post dilation stent achitecture was undistorted wih excellent patency to the SB. With proximal positioning of the SB access cell, SB inflation resulted in reflection of stents struts back into the lumen. This was only partially corrected by KB. In the same position KB immediately post stent rendered a perfect result. However with distal positioning of the SB access cell, SB inflation alone provided a perfect result. When pefect radial aligment was used therewas no stent distortion on the wall opposing the SB. Ex vivo CT analysis of the stented pig coronary confirmed these findings.

Conclusion: Using current stent techniques KB must be the next step following MB stenting. When perfect stent positioning is used the SB can be dilated with no MB stent distortion.

Impact of Final Minimal Luminal Diameter of the Stent on Long-term Results Following Sirolimus-eluting Stent Implantation for Diffuse in-stent Restenosis

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OBJECTIVES: We assessed the predictive value of minimal luminal diameter (MLD) for long-term patency of sirolimus-eluting stents (SES) implantation for diffuse in-stent restenosis .

BACKGROUND: By IVUS studies minimum stent area is a consistent predictor of in-stent restenosis. The value of angiographic MLD as a predictive value for SES failure still limited.

METHODS: From the RMC-ISR database, 110 patients were treated for diffuse ISR [Mehran class>1] using SES {Cypher}. Baseline angiography including pre- and post stenting QCA measurement were analyzed. Post-procedure MLD [<2.5mm] were correlated with 12 months target lesion revascularization [TLR].

RESULTS: Mean age 64±11 years with 70% male, 47% with DM and 16% with recurrent ISR. At baseline, 83% of the lesions were diffuse and proliferative and 16% total occlusions. The SES implantation was successful in all patients except one. Anti GP 2b/3a was used 45% of patients. The mean balloon pressure for stent deployment was 19±4 atmosphere. The mean stents length was 27±7mm. At 12-month follow-up, the total MACE rate was 12.7% (death 4.5%, MI .2.7%, CABG 3.6%, stent thrombosis 0.9%, TVR 12%, TLR 12%). Final MLD<2.5mm was positively correlated to 12 months TLR.

In a multivariate analysis adjustment to DM, time to restenosis, MLD<2.5mm [OR=4.2, 95% CI=1.1-16, P=0.03] was significant independent predictors of 12 months TLR. DM was borderline **[**[OR=3.12, 95% CI=0.8-12, P=0.08

CONCLUSIONS: In this study, reduced restenosis in the malignant type if in stent restenosis. MLD<2.5mm is a significant angiographic predictor of 12 months TVR

Do Drug Eluting Stents Improve Outcome in Patients Undergoing Primary PCI for ST Elevation Myocardial Infarction?

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Background: The role of drug eluting stents in primary PCI (PPCI) performed for ST elevation myocardial infarction (STEMI) is controversial. While a randomized trial suggested benefit, registry data suggest these stents may be associated with increased late mortality.
Aim: To investigate the clinical outcome of patients with STEMI treated with BMS or DES during PPCI.
Methods: We performed an observational study of 327 consecutive patients affiliated with Clalit Health Services who had PPCI for STEMI between 4/04 and 10/06. We compared patients who received DES (N=60 ,age: 60±13 years) to those who received BMS (N= 209, age:62±13 years). Patient data was obtained from computerized databases. Clinical, angiographic and angioplastic characteristics and one year clinical outcome were compared between the two groups.
Results: STEMI pts with DES more frequently had diabetes mellitus (38% vs, 24%, $p<0.04$) and moderate to severe left ventricular dysfunction (73% vs. 53%, $p=0.03$). The culprit lesion was more frequent in the LAD (65% vs 44%, $p<0.001$) and more often calcified (20% vs. 11%, $p=0.05$).Vessel diameter was smaller (3±0.4 vs.3.2 ±0.4 mm, $p=0.04$) and the stents longer (24±11 vs. 22±9 mm, $p=0.05$) when DES were implanted. Direct stenting was less frequent used with DES (22% vs. 43%, $p<0.01$). Immediate success was similar with both types of stents (99% vs. 100%). After one year follow up no differences were observed between patients given BMS or DES in all cause mortality (13% vs. 12%), myocardial infarction (2% vs 3%); surgical or angioplasty revascularization (15% vs. 8%) and a combined end points of those outcomes (29% vs. 20%, p=.NS) respectively .
Conclusion: In current clinical practice DES in the setting of STEMI is more frequently used in patients with diabetes and LV dysfunction and in LAD lesions. No clinical advantage of DES was found in this study.

Percutaneous Coronary Intervention for Chronic Total Occlusions: the Rabin Medical Center experience

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BACKGROUND: Percutaneous treatment of coronary chronic total occlusions (CTO) remains one of the major challenges in interventional cardiology. Bare metal stenting is limited by high rates of restenosis. Drug-eluting stents (DES) markedly reduce the risk of restenosis of relatively simple or complex nonocclusive lesions.

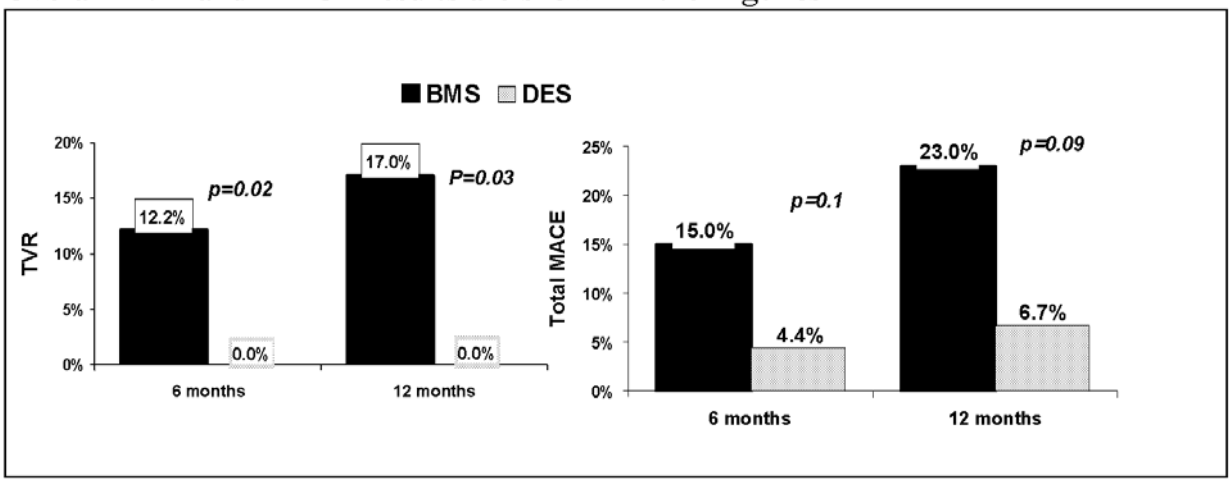
OBJECTIVE: This study sought to determine the clinical and angiographic outcomes after drug-eluting stent (DES)-supported PCI for CTO. .

METHODS: This study comprises 86 CTO lesions which were successfully treated with DES implantation [67% Cypher, 11% Taxus, 22% Endeavor stents)]. The control group consisted of 41 patients implanted with BMS only (n=26) or BMS and DES (n=15).

RESULTS:

	BMS [n=41]	DES [n=45]	P-value
Age [year]	62±12	63±12	.7
Male	90%	87%	0.5
LAD/DIAG	20%	33%	0.3
DM	34%	42%	0.4
CTO duration [m]	14±33	13±32	0.99

Overall TVR and MACE results are shown in the **Figures**



CONCLUSIONS: DES implantation for CTO is safe. Most events which are related to the need for repeat reintervention are decreased by the introduction of DES.

Aspiration During Every Stage of Primary PCI: "ADMIT"-Trial: Mid-Term Results

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Background: Distal embolic phenomena may appear during each stage of thrombus containing lesion intervention.

Aim: Assessing the role of active aspiration during each stage of primary PCI (PPCI) compared to the standard technique in a randomized prospective trial.

Material & Methods: So far, sixty nine patients eligible for PPCI were included. We excluded patients in cardiogenic shock. Demographic, clinical, angiographic, echocardiographic characteristics, ECG data and biomarkers in each group were collected. Clinical and echocardiographic records at 30 and 180 days follow – up are being investigated.

Results: The fallowing table presents the patients parameters in both groups:

*Parameter determined at the end of the procedure. N- Number of pts

Variable	Aspiration in every stage N= 34 (49.3%)	Standard –PPCI N=35(50.7%)	p-value
Age (years)	57.32±12.6	58.8±11.62	NS
Male n. (%)	30(88.2%)	27(77.1%)	NS
≥3 major risk factors	21(61.8%)	28(80.0%)	0.095
Killip FC (≥2) at admission	7(20.6%)	4(11.4%)	NS
Anterior wall infarct	18 (52.9%)	22 (64.7%)	NS
Inferior wall infarct	16 (47.1%)	12 (35.3%)	NS
*TIMI flow 3. N (%)	28(82.4%)	29(82.9%)	NS
*Mean TFC	25.23±12.2	30.4±15.8	NS
*Mean MBG 3. N (%)	22(64.7%)	15(42.9%)	0.069
Mean Peak CK	3012.7±2730	2143.9±2051	NS

Five MACE, defined as death, re- infarction and TVR had occurred during hospitalization period and 30 days follow- up. There was no significant difference between the arms.

Conclusion: This preliminary mid- term report show that performing repeated aspiration during every step of PPCI intervention neither improves nor damaging. Further data needs to be investigated as we are yet recruiting.

ADAM-15 Metaloproteinase Domain Derived Peptide as the Natural Ligand to GRP78 Receptor on Endothelial Cells for Therapeutic Angiogenesis

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ADAM15 is a membrane-anchored glycoprotein that contains a disintegrin and metalloprotease domains. The elevated levels of ADAM15 in endothelial cells prompted an evaluation of its role in neovascularization. Mice lacking the ADAM15 gene exhibit a strongly reduced angiogenic response compared to wild-type controls. It was found that neither VEGF nor bFGF induce changes in ADAM15 expression in human vascular endothelial cells.

The aim of the present study was to identify peptides derived from ADAM15 with angiogenic activity. **Results:** Three 12 aminoacid peptides were synthesized from the ADAM15 metalloprotease domain and termed ADoPep 1, 2 and 3. We studied binding, proliferation, migration and tube formation of endothelial cells under hypoxia with these peptides and found that ADoPep1 exhibited the strongest angiogenic activity invitro. In a mouse hind limb ischemia model, ADoPep1 at 0.1 microgram per mouse injected intramuscularly to the ischemic leg restored blood perfusion, as detected by laser Doppler imager. Histological examinations of the treated leg showed increase in capillary density, suggesting neovascularization. The Adam 15 derived peptides were found to bind glucose regulated protein GRP78 receptor on endothelial cells that increased after incubation with ADOPep1 under hypoxia conditions. The mean number of GRP78 positive cells was also significantly increased in ischemic limb histological sections 14 days post ADopep1 treatment. The role of ADoPep in prevention of apoptosis was studied using endothelial cell subjected to hypoxia or $CoCl_2$ induced apoptosis. ADoPep1 prevented only hypoxia induced apoptosis demonstrating that the inhibition of apoptosis by ADOPep1 is specific to the hypoxia stress conditions.

Conclusions: This study contributes to the search for new molecules for development of therapeutic angiogenesis in ischemic diseases.

Endothelial Nitric Oxide Synthase and Superoxide Dismutase are Crucial to Endothelial Progenitor Cells Function in Diabetes

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Background – Endothelial progenitor cells (EPCs), key regulators of vascular repair are impaired in diabetes. We postulate a tight crosstalk between endothelial nitric oxide synthase (eNOS) and superoxide dismutase (SOD) in regulating EPC levels and function in diabetes.

Methods – EPCs from diabetic patients and healthy subjects were compared ex vivo for their number and function. In another experiment healthy EPCs cultured under high glucose concentrations were either treated by insulin or SOD in vitro. Superoxide and NO production as well as SOD activity were assessed.

Results – EPC levels and function in diabetic patients were significantly reduced compared to those of healthy subjects ($P<0.05$). EPCs from diabetic patients produced excessive superoxide anions, lower NO levels but higher SOD activity compared to non-diabetic control subjects ($P<0.05$). NO produced from EPCs derived from diabetic patients correlated negatively with $HbA1_C$ and glucose levels ($r = -0.57$; $P = 0.003$ and $r = -0.49$; $P = 0.01$, respectively). NOS inhibition with N^G-nitro-L-arginine methyl ester (L-NAME) as well as SOD treatment attenuated superoxide generation and normalized functional capacity of EPCs treated with high glucose. Insulin treatment failed to suppress superoxide production but has restored NO bioavailability and improved EPC proliferation.

Conclusions – SOD seems to be essential for EPC regulation and may play an important role in modulating EPC function in diabetic patients.

In Vivo HIF-1 Alpha Expression in Experimental Murine Atherosclerosis

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Background **-** Hypoxia inducible factor-1 (HIF-1) regulates T cells activation, cytokine production and proliferation by inducing a shift towards T_H2-cell responses and inhibition of T_H1-cell pro-inflammatory response. T cells stimulation and cytokine secretion play a central role in the progression of atherosclerosis. We explored the effect of over-expression of HIF-1α in ApoE knockout mice lymphocytes, as a tool to regulate inflammation and atherosclerotic process.

Methods and Results –Intravenous hydrodynamic plasmid injection of empty pCDNA3 or pCDNA3-HIF-1αP564A (HIF-1α mutated stabilized construct) were performed to atherosclerosis prone Apolipoprotein E knockout mice. After 24 hours, HIF-1α over-expression in splenocytes (n=3) was validated by RT-PCR and ELISA. One week post-injection, spleens and aortas (n=3) were analyzed for expression of IL-10, INF-γ and TGF-β by RT-PCR. In addition, the cytokine profile of splenocytes was studied employing an inflammatory cytokine array. Increased expressions of IL-10 and TGF-β in splenocytes as well as a decreased expression of INF-γ in aortas were measured in HIF-1α-treated mice, compared to controls. Cytokine arrays revealed a shift of the T_H1 inflammatory response toward T_H2 cytokine expression. At day 30, systemic injection (n=8) was repeated. At day 60, animals were scarified and aortas were isolated for plaque progression assessment. Aortic sinus lesion size was significantly decreased in mice treated with pCDNA3-HIF-1αP564A and were characterized with reduced lipid cores as well as larger fibrous caps, compared with controls.

Conclusions – Over-expression of HIF-1α in mouse splenocytes is associated with attenuation of inflammatory response and attenuated plaque progression in experimental atherosclerosis.

Vitamin E Provides Renal Protection to Diabetic Mice Genetically Modified at the Haptoglobin Locus

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Background: The haptoglobin (Hp) gene is polymorphic with two classes of alleles denoted 1 and 2. Individuals with diabetes mellitus (DM) homozygous for the Hp 1 allele (Hp 1-1) are at decreased risk of developing diabetic complications, including nephropathy, as compared to individuals homozygous for the Hp 2 allele (Hp 2-2). Retrospective data from antioxidant studies suggests that vitamin E therapy provides benefit to Hp 2-2 individuals. We sought to recapitulate this pharmacogenomic effect in mice transgenic for the Hp 2 gene.

Methods: DM was induced in Hp 1-1 and Hp 2-2 mice with streptozotocin. After 3 months functional, morphometric and histochemical differences between the kidneys of Hp 1-1 and Hp 2-2 mice were assessed by measurement of creatinine clearance (CCT), albuminuria, glomerular area, glomerular collagen and iron. DM mice were treated for 10 weeks with Vitamin E at a dose of 40mg/kd/day.

Results: In the absence of DM we found no difference in any functional, morphometric or histochemical parameter between Hp 1-1 and Hp 2-2 mice. Moreover, no differences were found between Hp 1-1 mice with or without DM. However, there was a significant increase in CCT, albuminuria, glomerular area, glomerular collagen and iron in Hp 2-2 mice with DM. Vitamin E treatment prevented the functional, morphometric and histochemical changes seen in Hp 2-2 DM mice.

Conclusions: Vitamin E appears to provide protection against the development of nephropathy in Hp 2-2 DM mice.

Single Center Experience with Trans-Radial Approach for Primary PCI

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Background: More than 90% of the procedures in our Cath Lab are done as trans-radial approach. Lately we have extended this technique to primary PCI (PCI/TRA).
Methods: Since January 2007 we adopted the radial approach for all new patients with STEMI referred to primary PCI. Patients with weak radial pulse, severe dysrhythmias, CHF or hypotension were excluded. We used published world data for time table reference (NRMI, DANAMI) .
Results: 25 STEMI patients underwent primary PCI/TRA as a routine procedure (right radial all). IRA were: LAD: 11, LCX: 2, RCA: 12. Full patency restoration of the IRA was achieved in 100% of the patients. In 3 cases we used thrombus aspiration devices, in 5 patients a bifurcation PCI with kissing balloon was performed successfully. Six patients had slow reflow phenomenon resolved after IC Adenosine injection. In two cases IABP was inserted trough the femoral artery due to low blood pressure and slow reflow. There was no major bleeding, pseudo-aneurysm or fistula. In one case (treated by Integrilin Heparin and Plavix) there was a large hematoma in groin (IABP insertion site) and small one in the forearm. There were 3 more cases with minor hematoma in the forearm.
Time table:

	World data	Our experience in PCI/TRA
Symptom onset to Balloon	Median 218 min	90-840 (median 267) min
Hospital door to Balloon	83-120 (median 116) min	45-180 (median 72) min
Cath Lab door to Balloon	20-53 min	20-35 (median 27) min

Conclusions: Following a meticulous learning curve, the trans-radial approach can be applied for primary PCI with high success rate, short door to balloon interval, and low complication rate. This approach improves patient's convenience and well being. The very low vascular complication rate increases the safety margin for this procedure that involves intense use of anti-coagulation/aggregation medications.

Long Term Results of Mitral Valve Repair Using Autologous Pericardium Annuloplasty

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Objectives: Use of autologous pericardium for annuloplasty during mitral valve is controversial. We therefore sought to evaluate our long-term results using this technique.

Methods: We retrospectively reviewed 173 consecutive patients aged 19 years to 92 years (59.6 ± 16.25years) who underwent mitral valve repair complemented by annuloplasty between January 1998 and December 2003. Major causes of mitral regurgitation were annular dilatation and prolapse of the posterior leaflet. Annuloplasty was performed in all the patients using a strip of pericardium treated in glutaraldehyde 0.6% for 10 minutes. Two rows of continuous horizontal mattress Gore-Tex suture were used to secure the pericardium to the mitral annulus. Follow-up was performed in 100% of the patients, and the mean follow-up was 5.25 ± 1.62 years (range, 1.97 to 9.43 years).

Results: There were 3/173 (1.7%) 30 days deaths. Five (2.9%) patients with mitral regurgitation, with or without mitral stenosis underwent reoperation. Mean interval period between operation and reoperation was 3±2.7 years. Actuarial survival rate was 92.5% at 7 years after operation. Freedom from reoperation was 97.1% at 7 years after the initial operation. Follow-up echocardiography was performed on in 160 of the 160 patients (100%). No mitral regurgitation was detected in 34 patients (21.2%), 88 (55%) had grade 1 mitral regurgitation, 35 (21.8%) had grade 2, 3 (1.8%) had grade 3 and none had grade 4.

Conclusions: Our results indicate that autologous pericardium mitral annuloplasty is an effective technique. It provides a durable, reproducible annuloplasty of the mitral valve and avoids the use of foreign materials.

Sternal Wound Infection and Mediastinitis – The End of the "Sternectomy and Muscle Flaps" Era

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BACKGROUND: Postoperative deep sternal wound infection carries a high mortality, a high morbidity, and a poor cure rate. The prevailing approach of sternectomy and pectoralis muscle or omental flaps coverage significantly disrupts the heart's natural chest wall protection and the patients' quality of life. Besides increased mortality and morbidity rates, nearly all patients find it cosmetically repulsive. We present our 5-year experience of a new conservative approach which was gradually developed to improve the outcome of these patients.
METHODS: From January 2003 to November 2007, 2.5% of our patients (n=112) were treated for sternal wound infection and mediastinitis following open heart surgery. We have gradually developed treatment protocol entailing: early hospitalization, drainage and debridement of the sternal wound using the vacuum assisted closing (VAC) system, IV antibiotics administration, macrophages injection into sternal wound margins, and home discharge with IV antibiotics and granulation promoting dressings.
RESULTS: Sternectomy rates dropped down from 43% (n=12) during 2003 to 5% (n=1) in 2007 ($P< 0.001$), macrophages administrations increased from 18% to 95% ($P<0.001$), and the mortality of the patients with deep sternal infection and mediastinitis dropped down from 39% to 0% ($P<0.001$).
CONCLUSION: Our newly developed standard conservative protocol for the treatment of deep sternal infections and mediastinitis is effective and highly recommended. It spares the sternum, cures the infection, and leaves the patient physically functional without the use of soft tissue flaps. This treatment was associated with a dramatic reduction in mortality and a significant improvement in patients' quality of life.

Increased Incidence of Early Acute Rejection and Earlier Development of Cardiac Allograft Vasculopathy after Heart Transplantation Due to Donor-Recipient Ethnic Mismatch

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Aim: To investigate the possible linkage between donor-recipient ethnic mismatch (DREM) and incidence of early rejection and cardiac allograft vasculopathy (CAV), a major cause of graft loss in heart transplanted patients.

Materials & Methods: We studied all 111 patients who underwent heart transplantation between 1990 and 2006. Data were retrieved from patient records. Recipients ethnicity: 97 Jewish, 7 Arabs, 6 non-Jewish Caucasians and 1 Hispanic. Donors ethnicity: 47 non-Jewish Caucasians, 46 Jewish, 8 Asians, 7 Arabs and 3 Hispanics. Rejection based on cardiac biopsy was defined as mild (ISHLT 1, 2) or moderate/severe (ISHLT 3A, 3B, 4). CAV was diagnosed by coronary angiography.

Results: DREM was found in 60, and ethnic matching in 51 patients. No rejection was found in 57.7% of 275 biopsies in the ethnic matched group vs. 40.4 % of 241 among DREM patients. Mild rejection was identified in 31.9% in the ethnic-matched vs. 48.7% in the DREM group (p=0.0002). Rate of moderate/severe rejection were similar (10.4% vs. 10.9%). No such linkage could be established 3 months after transplantation. CAV diagnosed in 26.2 % and 19.6% (P=0.382) for the DREM and ethnic-matched groups respectively during average 7 years (1-14) follow-up. Average time to develop CAV was significantly shorter in the DREM group (4.6 Vs. 7.7 years, p=0.005).

Conclusions: Appropriate donor-recipient ethnic matching is associated with a significant decrease in early acute rejection rate following heart transplantation. In contrast, ethnic mismatching seems to be a risk factor associated with early rejection episodes and earlier development of CAV in the transplanted hearts.

Stentless versus Stented Prosthesis for Primary Aortic Valve Replacement: Midterm Results of Morbidity, Mortality and Quality of Life

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Objective: To compare midterm morbidity, mortality and quality of life after primary AVR between stentless and stented prosthesis groups.

Methods: Between August 1996 and August 2006, 310 patients (156 female, 109 (35.2%) >80 years old) underwent primary biologic AVR with or without concomitant CABG due to aortic stenosis. Biologic prosthesis was implanted in all patients older than 65, and in younger patients with a specific request. Clinical assessment, quality of life evaluation (the MOS questionnaire scores) and echocardiography measurements were performed during follow-up (mean 35 months).

Results: Overall hospital mortality was 2.6 %(8/310). Stentless valves were implanted in 31.3% (97/310) of patients. Post operative mean gradients was 18.5 ± 7.5 for patients with stented valves vs 14.5±6.7 for stentless valves ($p<0.001$). Multivariate analysis revealed that late mortality was associated with hyperlipidemia (O.R. =2.5, p=0.04). Overall mortality was associated with age over 80 (O.R. =2.0, p=0.003), CHF (O.R. =2.1, p=0.015), IDDM (O.R. =4.4, p=0.01), and CAF (O.R. =2.3, p=0.01) but not with any type of prosthesis. In addition, poor quality of life assessment (higher scores in the MOS questionnaire) was associated with CHF (O.R=4.2, p=0.001), moderate patient-prosthetic mismatch (O.R. =7.1, p=0.036) but not with any type of prosthesis.

Conclusions: although the use of stentless biologic prosthesis in the aortic position reduces post operative mean gradients more significantly, no difference in midterm morbidity, mortality or quality of life was seen between groups.

Postoperative Stroke after Cardiac Operations – Is there Light at the End of the Tunnel?

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Background: Ischemic stroke after cardiac operations is a devastating complication with an incidence that has remained constant during the past decade. Therapeutic options are limited since the increased risk for hemorrhagic complications with systemic thrombolytic therapy. Selective intra-arterial approach seems to be safer and more effective.

Patients and Methods: Three patients suffering acute ischemic stroke after surgery underwent emergency neuro-radiological interventions within a few hours from onset of symptoms.

Results: A 66 years old male underwent Mitral Valve Replacement and Tricuspid Valve Repair. On post-operative day (POD) 2 he developed sudden motor Aphasia and left hemiplegia. CT documented a thrombotic occlusion of the right middle cerebral artery. He underwent selective thrombolysis and balloon angioplasty 3 hours after onset of symptoms. Gradual resolution was documented.

The second patient, an 84 years old female, underwent Coronary Artery Bypass Grafting (CABG) and left carotid endarterectomy. On POD 2 she developed right hemiplegia. She underwent urgent carotid angiography and stenting of the left internal carotid artery within 90 minutes from onset of symptoms. Full neurological recovery was documented.

The third patient, a 78 years old female, underwent CABG and developed left hemiparesis on POD 4. She underwent selective thrombolysis and mechanical manipulation of a thrombus in the basilar artery within 6 hours from onset of symptoms. The thrombus was dislodged distally with no resolution of symptoms.

Discussion: Immediate neuro-radiological intervention has a role in the treatment of postoperative ischemic stroke. It may change the course of the disease and should be considered whenever feasible. Pros and cons of this approach will be discussed.

Mitral Regurgitation after Trans Aortic Myectomy for Hypertrophic Obstructive Cardiomyopathy

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Background: Systolic anterior motion of the mitral valve (SAM) causes left ventricular outflow obstruction and mitral regurgitation in hypertrophic obstructive cardiomyopathy (HOCM). It is therefore generally believed that effective relief of obstruction by transaortic septal myectomy (TSM) will subsequently result in resolution of mitral regurgitation (MR), even if significant.

Material and Methods: Between January 2004 and November 2007, 20 consecutive patients with HOCM and preoperative significant MR underwent TSM. We describe five patients in whom MR remained significant despite effective TSM. In all 5 patients a repairable cause of the residual MR was identified by intraoperative TEE and the MR was abolished in a second pump-run. In 3 of them, the additional repairable cause could have been detected by the preoperative study: in 1 patient it became apparent on the preoperative TEE only in hindsight, and in 1 patient the importance of the problem became apparent only after TSM. In 2 patients mitral valve replacement had to be performed in the absence of a detectable repairable cause, or due to intraoperative evidence of organic mitral valve disease unrelated to HOCM.

Conclusion: In up to 25% of the patients with HOCM and significant MR it may be difficult to predict whether abolishing SAM by TSM may also effectively abolish MR, because of: 1) intrinsic mitral valve abnormalities typical for HOCM – particularly leaflet redundancy; 2) changes in mitral valve configuration following TSM; and 3) the potential presence of coincidental organic mitral valve disease. Therefore, the mitral valve of patients with HOCM who are candidates for TSM should not only be carefully examined by preoperative TEE, but also by off-pump intraoperative TEE following TSM.

Tricuspid Valve Surgery in the Elderly : Is it Different ?

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Objective: We compared the outcomes of tricuspid valve [TV] surgery in the elderly and younger cohorts.

***Methods*:** In a prospective observational study, all 130 consecutive patients undergoing TV surgery between October 2004 and July 2007 were considered in 2 groups: group 1 included patients aged below 70 years (mean 55.76 ± 10.6 yrs) and group 2 - patients aged 70 years or more (mean 77 ± 5.3 yrs). Preoperative, operative and all outcome parameters were compared.

Results: All patients needed intervention on the tricuspid valve because of, at least, moderate tricuspid regurgitation. In 120 patients an annuloplasty ring implantation was done. Tricuspid valve replacement was needed in 10 patients. In group 1, the main indication for surgery was severe mitral regurgitation due to degenerative mitral disease; while more patients had rheumatic mitral disease in group II. The primary procedure was mitral valve replacement in both groups. Elderly patients had significantly more hypertension, diabetes, higher Euroscore, postoperative atrial fibrillation and behavorial confusion. Mortality was similar in both groups (12.9% in group 1 vs. 13.3% in group 2, P = 0.5).

Conclusions: In our cohort, although elderly age reflects a sicker group of patients, association of TV surgery in the elderly didn't carry any additive mortality risk compared to younger patient group.

Mitral Valve Leaflet Augmentation for Ischemic Mitral Insufficiency

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BACKGROUND: Chronic Ischemic mitral regurgitation (IMR) is a common complex clinical entity, associated with poor long-term survival. Numerous surgical techniques have been developed for IMR, but none has resulted in clearly improved patient outcome. Leaflet augmentation allows excellent leaflet coaptation and relief of leaflet tethering. We report our experience of mitral valve repair with anterior or posterior leaflet augmentation.

METHODS: Between March 2006 and August 2007 we used mitral leaflet augmentation technique in eight patients (7 patients – anterior and 1 patient – posterior leaflet augmentation). A mean age was 65 ± 9.5. The mitral valve leaflet was augmented with a patch of bovine pericardium. Non restricted annuloplasty with a semi rigid Physio ring was performed in all patients. Six patients presented preoperatively with severe MR and two had moderate MR. Annuloplasty ring size were 32 mm in 4 patients, 30 mm in 3 patients and 28 mm in one patient. Preoperative ejection fraction was 31.5 ± 11.7 % and NYHA class – 3.5 ± 0.5. All patents underwent concomitant CABG with a mean of 3.25 grafts/patients. Additionally, tricuspid valve repair was performed in one patient.

RESULTS: There was no operative mortality. Echocardiography performed after surgery showed none or trivial mitral regurgitation in all patients. Hospital mortality was 25% (2 patients). One patient died 48 days post operatively due to ischemic complications of severe peripheral vascular disease, another one developed sepsis and bacterial endocarditis with severe mitral regurgitation and died 31 days after the operation.

CONCLUSIONS: Leaflet augmentation for Ischemic MR showed promising short term results. Further studies are needed to assess long term outcomes.

Combined Carotid Endarterectomy and CABG, Long Term Results

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Background: The surgical approach for the treatment of concomitant coronary and carotid artery disease is still controversial. The options are either staged approach - carotid endarterectomy (CEA) first followed by coronary artery bypass grafting (CABG), or simultaneous approach - CEA and CABG under the same anesthesia. The reverse approach - CABG first and then CEA, was abandoned because of inferior results. In view of the newer options now available, such as percutaneous carotid artery angioplasty and stenting, we have reviewed our short and long term experience with combined CEA and CABG operations.

Methods: From January 1993 to January 2007 we operated on 82 patients (65 men, age 69.2±6.3 years). Carotid endarterctomy always preceded myocardial revascularization, performed either with or without cardiopulmonary bypass.

Results: Operative mortality was 3.6%. Perioperative neurological complications (5%) included irreversible hemiparesis (2) and TIA (2). Perioperative myocardial infarction (MI) occurred in 3 patients. During mean follow up of 10±3.2 years (1-14 years), six patients (7.6%) had neurological events: hemiparesis (4) and TIA (2). Seventeen patients (21.5 %) had cardiac events: MI (1), CHF (3), ischemia (11), VT (2). Five-year and 10-year survival was 74%±5% and 62%±6%, respectively.

Conclusion: Although the short term results of the new therapeutic alternative, namely carotid artery stenting before CABG, are similar to our surgical results, there are limitations to carotid artery stenting: the need for aggressive anti-platelets therapy for at least one month, and the hemodynamic changes during the procedure (bradyardia, hypotension) may be unacceptable for patients with unstable coronary artery disease. Therefore there is still a role for concomitant surgical CEA and CABG, yielding good results towards which the results of the other option should be compared while making the decision regarding the management of combined coronary and carotid artery disease.

Atrial Fibrillation Detection with a Novel Device "AF Alarm" in Mid-term Follow-up After Successful Maze Procedure.

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Background: Currently, determination of sinus rhythm after AF ablation procedure is done by using ECG, Holter monitoring and patients' subjective complaints. These methods may underscore periodic atrial fibrillation (AF) events. Underscoring of AF has serious implications such as discontinuation of anticoagulation and anti- arrhythmic therapy. A novel device "AF Alarm" was developed recently for automatic detection of cardiac arrhythmia.

Methods: From February 2004 till November 2007 we performed surgical ablation of AF in 150 patients. We tried to detect episodes of AF at 6 months and more after surgery in patients who were in normal sinus rhythm according to follow-up done by Holter monitoring and at least two follow up visits. We employed the device "AF Alarm" (Medtronic Inc, USA). The device was attached to the patient for 7 days. It automatically detected and stored in its memory all arrhythmia occurring in this period.

Results: Preoperatively seventy-five patients had persistent atrial fibrillation (50%), 65 suffered from permanent AF (43%) and 10 had paroxysmal AF (7%). One hundred eleven patients underwent left atrial ablation and 39 had biatrial ablation. Eighty four percent of patients were in sinus rhythm at follow-up. "AF Alarm" device was used in part of the patients with "normal" sinus rhythm [according to Holter monitoring and follow up visits without any subjective complaints of arrhythmia at 6 months and more after procedure]. In half of them short episodes of AF were found.

Conclusion: Determination of success after AF ablation is controversial. Some patients considered to be in normal sinus rhythm after ablation still can have some silent episodes of AF. These events can influence anticoagulation and anti-arrhythmic protocols after ablation. This new device gives more precise estimation of procedural success.

Echocardiographic Variables and Left Ventricular Morphology Patterns Associated with Right and Left Bundle Branch Blocks

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Background: Complete right and left bundle branch blocks (RBBB and LBBB) are associated with increased morbidity and mortality; however the mechanisms responsible for these relations are unclear.
Objectives: To determine independent echocardiographic variables associated with RBBB and LBBB.
Methods: We analyzed the data of 10,621 consecutive patients without pacemakers, non-specific intraventricular conduction delay, or significant valvular disease on the electrocardiogram, who were referred to stress echocardiography in our Institute. Left ventricle (LV) morphology patterns were categorized according to the American Society of Echocardiography recommendations. Logistic regression analysis determined independent variables associated with RBBB or LBBB.
Results: There were 479 (4.5%) patients with RBBB, 259 (2.4%) patients with LBBB and 9883 (93.1%) patients with no BBB. After adjustment for clinical and echocardiographic variables, independent variables associated with RBBB compared to no BBB included severely reduced left ventricle ejection fraction (LVEF <30%) and increased LV mass index. The independent variables associated with LBBB included: increased LV diastolic diameter index, any reduction in LVEF (< 50%) and increased LV mass index. A separate analysis revealed that both concentric and eccentric hypertrophy were independently associated with RBBB and LBBB; however for LBBB eccentric hypertrophy was significantly more prevalent than concentric hypertrophy.

	RBBB vs. no BBB		LBBB vs. no BBB	
	Odds ratio	P value	Odds ratio	p value
LV diastolic diameter/BSA > 3.2 cm/m2	1.37	NS	1.58	.016
LVEF 40-49% LVEF 30-39% LVEF<30%	.94 1.01 1.79	NS NS .015	2.70 5.46 15.07	.0001 <.0001 <.0001
Increased LV mass index	1.35	.005	2.21	<.0001
Eccentric hypertrophy Concentric hypertrophy Eccentric vs. concentric hypertrophy	1.46 1.57 .96	.015 .002 NS	4.03 2.27 1.70	<.0001 <.0001 .001

Conclusions: LBBB is strongly associated with increased LV mass index and eccentric hypertrophy. Its association gradually increases with reduced LVEF, whereas RBBB is moderately associated with severe LV dysfunction and increased LV mass index. These data may explain the increased morbidity associated with LBBB and RBBB.

Prediction of Left Atrial Appendage Thrombi in Non-valvular Atrial Fibrillation. The Role of D–dimer.

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Background: There is little knowledge about the prediction of left atrial appendage (LAA) thrombi in non – valvular atrial fibrillation (NVAF).

Aim: To evaluate the role of D–dimer to predict the presence of LAA thrombi in patients with NVAF.

Methods and results: In this prospective blinded study, 71 patients (56 % males, mean age 74.9 years) with NVAF were enrolled. Blood for D-dimer was taken at the time of transesophageal echocardiography (TEE). In 12 (16.9 %) patients, thrombus was found in the LAA. Significant predictors of LAA thrombi were the presence of congestive heart failure (25% vs 15%, p=0.04856), a history of recent embolic event (15.25% vs 8.33%, p=0.0412), severe spontaneous echo contrast (SEC) (66.67% vs 28.81%, p=0.0123), platelet count (248.000/ul vs 208.000/ul, p=0.0381), elevated fibrinogen levels (627.6mg/dl vs 534.3mg/dl, p=0.0480), and D-dimer levels (1445.64ng/ml vs 524.79ng/ml, p= 0.0002).

Receiver operating characteristic analysis detected an optimal cutoff value of ≥ 800ng/ml for D-dimer to detect LAA thrombi.

LAA thrombi were detected in 91% of patients with higher D-dimer values, whereas it was detected in only 9% of patients with lower D-dimer values. D–dimer cutoff level of 800ng/ml had a negative predictive value of 92% for identifying LAA thrombi.

Conclusions: In patients with NVAF, D-dimer may be helpful for predicting the presence of LAA thrombi. D-dimer level may be clinically useful to guide the management of patients with NVAF.

The Yield of BNP in Prediction of Ischemia During Dobutamine Stress Echocardiography

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Objectives: Dobutamine stress echocardiography (DSE) is a valuable tool for the noninvasive evaluation of myocardial ischemia. Recently, B type natriuretic peptide (BNP) has emerged as a biomarker with the potential of risk stratification & ischemia prediction. This study was performed to assess the correlation between BNP levels before and after DSE and myocardial ischemia as demonstrated by DSE.

Patients and methods: 26 patients referred for DSE were recruited for the study after signing informed consent. Before DSE, baseline echocardiography determined LV size, ejection fraction, and pulmonary artery systolic pressure. First NT pro-BNP sample was obtained after venous catheter insertion before dobutamine infusion. IV dobutamine was infused up to 50 mcg/kg/min to reach the target heart rate, IV atropine was used up to 1 mg if needed. Second NT pro-BNP sample was obtained immediately after the end of the exam. SPSS-13 software was used for statistical calculations.

Results: Mean age was 69 (47-83) years, 58% were females, 13 had established CAD, 9 had previous MI. Average LVEF was 58 (30-70)%, 80% of patients had EF $\geq$ 50%;: 5 patients had chest pain during DSE, 7 had ECG changes. 6 had wall motion abnormalities at baseline study. LV function did not improve or deteriorated in 3,
6 had evidence of inducible ischemia. Mean NT pro-BNP first sample value was 408 (17-2381) pg/ml, second sample was 401 (16-2292) pg/ ml, mean difference between the 2 samples was -7.67 (-89 to 82) pg/ml. There was a significant statistical correlation between 2 NT pro-BNP samples and baseline EF (p=0.031 & 0.027), when EF was divided into normal (>50%) and abnormal group, the correlation was even higher (p=0.001). There was no correlation between any of 2 NT pro-BNP value, their average, their relative change (and ratio between the change and the average) and the presence of inducible ischemia.

Conclusion: In this pilot study, NT pro-BNP levels before and after DSE and the difference between them did not correlate with the presence of inducible myocardial ischemia on DSE. Our study did not show any added value of NT pro-BNP levels during dobutamine stress echocardiography.

Nitrous Oxide Inhalation for Transoesophageal Echocardiography- An Alternative to Benzodiazepine Sedation?

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Background: Transoesophageal echocardiography (TEE) is usually performed using benzodiazepine sedation, which is a limiting factor for elderly patients or those with respiratory insufficiency. Kalinox®, an equimolar mixture of nitrous oxide and oxygen, with no depressive respiratory action and fast reversible effects, seems ideally suited for performing TEE but has never been evaluated. The aim of the present study was to evaluate TEE feasibility and efficiency using Kalinox compared to standard care using benzodiazepine.

Methods: We prospectively enrolled 80 consecutive patients referred for TEE. In the 35 first patients, TEE was performed using intravenous benzodiazepine (Midazolam) and in the 45 last patients using Kalinox (nasal delivery). Pain and tolerance induced by the examination were evaluated on a 0-10 scale. Remembrance of the examination by the patient and quality of the TEE by the operator were also evaluated.

Results: All TEEs were performed by the same experienced operator. TEE duration was not different (6±3 vs. 7±4 min respectively, p=0.57). Patients in the Kalinox group felt TEE to be more difficult (p=0.005) and remembered the procedure more clearly (p<0.0001) but pain experience was not different (7% vs. 9% had a pain score ≥5 respectively, p=0.75). Percentage of patients who agreed to have a second TEE if necessary was slightly lower (77% vs. 94% respectively, p=0.04). The operator judged TEE quality satisfactory in similar proportions (76% vs. 68% respectively, p=0.44).

Conclusion: These preliminary results show that TEE using Kalinox is feasible, provides similar pain relief despite more discomfort for the patient, and acceptable conditions for the operator. Thus, Kalinox use could be considered as an alternative to benzodiazepine sedation for patients intolerant to benzodiazepines such as elderly or respiratory-insufficient patients.

Accuracy and Reproducibility of Left Ventricular Outflow Tract Diameter Measurement Using Transthoracic as Compared to Transesophageal Echocardiography

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Background: Accurate measurement of left ventricular outflow tract diameter (LVOTd) is essential for reliable estimation of aortic valve area (AVA) using the continuity equation. Transesophageal echocardiography (TEE) can accurately delineate the LVOT. The purpose of this study was to assess the accuracy and reproducibility of LVOTd measurement using transthoracic echocardiography (TTE) with harmonic imaging as compared to TEE.

Methods: We prospectively studied 50 pts (mean age 69±14y, 20 with aortic stenosis (AS) and 30 without AS). LVOTd was measured offline in a blinded fashion in both systole and diastole by 2 experienced observers using TTE in the parasternal long axis view and TEE in the midesophageal aortic view (~130°).

Results: There was good correlation between TTE and TEE (r=0.91). LVOTd was significantly smaller by TTE as compared to TEE (2.11±0.21 cm vs. 2.16±0.22 cm, mean difference -0.05±0.09 cm, p=0.0003). Bland-Altman analysis showed 95% confidence interval of +0.14 and -0.24 cm for LVOTd measurement by TTE vs. TEE. Inter and intra-observer variability for LVOTd was 4.8±4.1% and 2.8±1.9% for TTE and 4.2±3.1% and 2.5±1.6% for TEE (p=NS). In patients with AS, estimated AVA was 0.93±0.22 cm^2 using TTE and 0.96±0.24 cm^2 using TEE, p=0.08. Diastolic LVOTd by TTE was smaller compared to systolic LVOTd by TEE (-0.07±0.08 cm, p<0.0001), especially when LVOTd was large, but there was excellent correlation between the two (r=0.95).

Conclusions: LVOTd is slightly underestimated by TTE as compared to TEE, but using harmonic imaging is accurate and reproducible. LVOTd measurements at end diastole can be used to predict systolic LVOTd when systolic images are suboptimal.

Comparison of Conventional and High-Frequency ECG Analysis in Detecting Ischemic Heart Disease During Dobutamine Echocardiography

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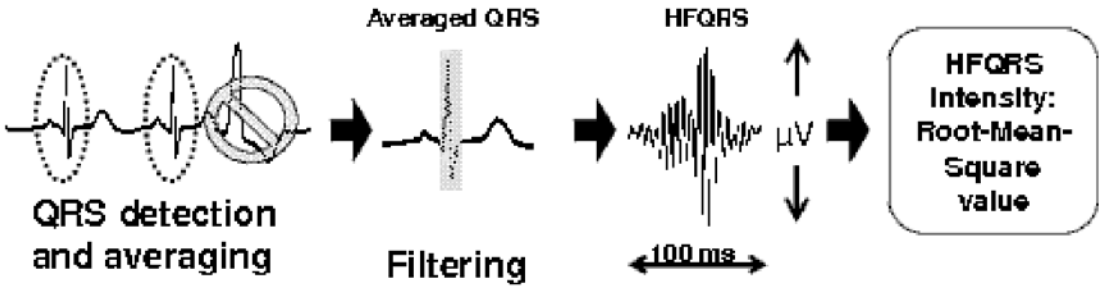
A novel technique for electrophysiological detection of stress induced ischemia, based on analysis of the high frequency mid-QRS potentials (HFQRS), has recently been reported to outperform conventional exercise ECG interpretation. Our aim was to test the performance of this technique in patients undergoing dobutamine echocardiographic imaging.

Methods: The study included 71 pts (67±14 y, 39 men) referred to clinical dobutamine echocardiography, which served as the comparative diagnostic test for ischemia. Conventional ECG was combined with high resolution ECG acquisition that was digitized and analyzed offline using the HyperQ™ System (BSP, Tel Aviv, Israel). HFQRS signals were extracted and time-intensity curves calculated (figure). Relative intensity change in HFQRS during the test was used as an index of ischemia.

Results: The dobutamine echocardiographic test was positive in ten patients, negative in 55 patients, while six patients had inconclusive results. HFQRS analysis was possible in 45 patients and conventional ECG interpretation was available in 33 patients. HFQRS analysis showed better specificity than conventional ECG interpretation (85% vs 55%, $p<0.01$), and overall accuracy was significantly improved (82% vs. 55%, $p<0.01$) when HFQRS was employed.

Conclusions: HFQRS analysis presents a significant improvement over conventional ECG interpretation in detecting ischemia during dobutamine stress and may thus aid in enhancing the non-invasive diagnosis of ischemic heart disease. Further testing in a larger patient population is required to accurately assess the diagnostic performance of this technique.



Correlates of Echocardiographic Left Atrium and Ventricular Parameters and GFR in Hospitalized Patients

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Introduction: Chronic kidney disease is associated with increased cardiovascular (CV) risk. Left ventricular hypertrophy (LVH) together with coronary artery disease has been considered the main target of intervention in these patients. LVH is highly prevalent in CKD even in early stages. The aim of the study was to investigate the relationship between Glomerular filtration rate (GFR) and LV, left atria (LA) echocardiographic parameters in hospitalized patients.

Methods: Retrospective chort analyses of all patients hospitalized in Internal Medicine A during the study period was performed. GFR was estimated by means of the serum creatinine level using the MDRD Equation formula. LVH, LA volume, area and diameter were determined according to echocardiographic criteria.

Results:

Data analysis was performed on 1000 consecutive patient's laboratory and echo files during 16 months (1/ 2006 -4/ 2007). In 397 pts (M/F 147/250) all data existed and thus were included. Mean Age was 76.5±8 (38-94y).The Correlation of GFR with LVH (posterior wall and septum) and LA Volume was good (r^2=0.68 and 0.62 respectively $p<0.05$). The Correlation of GFR with LA Area was Borderline (r^2 = 0.45, p=0.058) and no correlation was found with LA diameter (r^2=0.35, p=0.64).Creatinine clearance was inversely related to LVH (r=-0.132, $P<0.0001$).

Conclusions: GFR is associated with altered LV dimensions. These data may help explain the high cardiovascular mortality observed in patients with renal dysfunction. The incidence of LV diseases progressively increases as GFR deteriorates. This observation is more accurate when volumes are used and less when area and diameter are used.

Classification of Left Heart Functional Dimensions by Clustering Cardiac Echo-Doppler Measurements. A Mathematical Data Mining Technique Can be Used to Find Pathological Patterns

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Introduction: Cardiac Echo-Doppler (Echo) data may contain hidden information that cannot be revealed and identified by an experienced cardiologist. Thus, important relations between Cardiac dimensions (CD) may be misinterpreted. Clustering is commonly used in Data Mining (DM) and aimed to partition data into clusters.

Aim and methods: The aim was to find if mathematical tool such as clustering algorithms can find possible correlations between CD in order to upgrade and improve echo diagnostic abilities. Therefore clustering algorithms including K-means (KM), Kohonen (Koh) and TwoStep (TS) were applied on 24,400 data objects of Cardiac Echo measurements.

Results: The commercial DM tool Clementine (Clem) was used. Each algorithm generated different clusters. Despite this, between left atrial Area (LAad) and ascending aortic Diameter (AsAod), pathological positive correlations were identified and both negatively correlated with EF (table 1).

Conclusions: This work is an example from a series of works which shows that mathematical Data Mining technique can be apply on Echo measurements, find correlations between CD and thus may be used to look for hidden pathological patterns.

Cardiac Dimension vs. clustering algorithm	K-means	Kohonen	TwoStep
AsAod (mm)	29.2±4.8	*31.9±3.5	*33.8±4.2
Lad (mm)	*32.3±4.1	*36.6±5.2	*44.7±8.8
LAa (cm2)	*15.5±3.2	*19.4±3.8	*28.1±7.0
LVEDD (mm)	*46.5±4.1	*50.7±4.7	*55.7±8.5
LVESD (mm)	*28.9±3.2	*38.3±5.5	*42.4±10.8
EF %	*63.2±3.7	*41.4±11.1	*44.8±14.8
STH (mm)	*8.7±1.3	*10.2±1.4	*11.2±2.4
PWT (mm)	8.5±1.2	9.7±1.2	10.5±1.8

Table 1: LAd and left atrial area (LAa), LV end diastolic and systolic diameter (LVEDD)-LVESD), Ejection fraction (EF), Septal&Posterior wall thickness (STH-PWT).*= P<0.01 (in column only).

Routine Coronary Angiography pre Valve Surgery is it Time to Change the Paradigma ?

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Aim: To assess the usefulness for routine coronary angiography in patients referred for valve surgery.

Methods: Patients diagnosed with valve disease on clinical and echocardiographic findings and who underwent routine coronary angiography in the absence of clinical ischemia, were analyzed as to the presence and severity of coronary artery disease. Data was collected from the catheterization reports.

Results: 99 patients from private and public hospitals were catheterized . 40% were females. Average female age was 69years and males 63years. 67% of the patients had normal or non obstructive disease and 13% only 1 vessel disease. However in the patients under 60 years 88% were normal and 8% had only one vessel disease. In this subgroup no female had coronary artery disease. Only 13% underwent concomitant cabg.

Conclusions.High rate of normal and non obstructive disease especially in females under the age of sixty.

Recommendations..No need for routine coronary angiography prior to valve surgery in patients under 60. coronary CT scan can serve as an alternative.

Characteristics and Management of Hospitalized Old Patients with Severe Aortic Stenosis

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Introduction: Severe aortic stenosis (sev-AS) is common in old patients but there are no guidelines for its management at this age. We studied characteristics and management of these patients compared to younger sev-AS patients and to old patients without sev-AS.

Methods: Patients with sev-AS over age 70 (group 1 = 37 patients, age 84.6±4.2) were retrospectively compared to old patients with mild AS (group 2 = 20 patients, age 84.8±2.5) and to younger patients with sev-AS (group 3 = 17 patients, age 68±7.9, $p<0.001$ vs. other groups).

Results: Majority of patients were female (73, 50 and 67% in groups 1-3, respectively). Severity of AS was similar in groups 1 and 3 (mean gradient 56±24 vs. 54±17mmHg; valve area 0.61±0.18 vs. 0.69±0.14cm^2). Surprisingly, other echo parameters were similar in all groups as was the prevalence of hypertension (72-79%), atrial fibrillation (21-54%), diabetes (25-50%) and IHD (27-54%). Hyperlipidemia and smoking were more common in group 3 (67 and 22% vs. 29-35% and 0-4%, respectively). Common reasons for admission were heart failure (54-57%) and vertigo/syncope (19-33%). Blood pressures, heart rates, laboratory results on admission were similar but creatinine was higher in groups 1-2 vs. group 3. A cardiological consult was requested in 22% of group 1 but in 94% of group 3 patients. Accordingly, valve replacement was recommended in only 11% of group 1 vs. 72% of group 3 patients.

Conclusions: Old patients with sev-AS patients have similar characteristics to younger patients with sev-AS but are treated like old patients with mild AS.

Combined Surgical and Percutaneous Approach in the Cath Lab toTreat AF

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Background: Isolation of the major part of the left atrial posterior wall, including the four pulmonary veins, could become the treatment of choice in patients with paroxysmal and persistent AF, if a continuous transmural lesion could be made. Available epicardial monopolar ablation devices used in the minimally invasive surgical treatment of AF yield inconsistent results with this box-lesion. We therefore combined a mono-lateral right thoracoscopic approach with a standard percutaneous transseptal EP procedure to limit the shortcomings of both procedures.

Methods and results: Patients with paroxysmal or with persistent AF were operated on in the EP cath lab. In one case, endocardial evaluation of the lesion line in a patient with PAF showed a gap at the roof of the LA, which could be closed with another epicardial application. In another patient with persistent AF, the monopolar ablation device failed to create a continuous lesion in the connecting lines between right and left pulmonary veins, so endocardial RF ablation was necessary to close the gaps. Since the surgical device acts as an anatomical landmark for the box-lesion while serving as a protective wall between the atrium, the phrenic nerves, and the oesophagus, endocardial RF energy could be accurately and safely delivered.

Conclusion: A combined minimally invasive surgical and percutaneous EP approach in the cath lab appears feasible and safe. This procedure has the potential to overcome the shortcomings of each procedure, reduce complications, and increase success rate.

Implication of Exercise Training on Cardiomyopathy and Catecholamine-dependent Polymorphic Ventricular Tachycardia CPVT in Calsequestrin Deficient Mice

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Catecholamine-dependent polymorphic ventricular tachycardia (CPVT) is a lethal ventricular arrhythmia evoked by physical or emotional stress. Recessively inherited CPVT is caused by either missense or null-allele mutations in the cardiac calsequestrin (CASQ2) gene. It was suggested that defects in CASQ2 causing protein deficiency, impair Ca^{2+} uptake to the sarcoplasmic reticulum and Ca^{2+}-dependent inhibition of ryanodine channels, leading to diastolic Ca^{2+} leak, after-depolarizations and arrhythmia.

To examine the effect of exercise training on left ventricular remodeling and arrhythmia, CASQ2 knockout ($CASQ^{\square E9}$) mice and wild-type controls underwent echocardiography and heart rhythm telemetry before and after a 6-week training protocol using treadmill exercise. RT-PCR was used to measure the expression of A and B-type natriuretic peptide genes (ANP and BNP).

Left ventricular fractional shortening was impaired in $CASQ^{\square E9}$ (35±3% vs. 41±8% in controls, $p<0.05$) but improved after training (44±5% and 51±3 in $CASQ^{\square E9}$ and control mice, respectively, p=NS). The exercise tolerance was 16±1 min in $CASQ^{\square E9}$ mice vs. 29±2 in controls, $p<0.01$, but improved in trained animals (26±2 vs. 30±3 min, respectively, p=NS). The hearts of $CASQ^{\square E9}$ mice had higher basal expression of the BNP gene, but ANP was not significantly different from controls. After training, the expression of both natriuretic peptide genes was markedly decreased in $CASQ^{\square E9}$ and controls. Exercise training was not associated with a change in CPVT severity, but appeared to decrease the prevalence of ventricular arrhythmia during stress.

We conclude that in $CASQ^{\square E9}$ mice, recapitulating the phenotype of human CPVT, exercise training is beneficial and could offer a strategy for prophylactic and therapeutic interventions.

A Dominant Role of the Generated Force in Modulating the Cardiac Action Potential in Rat Trabeculae

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Mechanical inhomogeneities can elicit arrhythmias by triggering after-depolarization or generating spatial electrical disparity. However, the cellular mechanisms remain elusive. The prevalent hypothesis relates the phenomenon to stretch-activated channels. An alternate hypothesis postulates that mechanical perturbations affect calcium dissociation from troponin, and the ensuing changes in the intracellular free calcium concentration ($[Ca^{2+}]_i$) alter the action potential duration (APD). These stretch- and calcium-mediated hypotheses were investigated in trabeculae (n=7) isolated from rat right ventricle, by separately controlling sarcomere length (SL) and $[Ca^{2+}]_i$. SL was controlled by a rapid servomotor. $[Ca^{2+}]_i$ was clamped by utilizing tetanic contractions at different extracellular calcium concentrations ($[Ca^{2+}]_0$s). Tetanus was achieved by 8 Hz stimulation in the presence of cyclopiazonic acid. APD was evaluated by the voltage-sensitive dye Di-4-ANEPPS. SL was measured by laser diffraction and force by strain gauge. Sarcomere lengthening from 1.85 to 2.2μm at constant $[Ca^{2+}]_0$ =3 mM decreased the APD_{90} from 90.7±4.1 to 62±1.5 msec. However, an increase in $[Ca^{2+}]_0$ from 1.5 to 4.5 mM, at the same SL (2 μm) decreased the APD_{90} from 84.6±3.8 to 69.2±1.6 msec. Interestingly, a consistent identical inverse relationship between APD_{90} and force was obtained, and identical APD_{90} was observed at similar force with different pairs of SL and $[Ca^{2+}]_0$. The APD_{90} decreased from 89.8±2.1 to 62±1.3 msec as the force increased from 6.5±0.9 to 100.1±10.6 mN/mm^2. These conspicuous observations are readily explained by calcium-dependent reverse excitation–contraction coupling, where the cross-bridges determine the affinity of troponin for calcium and calcium extrusion via the Na^+-Ca^{2+}-exchanger affects the APD.

Effect of the Second Lebanon War on the Incidence of Appropriate Implanted Cardioverter-Defibrillator Discharge Among Israeli Patients – Final Results

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Background: Previous data have suggested that emotional stress may trigger malignant ventricular arrhythmias and hence Implanted Cardioverter-Defibrillator (ICD) Activations (Rx.). However, no data exist about the influence of a war on ICD Rx. Therefore, we retrospectively analyzed ICD interrogations of our entire ICD patients (pts.) (No= 233) and compared between the incidence of appropriate (app.) ICD Rx. (Anti-Tachycardia Pacing and shocks) during the Second Lebanon war period and three control periods.

Results: Mean age was 65.8 (22-90 yrs); 202 (86.7 %) were males; 166 (71.2 %) had ischemic heart disease; mean LVEF was 31.3 % (15-70 %); the indication for the implantation was aborted sudden cardiac death or sustained ventricular arrhythmia (i.e. secondary prevention) in 104 pts. (44.6 %), and 211 pts. (90.6 %) were exposed to alarms and/or rockets falls. The incidence of ICD App. Rx. was not significantly different during the war in comparison to the control periods.

Incidence of App. ICD Rx.

Patients N (%)	War period 13/07-14/08/2006	Control periods 12/06-12/07/2006	Control periods 15/08-15/09/2006	Control periods 13/07-14/08/2005
Exposed 211	10 (4.7 %)	9 (4.3 %)	9 (4.3 %)	5 (2.4%)

Conclusions:

1. The exposure of our ICD pts. to a huge emotional stress, such as the second lebanon war, did not cause a significant increase in ventricular tachyarrhythmias and appropriate ICD activations compared to the control periods.
2. As our findings are in contrast to previous studies, we suggest that the prolonged exposure of the Israeli pts. to emotional stress, precondition them to adapt stress during the war.

Admission for Syncope: Evaluation, Cost and Prognosis, According to Etiology

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Background: Syncope is a common clinical problem which often remains undiagnosed despite extensive and expensive diagnostic evaluation.

Objectives: to assess the diagnostic evaluation, costs and prognosis of patients hospitalized for syncope in a tertiary referral center (TRC) according to discharge etiology (DE).

Methods: We retrospectively reviewed medical records of patients admitted for syncope in a TRC throughout 1999. Mortality data were obtained, a year post-discharge, for each patient. Evaluation costs were calculated based on prices from the Ministry of Health basket services in 2002.

Results: 376 patients qualified for this study. DE's distributed as following: Vasovagal-26.6%, cardiac-17.3%, neurological-4.3%, metabolic-0.5%, unexplained-47.3%, and other-4%.

Cardiac and neurological tests were used more often, with higher yield in patients with cardiac and neurological DE respectively.

Mean evaluation cost was 11,210+8,133 NIS, higher in ICCU than in Internal Medicine (IM) wards (19,210+11855 vs.10443+7314 NIS, p=0.0015). Mean in-hospital stay was 4.9+4.2 days, longer in ICCU than in IM wards (7.2+5.6 vs. 4.6+3.5 days, p=0.024).

Short term mortality- 30 days and long term mortality (LTM) - 1 year rates were 1.9% and 8.8% respectively, and differed according to DE. LTM rates were significantly higher in patients with Cardiac, Neurological and Unknown DE (not vasovagal), compared with age adjusted general population of Israel (LTM = 2.2%) and higher in patients with cardiac compared with non-cardiac DE (15.4% vs. 7.4%, p=0.04).

Higher mortality rates were associated with higher evaluation costs.

Conclusions: hospitalization in a TRC for syncope is associated with increased mortality for most etiologies (except vasovagal), cardiac>non-cardiac. Despite high costs of in-patient evaluation, associated with more diagnostic tests, longer in-hospital stay and higher mortality rates, nearly half of the patients were discharged undiagnosed. Out-patient evaluation should be considered when medically possible.

Left Ventricular Lead Placement and Impact on Outcome of Cardiac Resynchronization Therapy

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Background: The response to cardiac resynchronization therapy (CRT) has been shown to be related to the location of the left ventricular (LV) lead in the posterior and lateral areas of LV. However, information is scarce about the difference between the two.
Objectives: To compare the clinical outcome between LV lead placement in the lateral and posterior cardiac segments for CRT.
Methods: We studied 102 patients with advanced heart failure, LV ejection fraction ≤35% and QRS duration >120 ms who underwent CRT device implantation. Clinical and echocardiographic variables before and after 3-month follow-up were compared between patients with lateral LV lead (lateral group) and posterior LV lead location (posterior group).
Results: The lateral group included 80 patients (71% with ischemic etiology) and the posterior group 22 patients (81% with ischemic etiology). There were no significant differences in baseline clinical and echocardiograpic characteristics of patients between the two groups. In a pre-defined positive clinical response (including 3 clinical criteria) there was no significant difference between the posterior group compared with lateral group (73% vs. 60% response respectively, p=.274). There was an improvement in 6-min walk distance (mean±SE 63±25 vs. 17±11 meters, p=.027) in the posterior group compared with the lateral group. We found no significant differences in improvement in LVEF, LV volumes, or intraventricular systolic dissynchrony between groups.
Conclusions: This study shows no different outcomes between LV lead placement in the lateral and the posterior cardiac segments. The best location of LV lead for CRT may depend on other measures such as scar tissue localization.

Clinical and Echocardiographic Predictors of Response to Cardiac Resynchronization Therapy in Patients Upgraded from Conventional Pacemakers

Roy Beinart [1,2], Eyal Nof [1,2], Osnat Gurevitz [1,2], David Bar Lev [1,2], David Luria [1,2], Hava Granit [1], Sharona Bachar [1], Micha Feinberg [1,2], Rafael Kuperstein [1,2], Shemy Carasso [3], Michael Eldar [1,2], Michael Glikson [1,2]

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Background: Most randomized controlled trials of CRT did not include patients with previous pacemakers therefore selection criteria for CRT in this population are poorly defined. We sought to evaluate potential predictors for response to CRT in patients upgraded from conventional pacemakers.

Methods: 48 consecutive patients who underwent successful upgrading from conventional pacemaker to CRT, and had complete follow-up within the first year were included in the study. Response was defined by a score combined of NYHA class, MLHF quality-of-life score and 6-minute walk. Each component was classified as improved (+1), unchanged (0) or worsened (-1) and responders were defined as patients who had a combined score of ≥1. We compared the occurrence of various parameters among responders versus non-responders.

Results:

	Responders (n=29, 60%)	Non-responders (n=19, 40%)	P value
Age	68±12	71±11	0.4
Male (%)	79%	74%	0.7
Ischemic cardiomyopathy	69%	83%	0.2
NYHA I-II, III, IV	7%,76%,17%	11%,84%,5%	0.5
6-min walk, m	254±127	324±146	0.1
Quality-of-life	65±23	55±24	0.2
QRS mean ± SD	183±35	179±29	0.9
Chronic atrial fibrillation	17%	16%	0.6
LVESV (average), ml	139±67	149±78	0.7
LVEF (average), %	24±8	24±6	0.8
Septal to lateral delay (>60 msec)	59%	53%	0.5
Yu standard deviation(>32)	79%	63%	0.2
Interventricular delay(>40 msec)	72%	63%	0.4

Conclusion: A positive response to upgrading to CRT in patients with previous pacemakers was observed in 60%. None of the parameters tested here was a significant predictor of response. Further studies are needed to define predictors of success in this population

Clinical Spectrum of Dual Atrioventricular Nodal Physiology

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Introduction

Dual atrio-ventricular nodal physiology (DAVNP) is longitudinal dissociation of AV conduction. It is the anatomic substrate of reentrant circuit responsible for the initiation and perpetuation of AVN reentrant tachycardia (AVNRT), which is the most common clinical presentation of DAVNP. Other forms of DAVNP may present as single nodal echo beats, or in rare occasions 2 for 1 ventricular response.

In this presentation we will discuss other forms of atypical clinical presentations of DAVNP. These include: AV conduction delay due to spontaneous conduction of sinus beats over the slow pathway, 2:1 ventricular responses or non reentrant AVN tachycardia, and the drug modulation of conduction over the slow pathway (see table below)

Patients Data

Age	Gender	Past History	Symptoms	ECG findings
24	Female	None	Asymptomatic	Long PR interval
36	Female	None	Asymptomatic	Long PR interval
74	Female	CAD S/P PCI	Angina Palpitations	Long PR interval & AVNRT
64	Male	CAD	Angina Palpitations	Irregular wide and narrow QRS tachycardia
67	Male	IDCMP ICD	9 ICD Shocks	2:1 ventricular responses

Discussion

DAVNP may present in different clinical forms. Non reentrant AVN tachycardia due to 2:1 responses via DAVNP, is an uncommon but an important form of irregular tachycardia. It may present as incessant form associated with tachycardia induced cardiomyopathy. It is usually misdiagnosed as atrial fibrillation. Treatment with antiarrhythmic agents may perpetuate tachycardia and convert it from paroxysmal to incessant form. Patients with prolonged PR interval are asymptomatic, and electrocardiographic finding could be interpreted as AV conduction delay. Pharmacologic agents or autonomic maneuvers may help in making the diagnosis.

Radiofrequency ablation of slow pathway terminates tachycardia and may restore LV function.

Echocardiographic Predictors of Response to Cardiac Resynchronization Therapy

Roy Beinart [1,2], Osnat Gurevitz [1,2], Eyal Nof [1,2], David Bar Lev [1,2], David Luria [1,2], Hava Granit [1], Micha Feinberg [1,2], Rafael Kuperstein [1,2], Stanislava Gilman [1], Shemy Carasso [3], Michael Eldar [1,2], Michael Glikson [1,2]

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Background: A significant number of patients currently selected for CRT by traditional clinical and electrocardiographic criteria do not respond to this therapy. We investigated the potential role of echocardiographic, Doppler and tissue Doppler imaging parameters as predictors of response to CRT.

Methods: 137 consecutive patients who were successfully implanted with CRT/CRTD system according to guidelines-based indications and had complete follow-up within the first year were included in the study. Response was defined by a score combined of NYHA class, MLHF quality-of-life score and 6-minute walk (6MW). Each component was classified as improved (+1), unchanged (0) or worsened (-1) and responders were defined as patients who had a combined score of ≥1. We compared the frequency of the various parameters among responders versus non-responders.

Results:

	Responders (n=78, 57%)	Non responders (n=59, 43%)	P value
LVEDV (average), ml	186±56	206±83	0.8
LVESV (average), ml	140±50	157±68	0.1
LVEF (average), %	23±7	23±6	0.9
RVFAC, %	37±12	40±11	0.2
LA area, ml	29±7	31±7	0.2
MR grade (1-4)	31%, 31%, 32%, 22%	45%, 30%, 19%, 6%	0.1
SPAP	45±13	44±13	0.8
Septal to lateral delay (>60 msec)	60%	59%	0.5
Yu standard deviation(>32)	85%	78%	0.2
Interventricular delay(>40 msec)	54%	56%	0.5

Conclusion: A positive response to CRT was observed in 57% of the patients. None of the measurements tested, including widely used parameters of mechanical dyssynchrony, was a significant predictor of response to CRT. Further studies are needed to define better predictors.

Clinical Predictors of Response to Cardiac Resynchronization Therapy

Roy Beinart [1,2], Osnat Gurevitz [1,2], Eyal Nof [1,2], Alon Barsheshet [1,2], David Bar Lev [1,2], David M Luria [1,2], Hava Granit [1], Shemy Carasso [3], Michael Eldar [1,2], Michael Glikson [1,2]

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Background: A significant number of patients currently selected for CRT by traditional clinical and electrocardiographic criteria do not respond to this therapy. We investigated the clinical predictors of response to CRT over the first year of follow up.

Methods: 137 consecutive patients who were successfully implanted with CRT/CRTD system for guideline-based indications and had complete follow-up within the first year were included in the study. Response was defined by a score combined of NYHA class, MLHF quality-of-life score and 6-minute walk (6MW). Each component was classified as improved (+1), unchanged (0) or worsened (-1) and responders were defined as patients who had a combined score of ≥1. We compared the frequency of the various predictors among responders vs. non-responders.

Results

	Responders (78, 57%)	Non responders (59, 43%)	P value
Age > 75	25 (32%)	27 (46%)	0.07
Male (%)	67 (83%)	46 (81%)	0.47
Ischemic Cardiomyopathy	57 (74%)	42 (74%)	0.56
NYHA I-II, III, IV	8%, 78%, 14%	17%, 78%. 5%	0.075
6MW	268±122	310±108	0.06
QOL	60±24	58±24	0.60
QRS mean ± SD	164±33	161±32	0.68
Chronic atrial fibrillation	5 (6%)	9 (15%)	0.08
Previous pacemaker implantation	37%	32%	0.34
RBBB	4 (7%)	5 (6%)	0.59

Conclusion: A positive response to CRT was observed in 57% of the patients, all of whom had been selected for CRT by usual criteria. Shorter 6MW distance, higher NYHA class and age < 75 were borderline predictors of response.

The Magnitude of Clinical and Echocardiographic Changes in Response to Cardiac Resynchronization Therapy

Roy Beinart [1,2], Osnat Gurevitz [1,2], Eyal Nof [1,2], David Bar Lev [1,2], David Luria [1,2], Sharona Bachar [1], Micha Feinberg [1,2], Rafael Kuperstein [1,2], Stanislava Gilman [1], Shemy Carasso [3], Michael Eldar [1,2], Michael Glikson [1,2]

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Background: Criteria for significant response of various parameters to CRT vary widely in the literature. We investigated the magnitude of response of clinical and echocardiographic parameters to CRT in our population.

Methods: 137 patients who had been successfully implanted with CRT/CRTD system and had complete follow-up within the first year were included in the study. We recorded clinical and echocardiographic parameters at baseline and up to 12 months post implantation and determined the percentage of responders of each parameter by commonly used criteria.

Results:

	Baseline	Follow-up	P value	Responders (%)*
NYHA (I-II, III, IV)	12%, 78%, 10%	41%, 56%, 3%	**0.0001**	38
Quality-of-life	59±24	41±28	**0.0001**	42
6-min walk	287±117	310±119	**0.02**	34
LVESV ml	147±59	131±60	**0.002**	30
LVEF %	23±7	27±8	**0.0001**	40
RVFAC, %	38±11	37±11	0.85	26
SPAP mmHg	45±13	42±12	**0.006**	18
MR grade (1-4)	30%,25%,22%, 23%	56%,31%,13%, 0%	**0.02**	26
Septal to lateral delay	34±53 (82/137>60msec)	33±56 (66/137>60msec)	0.65	20
Yu standard deviation	38±15 (112/137>32)	37±16 (94/137>32)	0.13	16
Interventricular delay	40±29 (75/137>40msec)	22±20 (50/137>40msec)	**0.0001**	33

* Response: NYHA≥1 class; QOL≥9 point; 6MW≥10%; LVESV≥15%; LVEF/RVFAC≥5%; SPAP≥10 mmHg; MR grade≥1. For dyssynchrony parameters response was defined as change from dyssynchrony to non-dyssynchrony.

Conclusion: Most of the clinical and echocardiographic parameters significantly improved following CRT implantation. However, these improvements were modest and met the commonly used definitions of response in only a minority. No improvement was observed in right ventricular function or in classical measures of intraventricular dyssynchrony in response to CRT.

Haptoglobin Genotype Determines Long-Term Survival and Affects Cardiac Remodeling after Myocardial Infarction in Diabetic Mice

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Introduction: Hp genotype predicts long term survival and congestive heart failure after myocardial infarction (MI) in individuals with diabetes mellitus. We have determined that Hp genotype determines the extent of myocardial necrosis after Ischemia-Reperfusion injury in diabetic mice. **We hypothesized** that Hp genotype would play a role in cardiac remodeling and left ventricular (LV) dysfunction after MI in diabetic mice.

Methods: The Hp 2 allele exists only in man. Wild type C57Bl/6 mice carry the Hp 1 allele. We genetically engineered a murine Hp 2 allele and targeted its insertion by homologous recombination to the murine Hp locus to create Hp 2 mice. MI was produced by occlusion of the left anterior descending artery in diabetic mice. MI size was determined with TTC. LV function and dimensions were assessed by echocardiography before the MI, 4 days and 30 days after the MI.

Results: MI size was similar in diabetic Hp 1 and Hp 2 mice 24 hours after MI. However, diabetic Hp 2 mice had a higher mortality rate than diabetic Hp 1 mice 30 days after the MI. Mortality rate was similar in sham operated mice. There was no significant difference in LV function between diabetic Hp 1 and Hp 2 mice at the different time points. LV end-diastolic area was significantly increased in Hp 2 mice compared to Hp 1 mice 30 days after MI.

Conclusion: In diabetic mice the Hp 2 genotype is associated with increased mortality and more severe cardiac remodeling 30 days after MI.

Myocardial Mechanics Explains the Time Course of Benefit in Septal Ethanol Ablation for Hypertrophic Obstructive Cardiomyopathy

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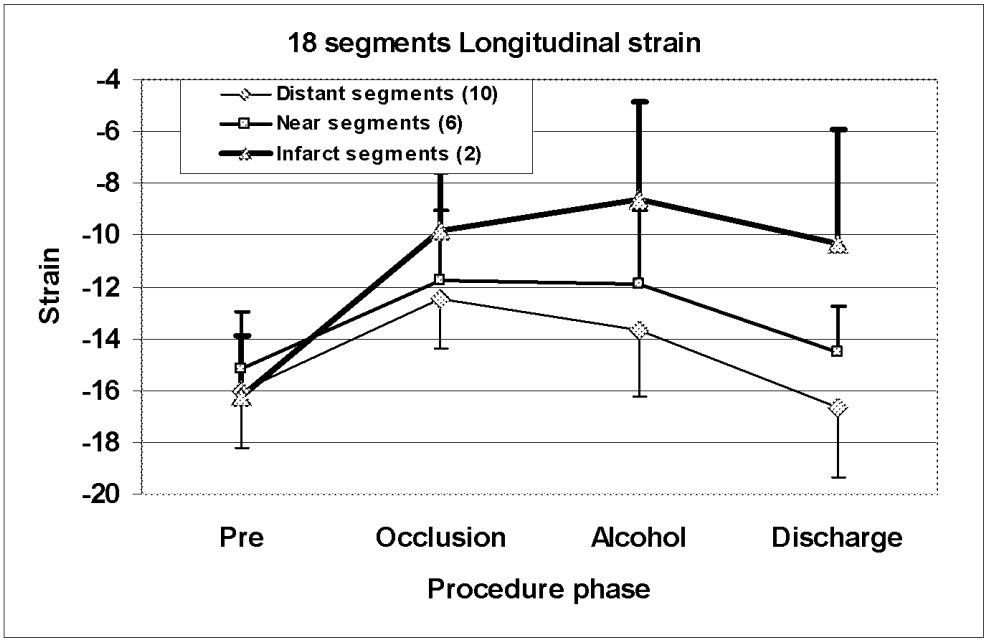
Background Septal ethanol ablation (SEA) alleviates left ventricular outflow (LVOT) obstruction in symptomatic patients with hypertrophic obstructive cardiomyopathy (HOCM) by controlled basal septal infarction. Relief of the gradient with SEA is complex and changes following ethanol injection: initially decreases during the procedure, increases pre-discharge then gradually decreases over the succeeding 6-12 months following the procedure. We hypothesized that the time course of LVOT gradient reduction during SEA is related to changes in regional and global myocardial mechanics.

Methods Baseline, immediately after septal occlusion, after alcohol injection and pre-discharge 2D echocardiograms were available in 21 patients with hypertrophic obstructive cardiomyopathy undergoing SEA. Echocardiograms were analyzed for mechanics using Velocity vector Imaging (VVI, Siemens) and correlated with hemodynamic data.

Results



LV outflow tract gradient decreased with septal balloon occlusion, further decreased post ethanol injection, and partially rebounded at discharge (5-6 days post procedure). During balloon occlusion longitudinal and circumferential strain significantly decreased in all analyzed segments, significantly improved with alcohol injection only at sites distant to infarction and normalized at all segments except infarcted ones at discharge. LV twist significantly improved with ethanol injection and remained high at discharge.

Conclusions Myocardial mechanics suggest that the decrease in LV outflow tract gradient during septal ethanol ablation coincides with global LV dysfunction despite only local ischemia during septal balloon occlusion. Global dysfunction is transient and the gradient rebounds when dysfunction is limited to the basal septum.

Segmental Wall Motion Abnormalities in Echocardiography of Patients with Acute Peri-Myocarditis.

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Background

Acute peri-myocarditis is a frequent inflammatory disease that may be associated with impaired cardiac function. Echocardiography is essential for acute peri-myocarditis diagnosis, assessment of the presence and amount of pericardial fluid and confirmation of concomitant heart disease. While, regional wall motion abnormalities have been observed a detailed description of these changes have not been described. In this study a detailed analysis of wall motion abnormalities are assessed.

Methods

Thirty consecutive patients 29(96.6%) males age 31±10, with first episode of acute peri-myocarditis were enrolled. Acute peri-myocarditis diagnosis was confirmed by the following: clinical history, ST elevation and/or PR depression on EKG, elevated inflammation markers and echocardiographic findings. Patients' echocardiography including pericardial fluid, detailed chambers measurements and wall motion abnormalities were measured on admission and after clinical recovery.

Results

Pericardial effusion was present in 20 (66.6%) of the patients with the majority of them having small to minimal effusion (90%) at the time of admission. After recovery, no effusion was noted in 17 (70.8%) of the patients, while the remaining had only minimal effusion. Sixteen (53.4%) patients had regional left ventricular dysfunction, affecting mainly the posterior, lateral and inferior wall while sparing the anterior and septal walls. Diffuse wall motion abnormalitis were observed in only 3 (10%) of patients.

Upon recovery significant improvement in Ejection Fraction (EF) (55.6±5.4 to 59±2.03 %(p=0.002)) and reduction in left ventricular end systolic dimensions (LVESD) were measured (3.1 ±0.51 to 2.85±0.4 mm (p=0.006)). No additional significant echocardiographic abnormalities were found.

Conclusions

Transient significant reduction in EF and increased LVESD were observed during AP.

The majority of the patients with decreased left ventricular function expressed poster-lateral and inferior wall anomalies. The reason for these predominantly regional wall motion abnormalities is not yet clear.

TNF- Alpha in Systolic Heart Failure Patients; Key for Inflammation and Myocardial Cell Destruction?

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Background: TNF- α participates in the inflammatory process of heart failure (HF). We examined serum TNF- α level in systolic HF patients, assessing its relation with other prognostic clinical and laboratory markers.

Methods: We tested sera samples of 67 pts (58 males, 9 females, age 65±13) for TNF- α level during a routine follow-up at our HF center. Mean LVF was 25±7% Based on median serum TNF- α level, pts were divided into two groups; detectable and non-detectable serum TNF- α level (group 1 and group-2, respectively). We evaluated both pts' groups for prognostic clinical markers including body mass index, NYHA class, six minutes walk test and QRS width. We also compared the two groups' sera for several prognostic laboratory markers including: matrix metaloprotease-9, Hs –C reactive protein, IL-10, Troponin I, NT-pro BNP, serum hemoglobin, serum total cholesterol level and renal function tests.

Results: There were no significant differences between the two groups in the clinical parameters. However, there were significant differences between the two groups in regarding to inflammatory cytokines, myocardial damage markers, serum hemoglobin and total cholesterol level as elaborated in **Table-1**:

Parameter	**Group-1 (Detectable TNF- α) m±sd/*inter quartile range**	**Group-2 (Un-detectable TNF- α) m±sd/*inter quartile range**	**P Value (*p<0.05)**
NT- pro BNP (pg/ml)	3666	1139	0.001*
Matrix metaloprotease-9	791 (2)	467 (2)	0.006*
IL-10	4.3 (30*)	0.0 (2*)	0.002*
Troponin I	0.02 (0.05*)	0.0 (0.00*)	0.001*
Hs-CRP (mg/dl)	0.6 (3)	0.8 (5)	0.6
Hemoglobin (gm/dl)	11.8 (1.6)	13 (1.7)	0.007*
Total cholesterol (mg/dl)	135 (32)	155 (36)	0.033*

Conclusions: Elevated serum levels of TNF- α in HF pts are associated with elevated markers of inflammation and myocardial cell destruction. This data reinforces the pivotal role of TNF- α in HF pathogenesis.

Everolimus as Maintenance Therapy in Heart Transplant Recipients: From Investigational Status to Everyday Practice, a Case Series.

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Purpose: Everolimus is a proliferation signal inhibitor recently approved for the use in heart transplantation (HTx). Besides its potent immunosuppression it has anti-cancer properties, it reduces the incidence of cardiac allograft vasculopathy and CMV infections and may improve renal function (RF). The purpose of the present study is to assess the role of everolimus in the common practice of HTx therapy.

Methods and Materials: The immunosuppressant protocol of the 75 pts transplanted at our center was assessed during their visits at the HTx clinic. Everolimus was introduced in 19 (25%) pts: 8 (42%) in the reduced CNI dose (CNIRD) and 11 (58%) in the CNI free (CNIF) protocols. The proposed trough levels of the CNI and everolimus were maintained.

Results: Results: Change to CNIRD was due to: worsening RF (n=5), mycophenolate mofetil (MMF) related symptoms (n=2), recurrent CMV (n=2), CNI induced neuropathy and delayed acute rejection (one each). Change to CNIF was due to: worsening RF (n=7), CNI related side effects (n=4), advanced cardiac allograft vasculopathy (n=4). Recurrent CMVand malignant melanoma (one each). Some had multiple reasons. Time from HTx to everolimus therapy in CNIRD and in CNIF was 57 and 75 months and mean follow up was 4 and 3.5 months respectively. The in-between therapies period was uneventful. Creatinine was reduced: from 2.02 to 1.8 and from 1.9 to 1.8 in pts with CNIRD and CNIF respectively. The MMF related symptoms and CNI induced side effects resolved. No recurrent CMV infection or acute rejections occurred in the relevant pts. CMV infection occurred in one CNIF pt so treated for reduced RF. One CNIF pt died due to septic shock and acute rejection. Acne like eruption occured in 2 pts treated with everolimus. Its severity was dose and time dependent.

Conclusions: Conclusions: Including everolimus in the maintenance therapy of HTx recipients has the potential of improving the tailored immunosuppressive therapy for each patient thus reducing side effects and maybe even improving prognosis.

V2-Receptors Antagonists Attenuate the Capability of Lungs to Clear Edema

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Active Na^+ transport and lung liquid clearance are regulated by apical sodium channel and basolateral Na,K-ATPase function in the alveolar epithelium. Vasopressin is a 9-amino acid neurohormone that is produced in the hypothalamus and stored in the hypophysis and plays an important role in the regulation of extracellular volume and its osmolarity. It has been shown to decrease lung liquid production in fetal lungs. Therefore, we aimed to study whether vasopressin has a role in alveolar fluid reabsorption in adult rat lungs in the isolated perfused rat lung model. Alveolar fluid reabsorption in control rats was 0.48±0.02 ml/h (all values are Mean ± SEM) and increased to 0.64±0.02 ml/h with vasopressin ($P<0.04$). The specific V_1 receptor antagonist, SR-49059, did not prevent the stimulatory effects of vasopressin, 0.64±0.02; whereas V_2 receptor antagonist, SR-1214638, inhibited the vasopressin effects, 0.31±0.04 ($P<0.001$). Treatment with amiloride (Na^+ channel blocker) inhibited the stimulatory effects of vasopressin, 0.23±0.02 ($P<0.001$). The albumin flux from the pulmonary circulation into the airspaces did not change significantly in the experimental groups indicating that lung permeability for large solutes was not increased. In conclusion, vasopressin increased alveolar reabsorption, apparently by regulating the active Na^+ transport in the alveolar epithelium. Conceivably, this effect is mediated via V_2 receptor receptors. Supported by Rappaport Institute for Research in the Medical Sciences and Chief Scientist Office; Ministry of Health, Israel.

The Utilization of ACE Inhibitors and ARB in Patients with Congestive Heart Failure: an Observational Study of Treatment Rates and Clinical Outcome

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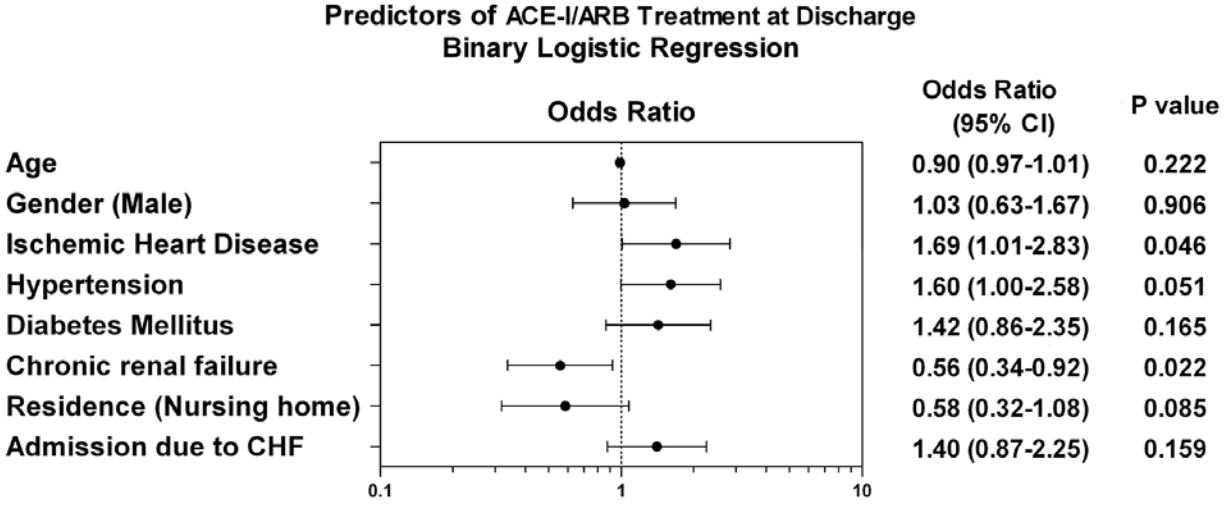
Background: Angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB) improve prognosis in congestive heart failure (CHF) and are the treatment of choice in these patients; despite this, the rates of ACE-I usage in heart failure patients remain low in clinical practice.

Objectives: To evaluate the rate of ACE-I/ARB treatment in hospitalized patients with CHF and analyze the causes of non-treatment.

Methods: We prospectively evaluated 362 consecutive patients hospitalized with CHF. Patients were evaluated for ACE-I/ARB usage at discharge and followed for a period of one year.

Results: On hospital discharge, 70% of the patients were prescribed ACE-I/ARB treatment. Only 69% of the patients received recommended target or sub-target dosages, proven to improve prognosis. This decreased to 63% and 59% at 6 months and 12 months of follow-up respectively, due to a shift from sub-target levels to low dosages. In the majority of patients that were not receiving optimal treatment (75%), there was no apparent justified reason for this. Common reasons for non-treatment at discharge were hyperkalemia and elevation in serum creatinine while hypotension and a cough were more prominent at follow-up. Clinical parameters associated with increased treatment rates were ischemic heart disease, hypertension and the absence of chronic renal failure. Patients receiving treatment had lower hospitalization and mortality rates.

Conclusions: ACE-I/ARB treatment is still underutilized in patients discharged from hospital with a diagnosis of CHF. Increasing the awareness of the importance of these drugs may increase the number of patients treated.



Surface Thoracic Impedance Monitor May Enable the Prediction and Prevention of de Novo Acute Heart Failure and the Decompensation of Chronic Heart Failure

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Background – Treating patients with Acute Heart Failure (AHF) is a challenge. Presently, there is no reliable method to predict AHF. The ability to predict the development of AHF can allow medical staff to initiate early treatment, which may curtail or prevent further deterioration.

Methods and Results – We used a new Surface Thoracic Impedance Monitor (STIM) in order to monitor lung impedance (LI) in patients at risk to develop AHF. We evaluated the sensitivity of measurements and their effectiveness to trigger early administration of therapy with the intention to prevent evolution of AHF. We observed LI readings in 542 patients hospitalized for acute myocardial infarction (AMI) and in 63 out hospital clinic patients. 389 patients did not develop AHF. Their individual LI decrease was 5.6% (CI 0.8 to -12%, p=0.7). 114 patients developed clinically overt AHF, which was supported by roentgenological evidence. The LI decrease was 35% (CI- 14.2 to -50%, $p < 0.001$) compared to baseline. Treatment for AHF development was initiated in 39 patients at the time when LI decrease was > 13%. As the result, AHF did not occur in 85% of patients ($\chi^2 < 0.01$). 75 episodes of decompensated AHF were observed in 63 hospital outpatients. Based on the accumulated evidence, LI decreased in all patients by more than 12% at 15.3±10.6 days prior to clinical deterioration.

Conclusions – STIM monitoring in patients at risk to develop AHF can reliably predict further deterioration. We have demonstrated that timely prediction may prompt medical professionals to administer early treatment that could successfully prevent the development of AHF.

Aldosterone Synthase Polymorphism is Associated with Atrial Fibrillation in Systolic Heart Failure Patients

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Background: Atrial fibrillation (AF) is common in heart failure (HF) .The activation of the renin-angiotensin system has an important role in AF pathogenesis. Aldosterone synthase is a key enzyme in the final step of aldosterone production. The *CYP11B2* T-344T polymorphism in this enzyme is associated with increased aldosterone activity. Accordingly, we examined the impact of this polymorphism on the prevalence of AF in systolic HF patients.

Methods: We analyzed the association between *CYP11B2* T-344T polymorphism in aldosterone synthase and the presence of AF in 178 {aged 65±13 years, 145 (81%) males} consecutive systolic HF patients who were followed at our HF center. Mean LVEF was 24±7% and 97 (55%) patients were in NYHA functional class 3 or 4.

Results: Atrial fibrillation was present in 57 (32%) patients. The -344 CC genotype was a strong independent marker for AF. Almost half (45%) of the patients with this genotype subtype had AF compared to only about a quarter (27%) of patients with out this genotype (p=0.02). In a multivariate stepwise logistic regression model, the *CYP11B2* CC genotype was the most powerful independent predictor of AF after age and left atrium size (Table-1).

Conclusion: Systolic HF patients with the CYP11B2 promoter T-344 C polymorphism have significantly higher prevalence of AF. This association may explain in-part the direct anti-aldosterone treatments success in systolic heart failure and in atrial fibrillation prevention.

Table-1:

Variable	OR	CI	P
Lt. atrium size	5.1	3.23-8.05	<0.0001
Age	1.1	1.03-1.07	<0.01
CYP11B2 -344 CC genotype	2.6	1.68-3.98	0.02

A Stable Minipig Model for Heart Failure

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Background: A number of chronic models of heart failure have been developed. Each of these models has specific limitations and in particular, is difficult, timely and expensive to create. We established a stable model based upon multiple interventions to impair compensatory mechanisms in a minipig. We sought to demonstrate that the acute heart failure model could be additionally used as a stable and recurrent chronic model.

Methods: Twelve minipigs were used in this study. All animals underwent alternate selective LAD and Cx injections of microsphere (90 μm). Fluid loading was performed with aliquots of 500cc of warmed NaCl. Afterload elevation was achieved with partial or complete descending aorta balloon occlusion. Hemodynamic parameters measured included RA, LA, aortic and LV pressures. The endpoints were stable elevation of maximum LA/LVED with maintained systemic blood pressure for a period of two hours. In selected cases TTE was performed to assess LV function. For the chronic group the animals were restudied at 4 weeks after the microsphere injection.

Results: Complete hemodynamic studies were performed acutely in 7 animals and in 4 chronic animals. A single animal was excluded due to an intercurrent illness. In the acute studies the time to stressing with afterload and fluid aliquots was longer and associated with larger amounts of preliminary IV fluid administration. LA and RA pressures (mmHg) are shown in the table.

	Baseline		Post beads		Post Volume		After load	
	RA	LA	RA	LA	RA	LA	RA	LA
Acute	13±4.7	17±4.4	15±6.0	22±7.4	19±6.7	32±8.0	21±6.2	38±9.3
Chronic			9±4.0	14±4.4	9.9±4.7	15±3.2	11±4.6	22±2.3

$P<0.05$ acute to chronic (non parametric)

Preliminary echocardiography was performed in 3 chronic animals prior to stressing with fluids and afterload. LV function normal to preserved in all cases.

Conclusions: The development of a stable and reproducible heart failure minipig model was achieved using a combination of selective coronary microshpere embolization, volume loading and intermittent afterload elevation apparently without impairing LV function. The model was effective both acutely and recurrently, with the chronic model providing less extreme LA pressure overload.

Clinical Predictors of Abnormal Tl-201 SPECT Myocardial Perfusion Imaging in Elderly Patients Without a Previous History of CAD

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Background: Myocardial perfusion imaging (MPI) has bee shown to be of value for the diagnosis of coronary artery disease (CAD) in patients with an intermediate pretest probability of CAD. Although elderly patients are not included in this category, MPI is routinely used in this group. The aim of this study was to identify the clinical predictors of abnormal myocardial perfusion imaging (AMPI) in this group of pts. without a previous history of CAD.

Methods: The study population included 339 pts, $\geq$ 80 years old (mean age= 83.3$\pm$ 2.7) who were referred to stress Tl-201 SPECT MPI for the diagnosis of CAD.

Results: An AMPI was present in 154 pts (45.4%). The incidence of AMPI was significantly higher in males in comparison with females (57% vs 37%, $p< 0.0003$) and in diabetics (57% vs 43%, $p= 0.038$). Anginal syndrome and pulmonary edema were more frequently in those with AMPI than with a normal MPI (49% vs 30%, $p= 0.0005$) and (6% vs 1%, $p= 0.0072$), respectively. In contrast to non-anginal chest pain more frequently reported with normal MPI (30% vs 19%, $p=0.016$). AMPI was present in 53% of pts with an abnormal resting ECG in contrast to 36% of with a normal ECG ($p= 0.0017$). Based on multivariate analysis the best predictive model of an AMPI (Chi-Square 44.8, $p< 0.0001$) included the following independent variables: male gender, Diabetes, anginal syndrome, pulmonary edema and resting ECG.

Conclusion: In very elderly pts without a previous history of CAD, male gender, Diabetes, anginal syndrome, pulmonary edema and resting ECG are clinical predictors of an abnormal MPI.

Pulse Pressure – A Readily Available Independent Predictor of Extent of Coronary Artery Atheroma on 64 Slice Coronary CT Angiography in Asymptomatic Patients with Type 2 Diabetes Mellitus

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Background and aims: Identification of high risk sub-groups for early initiation of preventive medical therapy requires widespread population screening using simple, inexpensive tests. High pulse pressure (PP) has been shown to predict adverse coronary events. We examined the predictive value of PP for the presence of coronary plaque on 64 slice coronary CT angiography (CTA) in asymptomatic pts with type 2 diabetes mellitus (DM) and no history of CAD enrolled in an ongoing prospective outcomes study.
Methods: Resting systolic and diastolic blood pressure were measured in both arms, mean pulse pressure calculated and CTA performed in 426 pts (63.5±5.3 yrs, 58% women) with DM (mean duration 10.3±7.8yrs) and no history of CAD.
Results: Risk factors included current or past smoking history in 44% and hypertension in 67%. Baseline therapy included insulin in 35%, ACE inhibitor or angiotensin receptor blocker in 67%, calcium channel blocker in 23%, beta blocker in 28% and statins in 70%. Prevalence of single vessel and multivessel plaque and of coronary stenosis in relaton to quartiles of pulse pressure are shown in table. Pulse pressure remained a predictor of multivessel coronary plaque after normalization for mean or systolic blood pressure. In a multivariate model including UKPDS risk score (age, gender, duration of diabetes mellitus, blood pressure, smoking history, cholesterol/HDL-C ratio and HBA1C), pulse pressure was an independent correlate of the presence of multivessel coronary plaque (OR 1.17/10mmHg increase in PP, 95% CI 1.01-1.32 , p=0.036).

Prevalence of coronary plaque in relation to pulse pressure

Pulse pressure Quartiles (mmHg)	Any plaque N (%) pts	Multivessel plaque N (%) pts	Stenosis (>50%) N (%) pts	Multivessel stenosis N (%)
1 (<49)	73 (69)	44 (42)	19 (18)	6 (6)
2 (49-58)	75(70)	55 (51)	28 (26)	8 (8)
3 (59-66)	82 (81)	62 (61)	23 (23)	5 (5)
4 (>66)	93 (88)	71 (67)	27 (26)	8 (8)
p-value	0.002	0.001	ns	ns

Conclusions: In asymptomatic pts with DM and no history of CAD undergoing 64 slice CTA: 1. Pulse pressure predicted the presence and extent of coronary plaque 2. This correlation was independent of mean or systolic blood pressure and independent of the UKPDS risk score. 3. Predictive value of pulse pressure should be further investigated as a readily available screening test for coronary disease in diabetic patients.

Characteristics of Ischemia and Prediction of Mortality in 1,488 Elderly Women

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The rate of cardiac vascular death is (CD) higher in elderly women than men, although severe CAD is more common in men. Hence it is not really obvious whether detection of severity of ischemia is correlated with CD in women.

Methods: During 2005-6 we recruited 1488 consecutive elderly women aged 75 and more (mean 79±3.6 ranges from 75 to 94) who underwent stress MPI. The women were followed for 29±18 months to determine the predictors of CD.

Results: There were 160 (11%) total deaths, 114 (8%) of cardiac origin, with annual rate of 3.3%. Reasons for referral were cardiac related symptoms in 77%, history of CAD in 36%, post MI 16%, and post CABG 14% and PCI procedures 24%. Risk factors: diabetes 26%, hypertension 75%, and hyperlipidemia 53%. The majority of women (83%) underwent stress test with dipyridamole and myocardial ischemia was detected in 30%, of them 12% was of moderate to severe.

The univariate predictors of CD were: age, abnormal rest ECG, diabetes, ST depression during stress test, LV enlargement (transient), increased lung uptake, abnormal MPI, ischemia and degree of ischemia. However, the major independent predictors of CD except of age were: LV dilatation (OR 1.7, 95% CI 1.2-2.4, p= 0.002) and increased lung uptake (OR 2.0, 95% CI 1.1-3.7).

Conclusion: The majority of the elderly women referred for MPI cannot perform exercise, and need to be assessed by pharmacological test. The predictors for CD in elderly women are more related to signs of global ischemia rather than regional ischemia.

The Predictive Value of Resting Electrocardiogram in Elderly Patients Without a Previous History of CAD for the Diagnosis of CAD by Stress Thallium Myocardial Perfusion Imaging

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Background: Resting electrocardiogram (ECG) has a limited value for the diagnosis of coronary artery disease (CAD. Therefore stress-testing ECG is indicated. Since elderly patients are not able to perform an exercise stress test, are frequently referred to myocardial perfusion imaging (MPI). The aim of the present study was to evaluate the predictive value of resting ECG for the diagnosis of CAD by MPI in elderly pts. without a previous history of CAD.

Methods: The study population included 339 pts, $\geq$ 80 years old consecutive who were referred to stress-redistribution Tl-201 SPECT for the diagnosis of CAD.

Based on the resting EGG at time of the MPI study, patients were classified in two groups for comparison.

Results: Group A included 182 pts (53.7%) with an abnormal ECG and group B 157 pts (46.3%) with a normal ECG. Group A pts compared with Group B were significantly older (82.9$\pm$ 2.4vs 83.6$\pm$ 2.6 years old, $p< 0.015$). More frequently males had an abnormal ECG in comparison with females (70.7% vs 41.7 %, $p< 0.0001$). No significant differences were observed between the groups regarding the prevalence of risk factors and the presence of anginal pain. By visual analysis an abnormal MPI was present in 154 pts (45%). A significant different MPI distribution was observed between the groups, the incidence of abnormal MPI was significant higher in Group A than in B in 97(53.3%) vs 57(36.3%), $p= 0.0017$, in addition a normal MPI was present in 100 (63.7%) group B pts.

Conclusions: In elderly pts without a previous history of CAD, resting ECG has a significant predictive value for the diagnosis of CAD by Thallium MPI.

In Asymptomatic Type 2 Diabetics in Israel do Differences Exist in Effort Tolerance and Prevalence of Coronary Atheroma on 64 Slice Coronary CT Angiography between Patients Living in Town and Country?

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Background: Residual life expectancy of kibbutz members reaching the age of 50 has been shown to exceed that of Israeli town dwellers by >2 years. The study examined whether pts with type 2 diabetes mellitus (DM) living in a rural setting had better exercise tolerance and less coronary artery atheroma than their urban counterparts.

Methods: The study examined asymptomatic individuals with DM and no history of coronary artery disease, 55-74 yrs participating in a prospective ongoing outcomes study. Pts underwent symptom limited treadmill exercise stress testing and 64 slice cardiac CT angiography preceded by calcium scoring.

Results: Pts in rural areas had less hypertension (53% vs 71%, p=0.002), a shorter history of DM (7.4 vs 10.7 yrs, p<0.001) less were treated with insulin (11.5% vs 31.3%, p=0.001) and HBA1C was lower (6.9% vs 7.7%). Maximal exercise achieved by women in the rural setting was greater than their urban counterparts (8.4 vs 7.3 Mets, p=0.005) and a similar tendency was found in men (10.9 vs 10.1Mets, p=0.08). Independent predictors of lower effort tolerance were older age (p=0.001), female gender (p=0.001), longer history of DM (p=0.014) and urban residence (p=0.07). Urban men had higher coronary calcium scores than rural men (p=0.025) but this was not the case among women. The extent of coronary atheroma was similar in both groups. Independent predictors of multivessel atheroma were older age, male gender and duration of DM.

Conclusions: 1. Multiple differences were found between baseline characteristics of rural and urban asymptomatic pts with type 2 DM. 2. Amongst women rural residence was an independent predictor of greater exercise capacity. 3. A similar extent of coronary atheroma was found in both cohorts although the calcified component of atheroma appeared to be greater in urban than rural men.

Israel Multicenter Perfusion Imaging Survey (IMPIS) 2007: Final Overall Results

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Background: Myocardial perfusion imaging (MPI) plays an important role in the non-invasive diagnosis of coronary artery disease (CAD) and pts risk stratification. Although quidelines recommendations and regulations have been published for the use of this diagnostic modality, significant differences through the world have been reported. The main purpose of this study was to prospectively collect data regarding the practice of nuclear cardiology units in 6 public hospitals in Israel.**Methods:** The study population included all consecutive pts who were referred for a MPI, to each of the hospitals during 1 calendar month (02/07). Overall data and percentage centers range data are presented.

Results: Within this period 1325 pts underwent a MPI study, 18% (3-41%) of them were hospitalized. The overall clinical characteristics of the pts were: mean age 65.5± 12 years old, 59% were males, with known CAD in 45%, angina syndrome was present in 51%, shortness of breath in 17% and 26% were asymptomatic. The stress protocols used were: Dipyridamole in 56% (42-59%), exercise in 41% (34-58%) and dobutamine in 1%. Gated acquisition was done in 45%(0-69%). MIBI was used in 41%(0-85%) and Thallium in 59%(15-100%). Normal MPI was observed in 48% (27-56%).

Conclusion: The overall findings of this multicenter survey reflect the wide heterogeneity in clinical practice. The different stress protocols used and the MPI results may reflect the different referral populations to each center.

Israel Multicenter Perfusion Imaging Survey (IMPIS) 2007 Comparison between Hospitalized and Ambulatory Patients

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Myocardial Perfusion Imaging (MPI) is widely used in the evaluation of coronary artery disease (CAD). Until now, there has been no multicenter data concerning the routine practice of nuclear cardiology in Israel.

Methods: A multicenter survey was performed during 1 month (February 2007). We prospectively reviewed all consecutive patients (pts) who had undergone MPI in the departments of nuclear cardiology in 6 public medical centers (Asaf Harofe, Beilinson, Ichillow, Hasharon, Kaplan and Soroka).

Results: Of 1316 MPI, 240 (18.3%) were performed in hospitalized pts. We found no differences between ambulatory and hospitalized pts in demographics or risk factors, except for a higher proportion of smokers (25% vs 16%, p=0.001) in hospitalized pts. Also the hospitalized pts were more likely to have a history of myocardial infarction (34% vs 24%, p=0.002) or PCI (33% vs 26%, p=0.003) and were less proportion of asymptomatic pts before the MPI (9% vs 22%, p<0.001), than ambulatory pts. Despite these differences, we found a similar percentage of pts with normal (49% vs 48%) and ischemic (37% vs 40%) MPI, but more hospitalized pts had fixed defects (30% vs 23%, p=0.03) in the MPI.

Conclusions: In this first multicenter registry of MPI in Israel, 18.3% of the studies were performed in hospitalized pts. They had more frequent history of CAD (myocardial infarction and PCI), and consequently more fixed defects in MPI. Nonetheless, the incidence of normal or ischemic MPI between the groups was similar.

Israel Myocardial Perfusion Imaging Survey(IMPIS) 2007. Comparison between Patients with Known and Unknown Ischemic Heart Disease

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There is little information on patients referred for nuclear cardiology studies in Israel. On behalf of the Israel Nuclear Cardiology Working Group we performed in February 2007 a survey of all myocardial perfusion imaging studies (MPI) performed during a period of one month in six major Israeli hospitals. We report about the differences between patients (pts) referred with known ischemic heart disease (IHD) and patients referred to evaluate potential IHD.

During the survey period of one month 1325 patients were studied in the participating hospitals. IHD was known in 569 pts (43%) and 695 pts (57%) were referred due to suspected IHD.

	Known IHD	**Unknown IHD**
Mean age	67 years	64 years
At least one risk factor	98%	90%
Diabetes Mellitus	40%	28%
Hypertension	76%	65%
Hyperlipidemia	84%	60%
Smokers	19%	16%
Hospitalized pts	18%	15%
Main reason for referral	Assessment of ischemia -72%	Roll out IHD - 81%
Exercise test	37%	45%
Pharmacological stress	63%	55%
Ischemic ECG changes	17%	14%
Abnormal MPI	69%	32%
Ischemic myocardium	53%	28%

Our survey shows that risk factors for IHD are relatively frequent in pts suspected of IHD, who are referred for MPI. The ability of MPI to detect significant ischemia in those pts was high. The results may indicate an under utilization of MPI in searching for significant IHD in pts with multiple risk factors for IHD.

Fast Triage of Patients with Acute Pulmonary Embolism by Grading the Reflux of Contrast to the Inferior Vena Cava on CT Pulmonary Angiography

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Purpose: To investigate whether fast grading of contrast reflux to the inferior vena cava (IVC) on CT pulmonary angiography (CTPA) could predict short term mortality in patients with acute pulmonary embolism (PE).

Methods: CTPA studies of 135 patients with PE and 123 patients without PE were assessed for: retrograde reflux of contrast to the IVC using visual grading of 1-6 on axial images, pulmonary obstruction index, diameters of pulmonary artery, right and left ventricles. Statistical analysis evaluated these parameters in relation to mortality.

Results: Moderate and severe degrees of reflux of contrast to the IVC (≥4) were found in 25(18.5%) with positive CT and 12(9.8%) individual with a negative CT (P=0.045). Kaplan-Meier survival curves in 30 days, demonstrated for the group of patients with acute PE, a significant reduction in survival only in individuals with moderate or severe reflux of contrast to the IVC (≥4) compared to lower grades (P = 0.006). On the contrary, there was no significant reduction in survival in patients with a severe reflux (≥4) and no PE on CT (P= 0.65). Pulmonary obstruction index, diameter of right and left ventricles, their ratio, and pulmonary artery diameter, did not show a statistically significant correlation with survival in patients with and without PE.

Conclusions: Moderate or severe degrees of reflux of contrast to the IVC during CTPA is a predictor of early mortality in patients with acute PE. Fast grading of reflux of contrast from the original axial CTPA images may be helpful for immediate patients' triage.

High Adenine Diet Induces a Reversible Inflammatory Process of Aortic Valve Calcification in Rats

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Objectives: Developing an animal model and exploring the pathophysiology of aortic valve calcification (AVC).

Background: AVC which is a major hallmark of aortic stenosis can result from renal failure (RF). A diet containing high levels of Adenine has been shown to induce RF and therefore might induce AVC.

Methods: 23 rats fed with adenine diet for 7 weeks followed by a normal diet for two additional weeks (diet group), were compared with 10 control rats. Renal function, PTH levels, echocardiography and multislice computed tomography (MSCT) were performed. Eight diet group's rats were further followed in order to asses the reversibility of AVC.

Results: After 4 weeks, all diet group rats developed RF with secondary hyperparathyroidism (PTH 2330 ± 40 pg/mL versus 281±53 pg/ml, in controls, $p<0.01$). At 9 weeks, RF resolved with improvement in hyperparathyroidism state. Echocardiography demonstrated valve calcifications in diet group rats, calcium score by MSCT was significantly higher in the diet group as compared with the controls (145 ± 30 versus 0; $p<0.01$). Von-Kossa stain in diet group valves revealed calcium deposits with positive staining for osteopontin (osteoblast marker), and CD68 (macrophage). PCR revealed over expression of osteoblast's specific genes and NFκB superfamily members. Serial MSCT scans revealed significant reduction in AVC after diet cessation.

Conclusions: We developed a unique, diet-induced model for AVC that can easily be quantifiable using MSCT. We showed that the process is reversible, involves macrophage accumulation and osteoblast transformation. This model may serve as an important tool in the study of AVC.

Impact of Revascularization on Outcomes in Patients with Non-ST-Elevation Acute Coronary Syndrome and Congestive Heart Failure. The Global Registry of Acute Coronary Events (GRACE)

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Background: Congestive heart failure (CHF) is a common and severe complication of Non-ST-Elevation (NSTE) acute coronary syndromes (ACS). It is associated with a major increase in short and long term mortality. Yet, patients with ACS and CHF are less likely to undergo coronary angiography or revascularization than ACS patients without CHF.
Aim: The aim of this study is to analyze the impact of early revascularization on outcomes.
Methods and Results: Of the 29 844 patients with NSTE-ACS enrolled in the Global Registry of Acute Coronary Events between April 1999 and June 2007, 4953 had CHF at presentation. One-fifth of the patients with CHF underwent in-hospital revascularization vs 35% in those without (P<0.001). Revascularized patients with CHF were younger (72 vs 76 years) and more likely to be male (65% vs 55%) than nonrevascularized CHF patients. They also had lower heart rate (81 vs 88 beats/min), higher ejection fraction (49% vs 40%), and less frequent history of stroke (11% vs 16%) or CHF (24% vs 42%) (all P<0.001). Patients who underwent revascularization were more likely to receive evidence-based cardiac medications during hospitalization (aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, thienopyridines, statins, and glycoprotein IIb/IIIa inhibitors) compared to patients who did not undergo revascularization. Patients with CHF had higher mortality rates in hospital (8.9% vs 0.9%) and from discharge to 6 months (9.6% vs 2.9%). After adjustment in a Cox model, patients who were revascularized had a lower risk of post-discharge to 6-month mortality (hazard ratio 0.64; 95% confidence interval 0.45–0.93).
Conclusions: Data from this large, multinational, contemporary observational study suggest that in patients with NSTE-ACS complicated by CHF, use of revascularization during the index hospitalization is associated with a significantly improved survival 6 months after discharge. These observations support current guidelines, which recommend early revascularization in high-risk NSTE-ACS patients and suggest substantial underuse of revascularization in this high-risk population.

The Obesity Paradox in Acute Coronary Syndrome Patients in Israel

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Background: While obesity is a coronary disease risk factor, its effect on acute coronary syndrome outcome (ACS) is inconsistent.

Methods: To explore the impact of body mass index (BMI) on short (30-day) and long (1-year) term clinical oucome, we retrospectively analyzed data of 5,751 patients [4,400 (77%) males, 2,754 (48%) with and 2,994 (52%) without ST-segment elevation ACS] from the Acute Coronary Syndrome Israel Survey (ACSIS), comprising data from ACS patients hospitalized in 2002, 2004 and 2006 during 2 months period in all coronary care units in Israel.

Results: Patients were divided into National Institutes of Health BMI-based 4 categories (Table). Mean BMI increased significantly during 2002, 2004 and 2006 (27.0±4.0, 27.2±4.3 and 27.7±4.5 kg/m^2, p<0.0001; respectively). Time from chest pain onset to hospitalization and invasive procedure, Killip class on admission, left ventricular ejection fraction, creatinine clearance and in-hospital therapy were the same in all 4 groups.

	Underweight BMI<18.5 (n=43)	**Normal 18.5-24.9 (n=1709)**	**Overweight 25.0-29.9 (n=2700)**	**Obese BMI≥30 (n=1299)**
Age (yrs)	69.9±17.7	65.3±13.7	63.3±12.6*	61.4±12.4*
30-d mortality	9.3%	5.6%	3.3%	4.7%
OR† (95% C.I.)	0.91 (0.24-2.69)	1.0	0.50 (0.38-0.67)	0.88 (0.62-1.22)
1-year mortality	20.7%	12.3%	8.2%	9.4%
OR† (95% C.I.)	1.0 (0.34-2.96)	1.0	0.63 (0.49-0.80)	0.78 (0.57-1.06)

Values are expressed as mean±SD; *p for trend<0.0001; †OR=odds ratio adjusted for age, sex, hypertension, past angina, past myocardial infarction, smoking, hyperlipidemia, renal failure, stroke, peripheral vascular disease, > Killip 2, previous procedures (coronary artery bypass grafting operation, percutaneous coronary intervention), ST-segment elevation; BMI= kg/m^2.

Conclusion: Overweight and obese BMI-based categories were associated with younger age and better survival than normal and underweight ACS patients. Our obserevation of a U-shaped relationship between increaseing BMI and mortality in ACS patients warrants careful propsective evaluation.

Bypassing the Emergency Room to Reduce Door-to-Balloon Time in Primary PCI Improves Clinical Outcome – Experience from the Acute Coronary Syndrome Israeli Survey (ACSIS)

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Background – Primary PCI (PPCI) is the reperfusion strategy of choice for patients (pts) with ST Elevation Myocardial Infarction (STEMI). *Door-to-balloon time* is a strong predictor of myocardial salvage and clinical outcome. Only 35% of STEMI pts meet the recommended goal of the 2004 ACC/AHA Guidelines of ≤ 90 minutes. The objective of this work is to assess the strategy of direct referral of STEMI pts to the CCU for PPCI as observed from the national ACSIS 2004 and 2006.

Methods and Results – Data were collected from the ACSIS 2004&2006. We examined the effect of admission pattern [*Emergency room(ER), Direct to CCU (CCU)*]; on the time line and clinical outcome in the STEMI pts who underwent PPCI. Out of 4171 pts with ACS, a total of 1924 (46%) presented with STEMI, of them *793* (41%) *underwent PPCI* [583 pts (73.5%) arrived to *ER*, 193 pts (24.3%) arrived directly to CCU, (for 17 pts (2.1%) full data were missing)].

		ER	CCU	Pvalue
Door-to-balloon time (median, min)		79	45	0.018
Adherence to Guidelines (≤90 min)		59.2 %	88.8 %	<0.0001
Mortality (%)	**30 days**	5.3	6.2	NS
	1 year	7.3	6.1	NS
30-d MACE (%)		30	22.3	<0.038

Conclusions –

In the ACSIS; direct referral to the CCU for Primary PCI, by bypassing the ER, significantly reduces the Door-to-Balloon time, increases the rate of adherence to guidelines, and improves the clinical outcome. A national system for bypassing the ER in STEMI patients should be encouraged.

Optimal Timing of Percutaneous Coronary Intervention after Successful Thrombolysis – Analysis of Data from ACSIS 2002-2006

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Introduction: Clinical guidelines recommend routine angiography and percutaneous coronary intervention (PCI) after successful thrombolysis. However, the optimal timing of PCI has not been determined yet.

Methods: We analyzed data of the Acute Coronary Syndrome Israeli Survey (ACSIS) from 2002 to 2006. We excluded patients with failed thrombolysis. Patients with successful thrombolysis were divided to 3 groups: Group A - patients (age 61.6±13.6) who did not undergo PCI (n=150), of whom 30.7% did undergo angiography; Group B (age 57.8±12.4) – underwent PCI within 48 hours from admission (n=34); Group C (age 58.3±10.6) – underwent PCI >48 hours after admission. Major adverse cardiac events (MACE) were defined as death and re-infarction at 7 & 30 days.

Results: Patient in group A were significantly older (p=0.01). Most patients (86.5%) underwent PCI >48 hours after admission. MACE at 30 days occurred in 17.4% in group C, lower than groups B (35.3%) and A (26.7%) (p=0.019). Mortality at 7 days was higher in group A versus groups B & C, respectively (4.7%, 2.9%, 0.9%, p=0.006). Post infarction angina occurred more in group B than A & C, respectively (11.8%, 2%, 7.3%, p=0.027). Killip II on admission was highest in group A vs. groups B & C, respectively (12.7%, 8.8%, 6.0%, p=0.001).

Conclusions: Patients who did not undergo PCI after successful thrombolysis had worse outcome at 7 & 30 days. Patients who underwent PCI >48 hours after admission had the best outcome. Heart failure and post infarction angina were significantly more frequent in those who underwent early PCI.

Comparison of Recurrent to First Acute Myocardial Infarction Patients in Israel in 1998-2006

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Rrecurrent acute myocardial infarction (AMI) patients, who represent 14 to 30% of patients hospitalized for AMI, are at increased risk for complications and death following their acute coronary event

Objective: We compared the outcome of recurrent to first acute ST-elevation myocardial infarction (AMI) patients hospitalized in coronary care units in 1998-2006.

Methods: We performed biennial prospective nationwide AMI/ACS surveys, collecting data prospectively during January-February 1998, February-March 2000, February-March 2002, February-March 2004 and March-April 2006 from all patients hospitalized in all 25 operating CCUs in Israel

Results: Our cohort comprises of 4,511 STEMI patients, 3,651 First and 860 Recurrent MI. In-hospital complications occurred significantly less frequently in first AMI patients.

	1998	2000	2002	2004	2006	P trend
First MI	**N=662**	**N=758**	**N=759**	**N=759**	**N=713**	
Age (yrs)	63	62	62	62	61	0.04
Primary PCI	8	10	28	44	48	0.0001
Thrombolysis	54	50	35	22	15	0.0001
7-day mortality	5.1	7.7	4.4	4.3	3.2	0.005
30-day mortality	8.8	10.8	6.3	6.7	4.8	0.0001
Recurrent MI	**N=148**	**N=190**	**N=188**	**N=173**	**N=161**	
Age	66	66	65	65	64	0.58
Primary PCI	5	17	18	40	42	0.0001
Thrombolysis	49	44	30	19	14	0.0001
7-day mortality	8.8	7.4	8.0	5.8	7.5	0.53
30-day mortality	11.5	13.7	10.6	9.2	9.3	0.23

Conclusions: In spite of high rate of primary PCI in both first and recurrent STEMI patients, while mortality and hospital complication rates significantly declined in First MI patients, they remain high in Recurrent MI patients. Improved therapeutic approach is needed in these high risk cohort of patients.

Trends in Management and Outcome of Elderly Patients with STEMI in Israel: Data from ACSIS 2000-2006

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Background: The management and outcome of AMI pts have recently undergone major changes, reflecting the implementation of new treatment guidelines.

Aim: To evaluate trends in management and their impact on early mortality of elderly (≥75yrs) pts with STEMI admitted to all 26 operating CCUs in Israel in 2000-2006.

Methods: The data were derived from biennial 2-monthly prospective nationwide ACS surveys (ACSIS 2000-2006).

Results: The age (81±5 y), prevalence of women (41-49%), risk factors, and Killip-class ≥II on admission (33-38%), were comparable throughout the study period.

	2000	2002	2004	2006
	(N=224)	(N=208)	(N=208)	(N=162)
Rx in-hospital♥:	%	%	%	%
Aspirin	93	95	98	99
Clopidogrel	9	37	53	73
b-blockers	59	65	77	70
ACE-I/ARB	63	67	74	77
Statins	17	40	61	88
*SCORE(4)	8	21	43	53
Primary reperfusion	38	45	46	54
TLx/primary PCI	80/20	56/44	38/62	18/78
Angio	34	48	64	91
PCI in hospital	21	38	50	60
Stent	10	27	43	56
30-day mortality	26.8	18.3	17.3	16.0
Covariate adjusted OR (95% CI)†	1.0	0.45 (0.26-0.75)	0.42 (0.25-0.70)	0.37 (0.20-0.67)

♥ *p for trend <0.001 for all comparisons.*

*SCORE(4)- management with 4 evidence-based medications (aspirin, b-blockers, ACE-I/ARB, statins).

†Adjusted for: age, sex, Killip (admission)≥II, Anterior MI, heart-rate>100bpm, SBP <100 mmHg, history of diabetes, hypertension, angina, renal failure, year performed.

Conclusion: In recent years the extent of both medical and interventional management of elderly STEMI pts changed substantially. The high degree of implementation and adherence to recommended guidelines was associated with a significant decline in early mortality.

Stent Thrombosis: A Poor Man's Disease?

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Objectives: Stent thrombosis (ST) is a rare but devastating complication of coronary stent implantation. ST incidence and potential predictors were assessed in a "real world" single center.

Methods: We searched our database for cases of "definite" stent thrombosis (according to the ARC Dublin definitions). Each case was matched by procedure date, age and gender, with 3 cases of stenting that did not result in ST. Demographic and clinical parameters were compared and socio-economic status was determined according to "Geocartography" polling and market survey database.

Results: 3401 patients underwent stent implantation at our hospital during 2004-2006. 29 cases (0.85%) of "definite" subacute / late stent thrombosis were recorded. No mortality was recorded during 30 days, which may imply a low rate of ST detection that is based on the strict angiographic criteria. Thrombosis occurred 2 days-3 years after stent implantation. Eighty percent of the patients were males and the mean age was 63±11. All presented with acute myocardial infarction (AMI). Premature clopidogrel administration was reported in 60%. Patients with ST had significantly higher rates of AMI at the time of initial procedure (76 vs. 32%, $p<0.001$), cigarette smoking (60 vs. 28%, $p<0.001$) and use of long stents (>15mm, 72 vs. 60%, $p=0.01$). Bare metal and drug eluting stents use were similar between the groups. Socioeconomic status was significantly lower at the ST group, 4±0.6 vs. 5.4±0.3 (mean±SE, scale 1-10, $p<0.05$).

Conclusions: Stent thrombosis incidence in our population is at least 0.85%. ST appears in patients of significantly lower socio-economic status in addition to certain clinical predictors. These results warrant stricter follow-up and support policy by healthcare providers on patients at risk for stent thrombosis.

Chronic Pre-treatment with Statins and the Outcomes of Patients with ST-Segment Elevation Myocardial Infarction Treated with Primary PCI

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Background: Beyond lipid-lowering effects, statins have favorable effects on platelet adhesion, thrombosis, endothelial function, plaque stability, and inflammation. These pleiotropic effects could contribute to the preservation of microvascular function during ischemia and reperfusion. There is limited data about the impact of chronic pre-treatment with statins on the outcome of patients with ST-elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PCI). Accordingly, our aim was to evaluate the effect of previous treatment with statins on clinical outcomes of such patients.
Methods: We studied 950 consecutive patients with STEMI treated with primary PCI, who were included in our primary PCI registry between 01/2001 – 07/2007. Excluded were patients with cardiogenic shock. Patients were allocated into two groups: those who received chronic pretreatment with statins (n=327) and those who did not (n=623).
Results: As shown in the Table below, despite significantly worse baseline clinical characteristics and similar procedural characteristics, patients who received previous treatment with statins had a lower 30 day mortality rate. At 6 months mortality differences were no longer significant. Multivariate analysis adjusted for factors such as diabetes and the CADILLAC score, showed that previous statin therapy was associated with an odds ratio of 0.4 (0.13-0.96, P=0.04) for 30 day mortality.
Conclusions: The present study suggests that chronic pretreatment with statins before primary PCI for STEMI may be associated with lower short-term mortality, possibly through preservation of the microvascular integrity. Large prospective trials should be performed to verify these findings.

Variable	Previous Treatment with Statins (n=327)	No Previous Treatment with Statins (n=623)	P value
Mean Age (yrs)	62±12	60±13	0.006
Women	22%	16%	0.03
Diabetes	34%	20%	0.0001
Hypertension	58%	38%	0.0001
Hyperlipidemia	79%	27%	0.0001
Smoker	40%	48%	0.01
Previous MI	18%	8%	0.0001
Previous CABG	5.8%	1.1%	0.0001
LVEF<40%	41%	43%	0.5
CADILLAC score	4.5±3.5	4.1±3.6	0.1
Post TIMI 3 flow	96%	95%	0.8
No Reflow	5.3%	6.2%	0.6
GP IIb/IIIa use	75%	78%	0.2
Procedural Success	96%	95%	0.8
Clinical Outcomes			
30 day death	1.5%	3.7%	0.05
30 day re-MI	3.4%	2.6%	0.5
6 months death	4.1%	5.8%	0.3
6 months re-MI	5.8%	4.4%	0.3

Comparative Analysis between Real World Percutaneous Coronary Intervention and Coronary Artery Bypass Grafting for Unprotected Left Main

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Background – Revascularization procedure for unprotected left main (LM) disease, in a real world scenario in our institute, is mostly dictated by assessment of the predicted operative mortality risk. In order to investigate the impact of patients' assessed operative risk and procedural type on early mortality we evaluated, in prospective manner, the outcome of consecutive patients who underwent percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG).

Methods – All patients who were referred for revascularization procedure were assessed for predicted operative mortality using the EuroScore system, which integrated patient-related, cardiac-related and operative-related parameters.

Results –270 patients underwent revascularization procedure for unprotected LM disease (PCI, n=71; CABG, n=199). Of note, 14 (5.2%) patients were presented with cardiogenic shock (PCI, n=12 (17%) vs. CABG, n=2 (1%), p=0.0001). Patients who underwent PCI were more often women (37% vs 26%, p=0.06), older (75±12 years vs. 67±10, p=0.0001), had a lower ejection fraction (48±13% vs. 54±10%, p=0.007), had higher rates of chronic renal failure (27% vs. 11%, p=0.01), history of previous CABG (10% vs. 1.5%, p=0.001) and previous stroke (20% vs. 10%, p=0.03). Presence of additional two or three-vessel disease was similar (86% vs. 88%, p=0.8). EuroScore was significantly higher among those who were referred to PCI (8±3.7 vs. 5.6±3, p=0.0001) with predictive mortality of 10.2% and 6.5%, respectively. Unadjusted mortality rate was higher, although not statistically significant, among those who underwent PCI (11% vs. 6.6%, p=0.2). Adjusted mortality increased in concordance with EuroScore (OR =1.4, 95% CI 1.2-1.7, p=0.01) per 1 score with no impact for the revascularization performed. Importantly, mortality rate among non-cardiogenic shock patients was identical (5.1% vs. 5.2%, p=1.0).

Conclusions – In a current real world scenario, patients who are referred for unprotected LM PCI compared to those who undergo CABG, have substantially higher risk profile and hemodynamic instability. Adjusted mortality rates are comparable between the two strategies. This observation suggests the need for studies aim to evaluate paradigm for unprotected LM revascularization.

Natural History of Saphenous Venous Grafts after Drug Eluting Stenting: Continuous Progression of Disease

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BACKGROUND: Percutaneous coronary intervention (PCI) of saphenous vein graft (SVG) lesions is associated with worse outcomes and high incidence of in-stent restenosis compared with PCI of native coronary arteries. Long-term prognosis is limited by the continuous progression of the disease even after successful drug-eluting stent [DES] implantation

OBJECTIVES: The purpose of the present report was to evaluate the long-term clinical and angiographic outcomes of DES implantation in SVG lesions.

METHODS: Data from consecutive patients who underwent PCI of SVG were imputed into a clinical Database. We evaluated the clinical outcomes up to three years after DES stenting. Included 88 patients [95-grafts] [87% male]. Major adverse cardiac events (MACE) including death, myocardial infarction, target lesion revascularization (TLR), and target vessel revascularization (TVR) were recorded.

RESULTS: The patients mean age was 69±9yrs and the mean age of SVG was 10.5±5.2yrs. The presenting diagnosis was ACS in 72% of patients. And 59% had DM and 15.7% of lesions were 'in-stent' restenotic. Distal protection device was used in 37% of cases and procedural success was achieved in all patients.

	Six months [n=88]	One year [n=84]	Two years [n=56]	Three years [n=38]
Death	1.1%	1.2%	7.7%	7.9%
MI	2.3%	3.6%	7.7%	13%
Stent thrombosis	0%	2.4%	5.9%	7.9%
TVR/graft	7.4%	12.1%	33%	56%
TLR/graft	6.3%	9.9%	28%	49%
CABG	1.1%	3.6%	9.8%	13%
MACE	11.4%	17.9%	41%	66%

CONCLUSIONS: DES implantation in SVG lesions appears safe with favorable and improved short-term outcomes. Nonetheless, long-term results are limited by disease progression in degenerated SVGs and prolonged need for repeat target lesions/vessel revascularization procedures.

A Comparative Analysis of Mortality/Myocardial Infarction Outcomes Using Drug-Eluting Stents vs. Bare Metal Stents in a Large Single Center Israeli Clinical Setting

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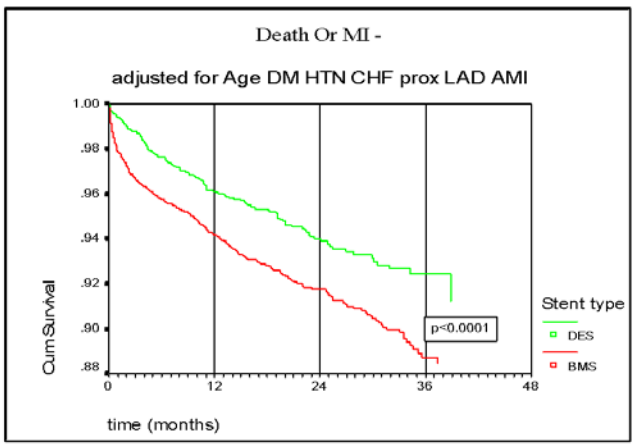
Background: The placement of drug-eluting stents (DES) decreases the frequency of repeat revascularization procedures in patients undergoing percutaneous coronary intervention (PCI) in randomized clinical trials. However, concerns have been raised about their long-term safety in 'all commerce' routine clinical practice among large population cohorts.

Methods: From our hospital and HMO Network Database we conducted a clinical registry of all patients undergoing PCI at our institution. We identified a cohort of 4750 patients who received at least one DES (n=2273) during PCI and compared the mortality and myocardial infarction (MI) risk-adjusted outcomes to patients treated using bare metal stents alone (BMS; n=2477) during an index PCI procedure between April 1, 2004, and July 1, 2007.

Results: Patients receiving DES were somewhat younger, had more diabetes, hypertension, sustained less heart failure, had less acute or recent MI, and had more proximal LAD culprit lesions (**Table**).

	All Pts	BMS	DES	P value
n	**4750**	**2477**	**2273**	
Male	75.3%	75.6%	75.1%	NS
Age	65.8	66.4	65.2	<0.0001
DM	38.7%	35.7%	42.0%	<0.0001
HTN	70.7%	69.0%	72.5%	0.01
PriorCABG	15.8%	15.4%	16.2%	NS
CHF	16.8%	18.7%	14.8%	<0.0001
SmokingHx	35.5%	36.0%	34.5%	NS
Prior MI	24.0%	29.9%	18.3%	<0.0001
Prox LAD (culprit)	16.6%	8.8%	25.1%	<0.0001

The 3-year mortality rate was significantly higher in the BMS group than in the DES group (9.7% vs. 4.7%, P<0.0001), whereas the 3-year rate of any MI was similar in the two groups (3.3% and 2.9%, respectively; P=NS). The risk-adjusted (for age, DM, HTN, CHF, MI, PCI in Prox. LAD) composite endpoint of Death/MI was significantly higher among BMS treated patients (12.1% vs. 7.5%, P<0.0001). Patients who were treated using DES alone had the lowest composite endpoint (7%).



Conclusions: According to our long-term experiences, DESs do not jeopardize the 3 year clinical outcomes (i.e. death/MI) among 'all commerce' group of patients in a wide variety of clinical scenarios. On the contrary, our risk-adjusted data would indicate a *prognostic benefit* for DES utilization which commences early and sustains for at least 3 years following index PCI.

Predictors and Prevalence of Early Stent Thrombosis in Patients with Acute Coronary Syndrome

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Background: While early stent thrombosis (EST) is an uncommon phenomenon, it has devastating consequences. Activation of platelets and coagulation system play a major role in the pathogenesis of acute coronary syndrome (ACS) and might impact on EST. The prevalence and predictors of EST in ACS patients have not been specifically examined.
Objective: To determine the incidence and predictors of EST in ACS patients from the ACSIS 2006.
Methods: Patients were followed for 30 days. Definite EST was diagnosed in patients with angiographic or autopsy evidence of thrombus. Probable EST was diagnosed if unexplained deaths occurred within 30 days after the procedure or in patients with acute myocardial infarction (MI) involving the target-vessel territory.
Results: Of 1202 ACS patients who underwent percutaneous coronary intervention (PCI) with stenting, 30 (2.5%) sustained EST (19 definite, 11 probable). ST-elevation MI (STEMI) versus NSTEMI/unstable angina patients were more than 4 times likely to sustain ST (3.9% vs. 0.9% p=0.001).The incidence of EST was even higher in STEMI patients who underwent primary PCI (5.6%). Other predictors of EST included: Killip class ≥2 (6.4% vs. 1.9%, p<0.01), multi-vessel coronary artery disease (3.6% vs. 0.7%, p=0.02). Drug eluting stent use was not associated with higher risk for EST (3.1% vs.2.2%, p=0.4).On multivariate analysis only STEMI [OR=6.7, 95% CI (2.5-23)], prior MI [OR=2.8, 95%CI (1.2-6.3)], and Killip class ≥2 [OR=3, 95% CI (1.3-6.6)], remained independent predictors of EST.
Conclusion: Among ACS patients, those with STEMI, prior MI and those hemodynamically unstable on admission, are at higher risk for EST.

The Impact of Calculated Patient Prosthetic Mismatch on Morbidity, Mortality and Quality of Life After Aortic Valve Replacement

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Objective: a midterm assessment of patient prosthetic mismatch (PPM) impact on morbidity, mortality and quality of life after aortic valve replacement (AVR).

Methods: Between August 1996 and August 2006, 459 patients (227 female, mean age 74.5±9.3 years, 41-93) underwent primary AVR with or without coronary artery bypass graft (CABG) due to aortic stenosis. Severe PPM was defined as Effective Orifice Area Index (EOAI) < 0.65 and moderate as 0.65>EOAI>0.85. Clinical assessment, quality of life evaluation (the MOS questionnaire scores) and echocardiografic measurements were performed during follow-up (mean 35 months).

Results: Overall hospital mortality was 4.3%. Severe and moderate mismatch were observed in 7.7% (35/459) and 33.2% (152/459) of patients, respectively. In patients ≥75 years, moderate or severe PPM was observed in 49.4% (126/255). Post operative mean gradients for patients with severe or moderate PPM were 19.0±7.5 mmHg and 15.2±6.9 mmHg for patients with no PPM ($p<0.001$). Multivariate analysis revealed that early mortality was associated with female gender (O.R. =3.3, p=0.027), age over 80 (O.R. =3.5, p=0.003), congestive heart failure (O.R. =3.0, p=0.012), IDDM (O.R. =10.7, $p<0.001$), and smoking (O.R. =3.7, p=0.015) but not with any degree of PPM. Late mortality was associated only with NIDDM (O.R. =2.25, p=0.031). In addition, poor quality of life assessment was not associated with any degree of mismatch.

Conclusions: PPM is common after AVR, particularly in the elderly population. Patients with PPM have higher postoperative gradients. However, PPM is not associated with reduced survival, functional capacity or poor quality of life, even if severe.

Incidence and Significance of Tricuspid Valve Insufficiency in Patients after Coronary Artery Bypass Surgery

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Introduction: Tricuspid regurgitation (TR) is usually functional and secondary to mitral valve disease. There is minimal data on new TR after CABG. We sought to determine the incidence and predictors, as well as late outcome of TR after CABG.

Methods: All patients undergoing pure CABG between 1999-2005 and having pre and post-operative echocardiogram in our institution were included. New TR was defined as moderate or greater after surgery, in patients having mild or less TR before surgery. Clinical, surgical and echocardiographic data was entered into our database. Univariate and multivariate analysis was performed in order to identify risk factors for development of new TR. All patients developing new TR underwent late follow-up, including echocardiography.

Results: There were 448 patients, 48 (11%) developed new TR. Predictors for TR were: pulmonary hypertension ($p=0.02$), disease in the RCA ($p=0.004$), elevated CPK levels ($p=0.003$), post-operative decrease in LV ($p=0.02$) or RV function ($p=0.03$), and deterioration of mitral regurgitation after surgery ($p<0.0001$). Four patients died in the follow-up period. Late echocardiogram was available in 32 patients at mean period of 26 months (range 3-84), and showed resolution of TR in 22 patients (69%).

Conclusions: Around 11% of patients will develop new significant TR after CABG. This was mainly correlated with peri-operative myocardial damage. In the majority of patients the TR will resolve spontaneously.

Routine Use of Bilateral Skeletonized Internal Thoracic Artery Grafting – Long Term Results

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Background: Skeletonized harvesting of the internal thoracic artery (ITA) decreases severity of sternal devascularization, thus reducing the risk of postoperative sternal complications in patients undergoing bilateral ITA grafting (BITA).

Methods: Between 1996 and 2001, 1515 consecutive patients underwent skeletonized BITA grafting. Of the 1179 male and 336 female patients, 641 (42.3%) were older than 70 years and 519 (34.3%) had diabetes.

Results: Operative mortality was 2.9%. Early postoperative morbidity included sternal infection (1.6%), cerebrovascular accident (3%) and perioperative myocardial infarction (1%). Multiple regression analysis showed chronic obstructive pulmonary disease (COPD) (OR 11.7, 95% CI 4.5-30.13), repeat operation (OR 13.6; 95% CI 3.4-5.4) and Diabetes Mellitus (NIDDM and IDDM: OR 4.26 95% CI 1.7-10.8 and OR 6.9 95% CI 1.4-35.6, respectively) to be associated with increased risk of sternal infection. Follow-up (between 6 and 12 years) revealed 305 late deaths. Kaplan-Meier 10 year survival for patients younger than 65, between 65-74, and older than 75 was 87%, 75% and 52%, respectively. Cox regression analysis revealed increased overall mortality (early and late) in patients with peripheral vascular disease (HR 1.8, 95% CI 1.39-2.33), patients older than 75 years (HR 7.23, 95% CI, 4.16-12.55), repeat operations (HR 2.19, 95% CI 1.19-4.03), patients with preoperative congestive heart failure (HR 1.56; 95% CI 1.22-1.99), and chronic renal failure (HR 1.49, 95% CI 1.07-2.07). Operations performed without CPB were associated with better postoperative survival (HR 0.69 95% CI 0.51-0.93).

Conclusions: BITA grafting is associated with low morbidity and good long term results. Use of skeletonized BITA is an appropriate technique for the elderly and most of the diabetics; however, it is not recommended for repeat operations or for patients with COPD.

Timing of Cardiac Catheterization and Acute Renal Failure after Cardiac Surgery

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Background: The incidence of acute renal failure (ARF) after cardiac surgery and the risk of mortality associated with it continues to be high. The aim of this study was to evaluate if timing of cardiac catheterization influences the incidence of postoperative ARF.

Patients and methods: Four hundred and eight patients undergoing cardiac surgery were prospectively evaluated. Mean age was 66+/-10 years, 22% were female, 38% diabetic, 69% had hypertension and 15% had peripheral vascular disease. Preoperative creatinine level and calculated creatinine clearance (CrCl) were 1.05+/-0.6 mg/dl and 82+/- 27 ml/min, respectively. Of the study population 39% underwent surgery within 24h of cardiac catheterization, 30% underwent surgery between the first and fifth day of catheterization, and 31% underwent surgery more than 5 days after cardiac catheterization. Endpoints were ARF, defined as a decrease in the calculated CrCl of 25% or more by the third postoperative day, and hospital mortality.

Results: 47% of patients who underwent surgery within 24h from cardiac catheterization have shown a decrease in calculated CrCl of 25% or more, as apposed to 29% in patients who underwent surgery between the 1st and 5th day after catheterization, and 23% in those who underwent surgery more than 5 days after catheterization (p=0.05). Mortality rate among patients who underwent surgery within 24h from catheterization was independently associated with acute renal failure ([OR]1.9, p=0.02). Preoperative calculated CrCl of less than 60ml/min and cardiac surgery within 24h from catheterization were independently related to hospital mortality ([OR]8, p=0.005).

Conclusion: Cardiac surgery performed within 24h from cardiac catheterization is a significant risk factor for acute renal failure, especially among patients with preoperative reduced renal function. Proper timing and patient selection is highly recommended.

Comparison between Surgical Arterial Revascularization and Drug Eluting Stents in Multivessel Patients with Diabetes Mellitus

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Background: Reduction of re-stenosis and re-intervention was recently reported with the introduction of drug-eluting stents (DES). This study compares mid-term outcome of surgical arterial revascularization in patients with diabetes mellitus to that of percutaneous interventions (PCI) incorporating DES (Cypher).

Methods: Twp hundred and two diabetic patients with multi-vessel disease who underwent left-sided arterial revascularization between May 2002 and December 2005 were compared with 187 diabetics who underwent Cypher stenting. Multi-vessel patients in the surgical group were treated with two ITAs. After performing propensity score with patients' characteristics, COX regression was used in order to evaluate predictors of outcome events.

Results: Follow-up ranged between 6-52 months. Four-year survival (Kaplan-Meier) of the two groups was similar (91.3% and 87% for the surgical and Cypher groups, respectively, p=0.87). However, angina-free survival (72% vs 47%, respectively, Log Rank p<0.001) and re-intervention-free survival (91% vs 76%, p=0.000) were better in the surgical group. After adjustment to propensity score, assignment to the Cypher group was associated with increased risk of angina return (OR 4.0, 95% CI 2.6-6.21, p=0.000), re-interventions (OR 3.36, 95% CI 1.7-6.62, p=0.000) and MACE (OR 3.47, 95% CI 1.85-6.49, p=0.000).

Conclusions: Outcome of diabetic patients who underwent surgical arterial revascularization is better than that of PCI patients treated with DES.

Quality of Mitral Valve Repair: Median Sternotomy Versus Port-Access Approach

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Objectives

The feasibility and safety of minimally invasive mitral valve (MV) repair using Port-Access was previously demonstrated. However long term quality of the repair, is not well investigated.

Methods

We studied 101 consecutive patients that underwent MV repair for isolated posterior leaflet prolapse. 50 patients underwent port-access approach, and 51 median sternotomy (MS) approach. In port-access approach we used EndoClamp® balloon (32) or Chitwood clamp (18). Patients in port-access group were younger; mean age of 55±11 versus 61±13 ($p<0.05$). Other patient's characteristics including MV pathology and mitral repair technique were comparable.

Results

Operative, bypass and aortic clamp times were significantly longer in the port-access group. There was no early death. There were more early postoperative pulmonary complications in port-access group. Early post operative echocardiography showed none of patients in both groups, had more then grade 2 mitral regurgitation. Mean hospital stay was 6.2±5.0 days in port-access group versus 7.6±4.2 in sternotomy group (NS). At mean follow-up of 31±30 months, NYHA improved from 1.9±0.9 to 1.5±0.6 in port-access group ($p<0.01$), versus 2.4±0.9 to 1.7±0.6 in sternotomy group ($p<0.01$). There were four (8%) late deaths in sternotomy group, versus none in port-access group ($p=0.04$). Freedom from reoperation was 98% and 100%, in port-access and MS groups, respectively. Echocardiography follow-up revealed 84% (42/50) and 86% (44/51) of patients (Port-access and MS groups, respectively) were free from moderate or severe mitral regurgitation (NS).

Conclusions

In mid term follow-up, quality of simple posterior mitral valve repair via port-access approach compares well with conventional MS approach.

A Novel Mutation in the HCN4 Gene Causes Familial Sinus Bradycardia in Two Unrelated Moroccan Families

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Background: HCN4 channel plays a major role in the diastolic depolarization of sinoatrial node cells. We and others have previously shown that mutant HCN4 channels are associated with familial sinus bradycardia (SB).

Methods and Results: Two 20 years old men of North African Jewish decent were admitted. One survived an out of hospital cardiac arrest during extreme exercise. The other presented with weakness and pre-syncopal events. Both had significant SB (minimum 35, mean 53), which was also found in several other first degree family members. Holter and exercise testing showed SB at rest with normal response to exercise. Echo demonstrated normal heart structure. Sequencing of the HCN4 gene in both patients revealed a C to T transversion at nucleotide position 1454, which results in an alanine to valine change in the protein (A485V). Multiple alignments of different species show a conserved alanine at this position. The mutation was also found in the bradycardic relatives of the second patient and was not found in the non bradycardic relatives as well as in 50 healthy controls. The mutation is located in a conserved locus in the ion channel pore. A mutation in the pore was found in expression systems to decrease the funny current.

Conclusions: We describe a new mutation in the HCN4 gene in two unrelated patients with symptomatic familial SB. The existence of this mutation in two unrelated SB individuals from the same ethnic backgrounds suggests that it may be a relatively common cause for unexplained congenital SB in this ethnic group.

Outcome of Patients with Drug-induced High-degree Atrioventricular Block

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Background: Since information is scarce regarding the natural history of patients with drug-induced (DI) AV-block (AVB), indications for permanent pacing are inconsistent. We sought to determine the outcome of patients with drug -associated AVB.

Methods: 165 consecutive patients with high-degree AVB receiving drugs that affect conduction (presumably DIAVB), were studied retrospectively. The culprit drug was discontinued and decision on permanent pacing was taken by the attending physician. Patients were followed up to pacemaker implantation or, in non-implanted cases, till death or last follow-up, and were divided into 3 groups. Group A: pacemaker implantation (PMI) during index hospitalization; Group B: Discharged without PMI, but re-hospitalized and underwent PMI later during follow up; Group C: no need for PMI till end of follow-up.

Results:

	Group A N=107	**Group B N=23**	**Group C N=35**	***P value***	***P value (B vs. C)***
Age (years±SD)	76±9	76±8	73±12	NS	NS
Males	41(38%)	8(33%)	16(47%)	0.53	0.29
Ischemic heart disease	59(55%)	6(25%)	14(41%)	0.02	0.20
Syncope	67(63%)	6(25%)	8(24%)	**0.0001**	0.89
Mobitz type II	19(18%)	3(13%)	9(27%)	0.36	0.19
CAVB	55(51%)	4(17%)	4(12%)	**0.0001**	0.59
Wide QRS	32(30%)	4(17%)	1(2.9%)	**0.003**	0.07
Chronic atrial fibrillation	27(25%)	11(46%)	6(18%)	**0.05**	**0.02**

Conclusion: Of patients discharged without PMI, 40% will need PMI at a later stage. The presence of atrial fibrillation predicted future need for PMI among those patients, while wide QRS was a borderline predictor.

Larger prospective studies are required to better characterize this group of patients in order to avoid unnecessary PMI

Tricuspid Incompetence after Pacemaker Implantation in 410 Patients- Incidence and Associated Factors

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Severe tricuspid incompetence (TI) after pacemaker implantation has been described in small series of patients but its incidence is not known.
We retrospectively analyzed the data of 545 patients who underwent pacemaker implantation and had an echodoppler performed before and after the procedure. We excluded 135 patients who had moderate TI or more at baseline.
Seventy-five patients (18%) had a worsening of TI by ≥ 2 grades and were defined as group1. The patients without significant change were defined as group 2.
We compared clinical and echocardiograhic data in both groups.
Patients in group 1 were older, 77 ± 7 years compared to group 2: 72 ± 10 years, $p< 0.001$.
There was no difference in systolic function, left ventricular size and function or systolic TI gradient before the implantation. The mitral E/A ratio was 0.98 in group 1 and 1.42 in group 2, $p<0.001$.
The systolic TI gradient after implantation was higher in group 1: 42 ± 12 mmHg than in group 2: 33 ± 8 mmHg, $p <0.001$.
We conclude that TI worsening after pacemaker implantation is not rare and occurs more often in older patients, with impaired left ventricular relaxation and who develop pulmonary hypertension after the procedure.

The Effects of Left Ventricular Lead Placement on QT Interval and Transmural Dispersion of Repolarization in Biventricular Pacing

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Background: There is controversy regarding the pro-arrhythmic effects of biventricular pacing. Left ventricular (LV) epicardial pacing using the coronary veins reverses the normal activation of the LV wall and may increase both QT interval and Tpeak-end which correlates with transmural dispersion of repolarization (TDR).

Objectives: We sought to analyze the relationship between LV lead position to QT interval and TDR in patients with cardiac resynchronization therapy (CRT) systems, with an LV lead implanted via coronary veins.

Methods: Twelve leads electrocardiograms at three pacing modes (no pacing, LV pacing only and biventricular pacing) were evaluated in 63 patients immediately following a CRT device implantation. The LV lead was located in the lateral cardiac segment in 41 patients and in the posterior segment in 22 patients.

Results: There were no significant differences in heart rate (HR), QT, QT corrected (QTc), QT dispersion, JT and Tpeak-end intervals between the two groups at baseline (no pacing). With biventricular pacing the QTc and Tpeak-end intervals were significantly greater in posterior vs. lateral position. With LV pacing only the Tpeak-end interval was significantly greater in the posterior vs. lateral position and there was a trend for longer QTc interval in the posterior vs. lateral position.

	No Pacing			Biventricular Pacing			LV Pacing Only		
LV Lead Location	HR (bpm)	QTc (msec)	Tp-e (msec)	HR	QTc	Tp-e	HR	QTc	Tp-e
Lateral Segment	67±16	482±54	113±29	71±13	499±49	114±26	80±18	558±102	128±28
Posterior Segment	68±15	496±59	119±28	70±13	530±59	143±24	85±17	602±63	148±35
P value	NS	NS	NS	NS	0.034	<.0001	NS	0.069	0.015

Data are presented as mean±SD

Conclusions: Our data suggest a pacing site-dependent increase in TDR and QTc interval in patients with both biventricular and LV pacing. Posterior lead placement may therefore be more arrhythmogenic.

Left Ventricular Strain Signatures in Dilated Cardiomyopathy Predict Response to Cardiac Resynchronization Therapy: Timing is Not Everything

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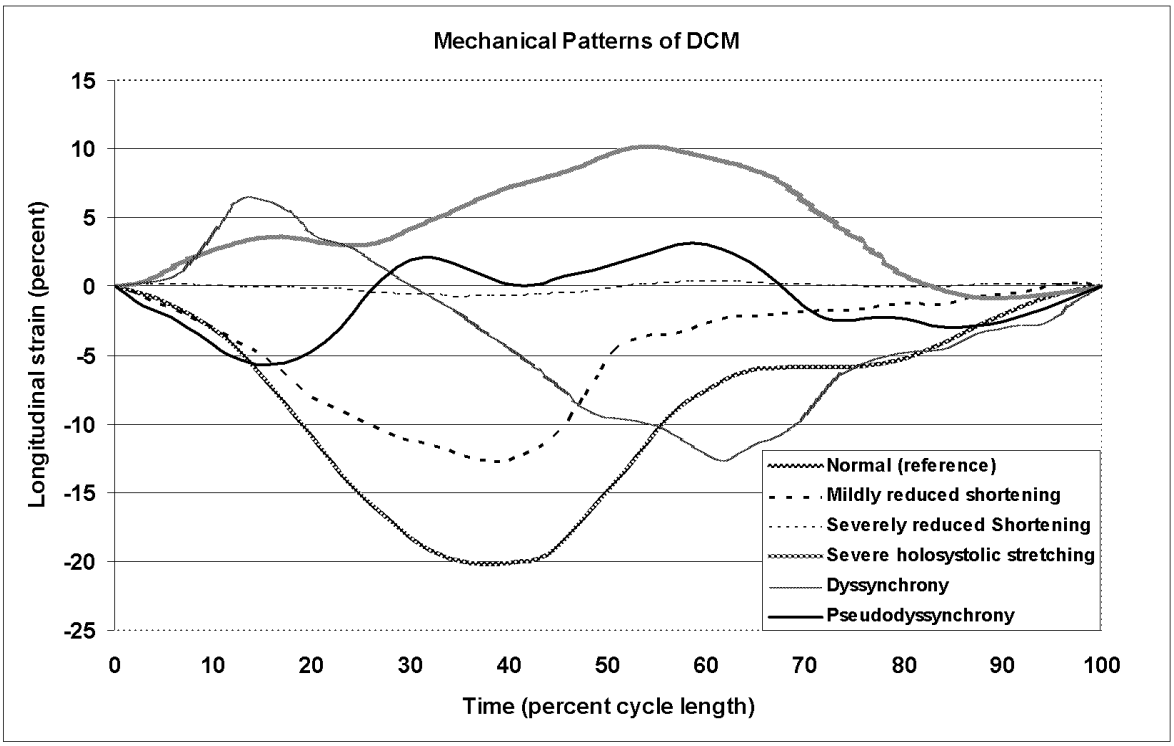
Background Cardiac resynchronization therapy (CRT) is helpful but not uniformly successful in patients with heart failure and ventricular dyssynchrony. Determination of dyssynchrony for patient selection does not consistently improve CRT success rate. We aimed to develop prediction rules for successful CRT based on mechanical strain patterns of LV function rather than just the timing of regional ventricular activation.

Methods 76 consecutive patients undergoing CRT were studied. Paired baseline and 3-6 months post procedural echocardiographic studies were analyzed. CRT response was determined by a ≥15% improvement in ejection fraction and/or a ≥15% decrease in end systolic volume. Longitudinal strain was measured using 2D speckle-tracking software (GE, Milwaukee) and Strain patterns correlated with CRT response.

Results Clinical and conventional echocardiographic characteristics were similar in responders (n=44) and non-responders (n=32). Resynchronization was achieved in both groups. Different strain patterns were identified and correlated with response.



Nonresponders had segments stretching ≥5% throughout systole. Absence of holosystolic stretching segments at baseline was 98% sensitive and 88% specific predicting response to CRT. When combined with presence of lateral delay pattern this model increased its sensitivity to 100% and specificity to 94% for response.

Conclusions LV strain pattern signatures are highly predictive of response to CRT, specifically, absence of holosystolic stretching. Strain imaging assesses the quality of resynchronization and its mechanical outcome.

Sinus Rhythm Restoration after Persistent Atrial Fibrillation: The Clinical Value of N-Terminal Pro-BNP Measurements.

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Aim: To examine effects of sinus rhythm (SR) restoration on N-Terminal pro-BNP (NTP-BNP), in patients with atrial fibrillation (AF).

Methods: Subjects with paroxysmal and persistent AF in the absence of organic heart disease were prospectively studied. Chemical or electrical restoration of SR was attempted within 48h (n=37) or >3 weeks (n=73). Clinical and laboratory (N-terminal Pro-BNP, 72 hour Holter monitor and EKG) assessments were obtained at baseline and 1, 30, and 180 days after an attempt to restore SR. Patients were divided into 3 predefined "outcome groups": (a) Maintenance of SR for 1 month. (b) SR with periodical recurrent AF (PeAF) (c) Early (<30 days) recurrence AF (RAF).

Results: 110 patients enrolled; 93 had successful SR restoration. Baseline NTP-BNP was 936 pg/ml ($_{q25\text{-}75}$ 333-2026); Ratio between baseline and 30 day NTP-BNP was 10.2 ($q_{25\text{-}75}$ 6.42-22.0) for SR group, 3.3 ($q_{25\text{-}75}$ 2.45-7.34) for PeAF, and 1.07 ($q_{25\text{-}75}$ 0.87-1.22) for RAF ($p<0.001$), and was higher with early cardioversion. Patients with ratio ≤3 were more likely to have PeAF. (46% versus 3%, OR 30, $P<0.001$).

Results NTP-BNP Levels	ALL (n=110)	SR (n=38)	PeAF (n=32)	RAF (n=23)	Control (n=17)	p Value (chi²)
pre-cardioversion (pg/ml) median (q25-75) n=110	970 (344-1966)*	1415 (561-2626)*	641 (249-1410)*	896 (274-1110)*	1259 (755-2215)*	0.047
24 post-cardioversion (pg/ml) median (q25-75) n=67	471 (194-949)	451 (212-1041)	348 (164-1140)	650 (340-908)	-	0.614
1 month (pg/ml) median (q25-75) n=110	272 271-816	114 (271-816)	167 (56-290)	777 (276-1061)	1209 (749-2406)	<.001
6 months (pg/ml) median (q25-75) (n=45)	171 (53-336)	122 (15-249)	216 (89-444)	-	-	.031
12 months (pg/ml) median (q25-75) (n=25)	207 (83-474)	144 (21-376)	318 (171-1118)	-	-	.062
Ratio of pre and 1 m post CV median (q25-75) (n=110)*	2.98 1.13-8.87	10.2 6.42-22.0	3.3 2.45-7.34	1.07 0.87-1.22	1.04 0.85-1.17	<.001
*Ratio of pre and 6 m post CV * median (q25-75) (n=44)*	4.91 2.8-18.6	15.2 4.60-32.11	2.9 1.92-4.83	-	-	<.001

*CV-cardioversion

Conclusion: Patients with AF have elevated NTP-BNP, which is not predictive of SR restoration. When restoring SR dramatic reduction of NTP-BNP is observed up to 1 month. The NTP-BNP drop is partially or completely abolished by PeAF and RAF respectively. Post-cardioversion NTP-BNP may predict recurrent AF and embolic events.

Overexpression of MEF2c and IGF-1 in Transplanted Mesenchymal Stem Cells Increases Myogenic Differentiation, Cell Survival and LV Function in Rats

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Background:

We evaluated the synergistic effect of myocyte enhancer factor-2c (MEF2c), which modulates myogenic differentiation, and insulin-like growth factor 1 (IGF-1), which affects cell proliferation and apoptosis, on the efficacy of transplanted mesenchymal stem cells (MSC) for myocardial repair.

Methods and Results:

Female Lewis rats underwent LAD ligation 3 weeks before transplantation with $3x10^6$ male untransfected MSC, MSC transfected with MEF2c (MSC+MEF2c), IGF-1 (MSC+IGF-1), MEF2c+IGF-1 (MSC+MEF2c+IGF-1) or medium without cells (Control). At 2 and 4 weeks MEF2c and IGF-1 expression, donor cell survival and LV function were evaluated. MSC were characterized by flow cytometry prior to transplantation and by immunohistochemistry in the recipient heart.

After 2 weeks, MEF2c expression was greatest in MSC+MEF2c and MSC+MEF2c+IGF-1 ($P<0.001$). IGF-1 expression was greatest at two and four weeks in MSC+IGF-1 and MSC+MEF2c+IGF-1 ($P<0.001$). Donor cell survival was lowest in MSC and MSC+MEF2c, and highest in MSC+IGF-1 and MSC+MEF2c+IGF-1 ($p<0.05$). At 2 and 4 weeks, LVEF was lowest in control, intermediate in MSC and MSC+IGF-1, higher in MSC+MEF2c and greatest in MSC+MEF2c+IGF-1 ($P<0.05$). Immunohistochemistry demonstrated increased expression of both α-SMA and MHC in donor cells in MSC+MEF2c and MSC+MEF2c+IGF-1, indicating myogenic differentiation of the transplanted cells.

Conclusions:

Transplantation of MSC transfected with MEF2c and IGF-I augments myogenic differentiation, improves transplanted cell survival and enhances LV function in infarcted rat hearts. This approach may maximize the efficacy of MSC transplantation for myocardial repair.

Therapeutic Fusion: A Novel Strategy for Reprogramming and Generation of Immune-privileged Cardiomyocytes for Heart Repair

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Background: Some stem cell repair properties originate from their ability to fuse with naturally resident cells in the organs they repair. We hypothesized that *ex vivo* fusion of autologous mesenchymal stem cells (MSCs) and donor cardiomyocytes could provide an invaluable resource of semi-autologous myogenic hybrids with improved regenerative capacity.

Methods and Results: Cell hybrids were engineered by polyethyleneglycol-mediated fusion of fetal mouse cardiomyocytes ($5x10^5$) isolated from LacZ transgenic mice with autologous MSCs ($5x10^5$) from bone-marrow of GFP transgenic mice. Unfused cells were eliminated using specific antibiotics. We used a mixed lymphocyte reaction assay, in which the cells were co-cultured with *GFP* transgenic splenocytes to assess immune response against the hybrids. By lymphocyte proliferation and destruction rate, we showed that MSC-cardiomyocyte cell hybrids were significantly less immunogenic (12% less lymphocyte proliferation). Gene expression analysis by Affymetrix Genechip® array was performed and fused and MSC gene expression were compared. We found that genes related to the major histocompatibilty complex were down-regulated by 2^7 fold. An in vivo experiment was performed in which MI mice were randomized into 5 groups: Cell hybrids (n=10), MSCs (n=10), cardiomyocytes (n=10), mixed MSC and cardiomyocytes (n=9) or saline injection (n=8). Cells were administrated 10 minutes after MI was induced. Echocardiography analysis was performed 3 days and 1 month after the operation and showed that cell hybrids improved left ventricle area change (33.26% ± 5.68 before vs. 39.21% ± 4.87 after, p=0.05) and left ventricle fractional shortening (21.76% ± 5.68 before vs. 27.31% ± 3.82 after, p=0.07).

Conclusion: Our results suggest that the unique power of stem cell fusion can be translated to reprogramming and generation of immune-privileged, therapeutic, hybrid cardiomyocytes.

Acute Decompensated Heart Failure is Associated with Elevated Serum Oxidative Stress

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Background: Oxidative stress (OS) is one of the features of the inflammatory process, a key player in heart failure (HF) pathogenesis. We examined OS serum level in patients who were admitted with acute decompensated heart failure (ADHF), followed OS changes over two months course along with patients' clinical progress and serum NT-pro BNP level.

Methods: We examined sera of 25 (6 females, 19 males, mean age 71) consecutive HF patients who were admitted due to ADHF. Patients' sera were analyzed for OS on admission, discharge and two months after. Simultaneous serum levels of NT-pro BNP were measured as well. We followed patients for HF readmissions. In addition we compared the HF patients OS level to an age and sex matched control group of 36(7 females, 29 males, mean age 74) volunteers with out HF syndrome. Serum OS level was determined using a new technique based on a real time on line assay, thermochemiluminescence (TCL) oxidizability. TCL assay measurement is based on heat induced oxidation of the biological sample and provides a ratio calculating the oxidability measurement in respect to the OS potential. **The lower the TCL ratio, the higher is the OS level.**

Results: The mean OS measurements on admission and on discharge were similar (170±23 and 174 ±25, respectively, p=NS). During the following two months, one patient died and 10 patients were readmitted for ADHF. The OS level was significantly higher in the 10 readmitted patients compared with the 14 patients who were not readmitted (171±15 vs.188±21 respectively, $p<0.05$). The control group mean serum OS level was 193±13. This control group OS level, was significantly better than the OS level of the HF patients measured in the hospital, on both admission and discharge days ($p=0.02$). Two months after hospital discharge , only HF patients who were not readmitted due to ADHF, the OS level was "normalized" , to the same OS level of the control group (188±21 and 193±13 respectively, p=NS). Of note, there was a high correlation between OS values as reflected in TCL ratio measurements and the serum NT-pro BNP values ($r=0.6$, $p<0.01$).

Conclusion: Serum OS level is elevated in ADHF. The OS serum level improves significantly two months after hospital discharge but only in those patients who are not readmitted. Serum OS level correlates with clinical deterioration and with serum NT-pro BNP level. Accordingly, OS is an important factor in acute HF either as a cause or as a reflection of disease severity.

The Clinical Outcome of Patients with Congestive Heart Failure: A Poor Prognosis Despite Preserved Left Ventricular Function

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Background: The clinical outcome of patients with congestive heart failure (CHF) is poor. However, it was presumed that patients with preserved left ventricular function (PLVF) may have a more benign prognosis. Recent data would suggest otherwise.
Objectives: To evaluate the clinical outcome of patients with CHF with PLVF compared to patients with reduced function and the factors affecting prognosis.
Methods: We prospectively evaluated 289 consecutive patients hospitalized with a definite diagnosis of clinical CHF based on typical symptoms and signs. Patients were followed clinically for a period of one year.
Results: More than a third (36%) of the patients had preserved LVF based on echocardiography. These patients were more likely to be older, female, hypertensive and suffer less from ischemic heart disease. The survival rate at 1 year in this group was poor and not significantly different from patients with reduced LVF (75% vs 71%, respectively). The adjusted survival rate by Cox regression analysis was also not significantly different (Figure 1, P=0.25). However, patients with preserved LVF had less re-hospitalizations due to CHF (25% vs 35%, P<0.05). Predictors of mortality in the whole group by multivariate analysis were age, diabetes, chronic renal failure and Sodium < 135mEq/l.
Conclusions: The prognosis of patients with clinical heart failure with or without preserved LVF is poor. Better treatment modalities are needed in these patients.

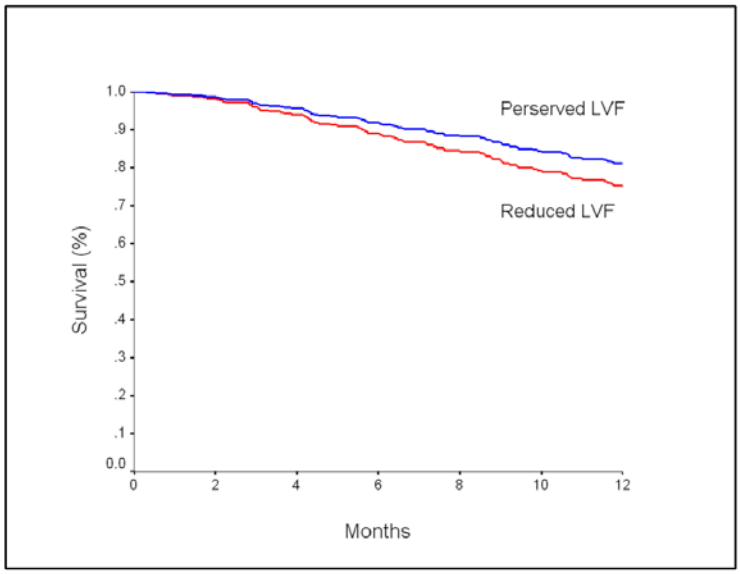

Figure 1. The adjusted survival rate of patients with preserved versus reduced LVF (N=289) by Cox regression analysis. There was no significant difference in survival between the groups.

Hypertrophic Cardiomyopathy with Extreme Left Ventricular Hypertrophy: Risk Profile and Outcome with and without ICD Implant

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Background: Implantation of ICD had been recommended for prevention of sudden death **(SD)** in patients (pts) with Hypertrophic Cardiomyopathy **(HCM)** and extreme (≥ 3.0cm) left ventricular hypertrophy **(ELVH)**.

Objectives: to compare the risk profile and clinical outcome of pts with ELVH who did and did not undergo ICD implantation.

Methods: In the *ISAAC* database, ELVH was diagnosed in 17 pts, aged 1-72 (32.4 ± 17) years, 14 (82%) were male, and follow-up lasted 1-10 (5.3 ± 3.2) years. Presence of major and minor risk factors for SD, survival and type of death were specifically recorded. Major risk factors were considered aborted SD, family history of SD, syncope, nonsustained VT (**NSVT**), and abnormal blood pressure response to exercise, whereas young age at diagnosis, outflow gradient and ischemia on imaging were considered minor risk factors. A Risk Factor Burden was calculated by summation of predefined scores assigned to each risk factor.

Results: The two groups had similar age and similar prevalence of family history of HCM, syncope and minor risk factors for SD. Pts with ICD tended to have a higher NYHA class (2.0 ± 0.7 vs 1.7 ± 1.2, p=0.08) and LV wall thickness. They had a higher Risk Factor Burden due to higher prevalence of family history of SD and NSVT on Holter, as shown in the Table.

	LV Wall thickness	Fam History of SD (n)	NSVT (%)	Nr of Major Risk Factors	Risk Factor Burden
ICD (n=10)	37 ± 6	6	75	1.8 ± 0.6	3.6 ± 1.3
No ICD (n=7)	31 ± 5	0	17	0.9 ± 0.7	1.9 ± 0.9
p	0.08	0.04	0.05	0.02	0.03

Among the patients without an ICD, one died suddenly. One patient had aborted sudden death and had an ICD implanted without further arrhythmic events. In the ICD group one pt died following infective endocarditis and sepsis related to the implant of the device. During the follow up of the 10 pts with an ICD arrhythmia triggered discharges were not recorded.

Conclusions: In our pts with ELVH the decision to implant an ICD was related to presence of additional major risk factors, particularly family history of SD and/or NSVT on Holter. Although SD or aborted SD occurred only in pts without ICDs, one pt died of complications related to device implantation. There is need for further evaluation in a larger population, of the appropriateness of ICD implantation criteria and of the effectiveness of these devices to prevent death in this type of pts.

Immune Cell Function Testing for the Optimization of the Therapeutic Drug Monitoring in Selected Heart Transplant Patients, a Case Series

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Purpose: The Immuknow assay determines the cellular immunity status by quantitative measurement of intracellular ATP level in $CD4^+$ lymphocytes after PHA stimulation. Levels below 225 and above 525 indicate over and under immune suppression respectively. The purpose of the present study was to assess the contribution of Immuknow assay measurement in tailoring the immunosuppressive therapy of heart transplant (HTx) recipients.

Methods and Materials: Between June and August 2007, the immunosuppressive protocol of 15 of the 75 pts transplanted at our center needed re-assessment. Seven pts suffered from infectious episodes (2 recently transplanted with severe fungal infections, 2 pts had 2 episodes of CMV infection despite prophylactic Gancyclovir and 3 had recurrent respiratory tract infections), 5 experienced biopsy proven rejection and 3 pts were started on a CNI free protocol due to CNI side effects. The contribution of the Immuknow assay measurement was assessed.

Results: Mean Immuknow levels were low in the infected pts (235) and high in the pts with rejection (575). During the change to CNI free protocol, mean Immuknow levels were appropriate (426). In the fungal infected pts, the immunosuppressive treatment was diminished to low doses of steroids, lower trough CNI levels, omitting mycophenolate moefetil. The lower Immuknow levels encouraged us to continue the low potency immunosuppression. In the CMV and the respiratory tract infected pts, the Immuknow levels were low despite CNI therapeutic drug levels. Their immunosuppressive regimen was changed to a less potent one. In the pts with rejection, steroids were added and MMF was changed to everolimus. The appropriate Immuknow levels during the change to the CNI free protocol reflect the uneventful protocol change.

Conclusions: Monitoring the Immuknow levels is a valuable and simple tool for immunosuppressive therapy monitoring. It helps decision making in complex situations allowing therapeutic changes that can favorably affect the outcome of HTx recipients.

Effect of Atrial Fibrillation on Mitral Incompetence Severity Established by Echocardiography

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Background: Presently there is no data on the effect of atrial fibrillation (AF) on the severity of mitral insufficiency.
We have observed that some patients with AF experience improvement of their mitral regurgitation (MR) upon return to sinus rhythm.
Objective: 1) to measure the influence of heart rhythm (sinus or atrial fibrillation) on severity of MR
2) to define clinical and echocardiographic parameters that influence the changes in MR severity in these patients
Methods: Between 1992-2006 we found 335 patients (51% males, mean age 62.27±16.07 years) with significant mitral insufficiency while in atrial fibrillation who underwent follow up echocardiography within 6 months, while in sinus rhythm. These patients were divided into 2 groups according to degree of MR improvement after returning to sinus rhythm: patients who improved by two grades or more (group 1) or by less than 2 grades (group 2).
Results: There were 98 patients (29.25%) in group 1 (55% males, mean age 66.1yrs). There was no difference between the groups in relation to hypertension, diabetes, stable or unstable coronary artery disease.
Left ventricular dimensions improved significantly (left ventricular end diastolic (LVEDD) from 5.13 cm to 4.98cm, p=0.0363, left ventricular end systolic (LVESD) from 3.62cm to 3.40cm, p=0.0314) compared to group 2 (LVEDD 5.18 cm to 5.25cm, p=0.3410, LVESD 3.69cm to 3.71cm, p=0.2995).
Patients in group 1 had a morphologically normal mitral valve in 32.6% vs only 23.6% in group 2 (p=0.087).
In addition, left atrial (LA) dimensions improved significantly (4.73cm to 4.31cm, p=0.0425) in group 1 compared to group 2 (4.71cm to 4.72 cm, p=0.4270) and pulmonary artery pressures improved marginally (from 44.41 mmHg to 37.48 mmHg, p=0.0587) in group 1, compared to group 2 (44.71mmHg to 41.57mmHg, p=0.1624).
Conclusions: In 30% of patients with paroxysmal AF, MR improves significantly after cardioversion to sinus rhythm. Clinical decisions should be based on echocardiographic data when the patient is in sinus rhythm.

The Natural History of Moderate Aortic Regurgitation

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Background: Whether to replace the aortic valve for moderate aortic regurgitation (AR) in patients refer for cardiac surgery primarily for CABG or MVR is still debatable. Therefore, we sought to study the rate of progression of moderate AR and the need for future surgical intervention.

Methods and Results: Two hundred and sixty-two consecutive patients (162 men,100 women; mean age 65 ± 15 year ,range 21 to 93) with moderate AR and no more than mild aortic stenosis, were followed for 42 ± 31 months. AR resulted from disease of the aortic leaflets in 145 patients (55%): 85-degenerative disease, 54-rheumatic and 6 infective endocarditis. In 70 patients (27%) the AR was secondary to dilatation of the aortic root and/or ascending aorta (average aortic diameter 48 ±6 mm).In the remaining 47 patients (18%) the cause of the AR could not be determined. Progression to severe AR occurred in 18 of the 262 patients (6.8%) , an average rate of progression of 5.1% per year. Progressors were evenly distributed between valvar disease and aortic root dilatation. Three of the patients with aortic dilatation underwent aortic valve replacement : one of them due to type A aortic dissection.

Conclusions: A small proportion of patients with moderate AR progress to severe disease in the mid-term. Etiology of the disease doesn´t seem to influence the rate of progression. A minority of patients needed aortic valve replacement during follow-up. Therefore, the indication of prophylactic valve replacement in patients with moderate AR who undergo coronary artery bypass or mitral valve surgery is questionable.

Comparison of Fast Instantaneous 3 D Echocardiography Analysis with Cardiac MR Imaging for the Evaluation of Left Ventricular and Left Atrial Volumes - A Pilot Analysis

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Introduction: Left ventricular (LV) ejection fraction (EF) and Left Atrial (LA) volume are an important predictors of morbidity and mortality in a wide range of patients and clinical scenarios. LV and LA volumes and EF measurements from two-dimensional echocardiographic (2DE) images are subjective, time-consuming, and relatively inaccurate. Real-time 3DE technique is a novel technique capable of instantaneous acquisition of volumetric images. The aim of this pilot analysis was to validate a new method for rapid, online measurement of LV and LA volumes from 3DE data using cardiac magnetic resonance (CMR) as the reference

Methods: CMR and 3DE data from 8 unselected patients (aged 15-61) that underwent cardiac evaluation for various reasons were obtained. The 3DE parameters: end systolic (ES) and end diastolic (ED) of LV and LA were analyzed using iE-33 machine designed to automatically detect the endocardial surface calculate ESV and EDV from voxel counts. 3DE-derived LV and LA volumes were compared with CMR volume measurements that were performed by the CMR physician corrected analysis (linear regression, Bland–Altman analysis).

Results: The analysis results, comparison and the correlations are presented in the table:

Parameter	CMR ml	3DE ml	r^2 (3DE vs. CMR)	Limits of agreement
LV EDV	108.6±26.9	105.9±27.1	0.81	SD: 11 ml, 9.3%
LV ESV	43.4±9.	41.2±8.1		
LA EDV	39.4±46.9	37.9±41.8	0.76	SD: 14 ml, 11.5%
LA ESV	64.4±44.0	59.8±39.1		

Conclusions: The 3DE have good correlation and close limits of agreement with CMR for calculating LV and LA volumes. The 3DE analysis offers a rapid, and accurate method for LV, LA volume and therefore LVEF calculation. This novel tool can mitigate the errors inherent to 2DE.

Is the Common Cut-Off Point for Prophylactic Surgery to Prevent Aortic Dissection Too High?

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Background: Aortic diameter ≥5.0 to 5.5cm is the cut-off point, under which it is recommended to perform elective surgery to prevent aortic dissection (AD), in non-Marfan patients with tri-leaflet valves.
We summarized the data of patients with AD, undergoing echocardiography in our hospital, with special focus on maximal ascending aortic diameter.
Methods: Computer records of all transesophageal echocardiograms (TEE) of acute type A AD by Stanford classification, performed in our hospital in the last 10 years were reviewed. Patients' characteristics and cardiograms were reviewed. TEE's were performed on presentation or intraoperatively.
Results: The study group included 47 patients, mean age 58±13 (range 27-79), 68% male. 70% had DeBakey type I dissection, and 30% had DeBakey type II dissection. The average aortic diameter was 5.2±1cm: It was >5.5 cm in 15 patients (32%), 5.0-5.5 cm in 12 patients (25%) and smaller than 5.0cm in 20 patients (43%). Thirty-day mortality was 23%, all with aortic diameter <5.5cm. Aortic diameter was <5.5 cm in 3/4 patients with Marfan syndrome, 2/2 patients with bicuspid aortic valve and 9/11 patients with atherosclerosis.
Hypertension was common (68%) and was evenly distributed among those with diameter <5.5cm and >5.5cm.
Conclusions: The majority (68%) of patients with AD had aortic diameter <5.5cm, i.e. below the threshold for prophylactic surgery, including non-Marfan patients with tri-leaflet valves. This calls for reconsideration of the cut-off values for prophylactic surgery.

Reproducibility of Visual Assessment of Segmental Wall Motion on Echocardiograms: A Multicenter Study by the Israeli Echocardiography Research Group

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Background: Quantification of wall motion abnormalities (WMA) is of paramount importance in interpretation of echocardiograms. Visual assessment of WMA is widely used but data are lacking on its accuracy. We determined this method's accuracy in expert hands using contemporary echo-technology.

Methods: Echo studies of 105 patients (28 healthy, 62 IHD, 15 DCM) were performed using Vivid 7 (GE) echo machines and analyzed blindedly by 10 experienced readers. Readers scored (1=normal to 4=dyskinetic) 18 segments from 3 apical views per-patient. A segmental "gold-standard" score (GSS) was constructed by the majority score.

Results: Of 1890 segments, 66% were normal by GSS, 30% abnormal and 4% unreadable. The overall readers' **inter-observer** variability when dichotomizing segments into normal (score 1) vs. abnormal (scores 2-4) had a Kappa of 0.65 ($p<0.0001$). For scoring WMA from 1 to 4, Kappa was 0.65, 0.28, 0.5 and 0.26 respectively, mean 0.5 ($p<0.0001$ for all) and Kendall's coefficient of concordance 0.73. **Intra-observer** variability was assessed in 10 patients: for dichotomizing segments (normal/abnormal) mean Kappa was 0.71 (individual reader's Kappas 0.5- 0.91). For scoring WMA from 1 to 4, Kappa was 0.71, 0.36, 0.55, 0.39, respectively, average 0.57 and Kendall's statistic 0.88. Compared to GSS scores: for dichotomizing segments (normal/abnormal) mean Kappa was 0.77 (individual Kappas 0.67-0.84). For scoring segments from1 to 4, Kappa was 0.77, 0.46, 0.65 and 0.37, respectively, mean was 0.64 and Kendall's statistic was 0.90.

Conclusion: Experienced readers had considerable inter- and intra-observer variability in quantifying WMA. Introduction of standardization methods or development of objective/ automated methods are necessary to assist visual WMA assessment.

Posterior Descending Coronary Artery Blood Velocities: Value and Feasibility of Non-invasive Sampling

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Recent developments in echocardiography made transthoracic echocardiography (TTE)-Doppler sampling of coronary artery velocities possible. Left anterior descending coronary artery (LAD) velocities by TTE- Doppler is feasible almost in all subjects even without echo-contrast. Aim: Evaluation of feasibility of TTE-Doppler sampling of posterior descending coronary artery (PDA) velocities. Methods: Forty seven subjects, were studied, 27males, age 51.8±24.9 years, range 6-94 years, weight 74.6±16.7 kg. range 46-111 kg. Sampling of TTE-Doppler of the PDA were attempted from modified apical two-chamber views using 3.5 MHZ transducers. Results: Peak velocities in diastole 51.1±15.9 cm/sec were higher than in systole 23.2±6 cm/sec, $p<0.001$. Time velocity integral in diastole 15.9±5.4cm were higher than in systole 5.1±2.1 cm, $p<0.001$. Diastolic pressure half time averaged 178.3±65 msec and deceleration time 597±212.6 msec. Flow in the PDA in diastole 43.7±20.6 ml/min was higher than in systole 13.8±6.7 ml/min, $p<0.001$. Diastolic to systolic velocity ratio averaged 2.28±0.67, and was less than 1.5 in 3 subjects with severe PDA stenosis. Conclusions: Sampling of Doppler velocities of the PDA using TTE is feasible. Diastolic velocities, time velocity integrals and flows were higher than the systolic parameters. Sampling of PDA velocities may be used in the evaluation of subjects with coronary artery disease and can detect severe PDA stenosis.

Both Lean Hypertensive and Frankly Obese CHD Patients are at Increased Risk for Long-term Mortality

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Background. The issue of excess weight in apparently healthy men and women as a risk factor for disease and mortality has gained increasing interest. Less is know about the significance of weight in coronary heart disease (CHD) patients. This association may differ according to hypertension status.

Patients and Methods. We used data from a screening of 15,700 CHD patients, screened for eligibility to participate in the secondary prevention trial Bezafibrate Infarction prevention (BIP). Follow-up lasted from 1990/2 to 1999, over a mean period of 8 yrs. Mortality was obtained by matching with the National Population registry and incident stroke leading to hospitalization was assessed in a special project. Groups of relative weight were defined as **1** [lean patients] for body mass index (BMI) below 20 Kg/squared meter, **2** for 20-22.99, **3** for 23-24.99, **4** for 25-26.99, **5** for 27-29.99 and **6** for >30 Kg/SqM meters [obese patients]. Multivariate analysis using a proportional hazards model yielded hazard ratio (HR) estimates controlling for age, sex, diabetes, hypertension and MI history.

Results. Among 9520 patients who were normotensive at entry, crude mortality rates during follow-up were 19, 19, 16, 17, 17, and 19% in BMI groups 1 to 6, respectively. Among 4630 hypertensive patients the corresponding rates were 30, 23, 20, 16, 19 and 24%, respectively. These findings, indicating that the "desirable weight" as well as the "mildly overweight" CHD patients (25-27 Kg/SqM) do better were substantiated by a multivariate analysis which produced the following adjusted HRs: 0.87, 0.70, 0.71, 0.76 and 0.93 for groups 2 to 6, with the leanest patients as the reference. Specifically for women, the "mild overweight" group enjoyed the longest survival.

Comments. Lean and obese CHD patients fared worse than "desirable" and so-called "mildly overweight" counterparts over 8 years after being assessed for eligibility in a trial of stable CHD, and the combination of leanness and hypertension appeared particularly undesirable, adding to the accumulating doubts concerning a universal recommendation to maintain weights yielding BMI below 25 Kg/SqM. Dietary and lifestyle advice should be weighed against these and similar findings**.** Further research needs to be pursued examining how these associations interact with patients' ages and previous smoking habits.

Elevated C-Reactive Protein Levels Predict Poorer Cognitive Function Among Coronary Heart Disease Patients

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Background- Chronic low-grade inflammation may be a risk factor for dementia in elderly persons. Our aim was to test the hypothesis that elevated concentrations of high sensitivity CRP (hsCRP) predict poorer cognitive function and in-particular executive function among patients with CHD.

Methods- A subgroup of CHD patients who previously participated in a trial of lipid modification (BIP trial) was assessed. CRP was measured by a high-sensitivity assay from thawed frozen (-70^{0}c) plasma samples collected at baseline. Cognitive scores were assessed more than 10 years later, using a validated set of computerized cognitive tests (Mindstreams Computerized Cognitive Battery; computing index scores summarizing performance in each cognitive domain and a global cognitive score). We compared means of cognitive scores normalized to age and education, between patients in the highest CRP tertile (CRP ≥3.6mg/L) and patients in the lower tertiles.

Results- Among 346 patients (mean age 72±6 yrs, 95% males, 19% diabetics) CRP levels at baseline were inversely correlated with both the global cognitive score (p=0.04) and with executive functions (p=0.02). The mean global and executive scores were lower among patients in the upper CRP tertile as compared to those in the lower two tertiles (91.6±11.3 vs. 95.4±11.3; p=0.004 and 93.3±11.5 vs. 97.9±12.4; p=0.001, respectively).

Conclusions- Increased CRP levels are associated with cognitive impairment and poorer executive functions among CHD patients. These results support the hypothesis that chronic low-grade inflammation may be involved in vascular cognitive impairment.

The Effect of Secondary Prevention on Recurrent MI; Results from the 2004 and 2006 ACSIS Survey

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Background:
The preventive effects of cardiovascular drugs after an acute myocardial infarction (AMI) are well established, but little is known concerning the effect of such secondary prevention on the characteristics of recurrent events. We therefore studied the characteristics of events and the patients who presented with recurrent MI (PMI - Previous MI group), in relation to their secondary prevention medications.

Methods:
Data was summed up from the 2004 and 2006 ACSIS. In the two surveys, there were 1207 PMI patients. This combined group was analyzed according to multiple variables.

Results:
65% of PMI patients were treated prior to admission with 3-4 secondary preventive drugs (platelet inhibitors, beta blockers, angiotensin enzyme inhibitors or statins), 28% with 1-2 drugs and 7% were not treated with any drug. Seven day mortality was 5% for patients with 3-4 drugs, 2% for 1-2 drugs and 0% for the 0 drugs group (P=NS). Thirty day mortality was 6%, 5% and 0%, respectively (P=NS). However, an analysis according to the TIMI score showed that in the high TIMI group, when adjusted for age, diabetes and ST elevations, there was a statistically non-significant opposite trend for lower mortality rates in the 3-4 drugs patients (OR= 0.88, confidence limits 0.49 to 1.61), whereas adjusting for sex, diabetes and ST elevations in the low TIMI group showed no difference in risk of death in patients treated with more or less drugs.

Conclusions:
PMI patients are under-treated with secondary preventive drugs prior to admission. Overall, there is a trend for higher mortality rates in those who are treated with more drugs. However, when adjusted for confounding factors, there is no change in mortality in the low TIMI score patients, and a non significant trend for a reduced death rate for the high TIMI score patients, when treated with more drugs. Thus, the higher risk found in PMI patients treated with more drugs is due to more co-morbidities and risk factors, and not the medical treatment itself.

Low Grade Inflammation in Asymptomatic Healthy Adults During Bouts of Respiratory Tract Infections in the Community: Potential Triggers for Cardiovascular Events

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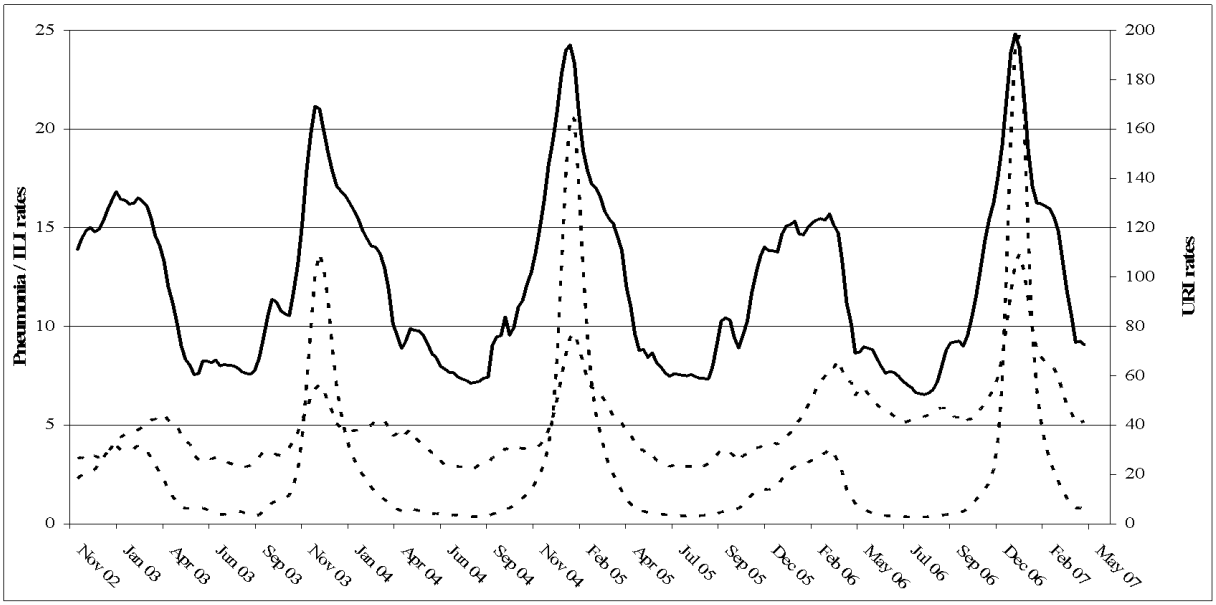
Background: Cardiovascular morbidity and mortality demonstrate a well documented seasonal pattern. We explored the possibility that low grade inflammation is evident in asymptomatic adults during bouts of acute respiratory tract infection/inflammation in the community.

Methods: We examined the concentration of high-sensitivity C-reactive protein (hs-CRP) as well as quantitative fibrinogen in completely asymptomatic adults during a routine screening health program and correlated the results with weekly epidemiological data related to the appearance of acute respiratory tract infection/inflammation in the community (figure 1).

Results: Included were 5315 male and 2795 female at the mean (SD) of 45 (11) years. We demonstrated a statistically significant seasonal variation in the concentrations of hs-CRP and fibrinogen using the cosinor analysis. Following adjustment for a relatively large number of possible confounders, the weekly burden of acute respiratory infection/inflammation had a significant influence on the inflammation-sensitive biomarkers in the asymptomatic cohort. The magnitude of this influence could reach as much as 10% (2%-17%) in hs-CRP concentrations in women and 8.16 (5.44-10.88) mg/dl in fibrinogen concentrations in men.

Conclusion: Changes in the concentrations of two inflammation-sensitive biomarkers can be noted in completely asymptomatic adults at the time of increased burden of acute respiratory tract infection/inflammation in the community. The possibility exists that these inflammatory changes represent occult and asymptomatic infections that could by themselves trigger acute atherothrombotic events.

Respiratory illness rate curves in the community during the time period of the study.



Relation of Exercise Capacity to Sub-Clinical Coronary Artery Disease in Asymptomatic Patients With Type II Diabetes

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Background: Patients with type 2 diabetes mellitus (DM) may have limited exercise capacity (ExC) despite no clinical history of coronary artery disease (CAD). The importance of sub-clinical CAD in determining ExC is unclear. We examined relation of ExC to sub-clinical CAD, defined by 64 slice coronary computed tomographic angiography (CTA), in diabetic subjects with no history of CAD.
Methods: 423 pts (63±5.3 yrs, 56% women) enrolled in an ongoing prospective study of cardiovascular outcomes in asymptomatic subjects with DM, underwent 1) maximal, symptom limited graded treadmill exercise testing to define ExC (in metabolic equivalents [Mets]) and ECG defined, exercise induced, myocardial ischemia and 2) CTA to define presence of significant (>50%) coronary luminal stenosis, non-obstructive coronary atheroma and coronary calcium score.
Results: Determinants of peak exercise capacity differed in men and women. In men coronary plaque was related to duration of exercise but not in women (Table).Duration of DM correlated with duration of exercise in women (r=0.27, p=0.001) but not in men (r=0.09, ns).

Exercise Capacity

	METS(MEN)	P-VALUE	METS (WOMEN)	p-value
Calcium score <median	11.2±2.3		7.8±2.1	
Calcium score >median	9.6±2.6	<0.001	7.3±2.2	ns
Plaque any +	10.1±2.6		7.6±2.1	
Plaque any -	12.2±1.9	<0.001	7.5±2.4	ns
Multi-vessel plaque+	9.8±2.5		7.2±2.1	
Multi-vessel plaque-	11.6±2.3	<0.001	7.8±2.3	0.07
Stenosis+	9.8±2.5		7.1±2.4	
Stenosis-	10.8±2.6	0.06	7.6±2.1	ns
Multi-vessel Stenosis +	9.4 ±2.0		6.7±2.4	
Multi-vessel Stenosis -	10.5±2.6	ns	7.6±2.2	ns

Conclusions: In **men** peak exercise capacity decreased in presence of non-obstructive or obstructive coronary artery disease on CTA but was was unrelated to longer history of diabetes mellitus. In **women** peak exercise capacity was not significantly related to presence of sub-clinical coronary artery disease but correlated inversely with duration of DM.

Combined Assessment of C-Reactive Protein and Uric Acid Levels for Risk Stratification in Coronary Heart Disease Patients

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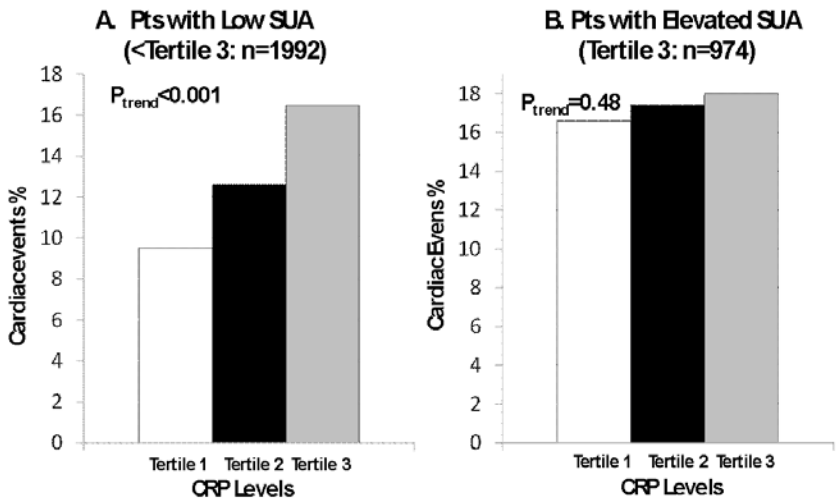
Background: C-reactive protein (CRP) is an established risk factor for cardiac events in coronary heart disease (CHD) patients. Recently, elevated serum uric acid (SUA) was also suggested to be associated with adverse outcome in this population. We hypothesized that combined assessment of CRP an SUA would provide incremental prognostic information to single marker measurement.

Methods: The risk of major cardiac events (comprising fatal or nonfatal myocardial infarction or sudden cardiac death) during mean follow-up period of 6.2 years was related to increasing tertiles of CRP and SUA levels, in a population of 2966 CHD patients enrolled in the Bezafibrate Infarction Prevention (BIP) trial.

Results: The rate of major cardiac events was directly related to increasing tertiles (1 to 3) of both CRP (11.4%, 14.2%, and 17.3%, respectively; p for trend < 0.001) and SUA (12.6%, 12.9%, and 17.6%, respectively; p for trend = 0.002). However, when combined assessment of the 2 markers was employed, CRP levels were shown to be associated with adverse outcome only in patients with low SUA (Figure 1A), whereas among patients with elevated SUA cardiac event rate was increased at all levels of CRP (Figure 1B). Consistently, in multivariate analysis elevated CRP was independently associated with outcome in patients with low SUA (HR=1.55; p=0.007), but was not a risk factor among patients with elevated SUA (HR=1.04; p=83).

Conclusions: Combined assessment of CRP and SUA improves risk stratification in CHD patients. Patients with elevated SUA exhibit a high risk of cardiac events regardless of CRP levels.

Figure 1: Rate of Cardiac Events by CRP Tertiles



Aspirin Resistance among Stable Coronary Artery Disease Patients

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Background: Low response to aspirin has been associated with adverse clinical outcome. There is limited data that characterizes patients with stable coronary artery disease (CAD) who are resistant to the anti-platelet effects of aspirin. Our objectives were to identify the prevalence and the characteristics of patients with stable CAD who have reduced anti-platelet response to aspirin treatment.

Methods: We evaluated 227 stable patients with CAD who have been treated with aspirin for at least one week. Aspirin resistance was defined by at least 2 of 3 criteria: VerifyNow Aspirin (Accumetrics) score≥550, 5μM adenosine diphosphate-induced platelet aggregation ≥70% and 0.5mg/ml arachidonic acid-induced platelet aggregation ≥ 20%.

Results: Of the patients studied 13 (6%) were aspirin resistant. Aspirin resistant patients were more likely to be women and less likely to have hypertension. Other characteristics are shown in the table.

Conclusions: A relatively low percentage of patients with stable CAD are resistant to the effect of aspirin. The main clinical feature found in our study is a higher proportion of women among aspirin resistant patients. This finding may contribute to the low benefit of aspirin treatment in women, recently reported in primary prevention trials.

	Aspirin resistant (n=13)	Aspirin sensitive (n=214)
Age (years)	68.8±9.6	68±9.7
Gender (women)	38.5%*	13.6%*
Weight (kg)	70.7 ±12.8†	77.5±12.9†
Height (cm)	163.5±9.1*	169.1±8.5*
BMI (kg/m^2)	26.5±4.6	27±3.6
Diabetes Mellitus	30.8%	41.5%
Hypertension	38.5%†	63.8%†
Hypercholesterolemia	84.6%	78.7%
Smoker	22.2%	17%
Family History	58.3%	57.9%
Previous MI	61.5%	58.1%
Previous PCI	84.6%	90.5%
Previous CABG	53.8%	36.9%
Clopidogrel	7.7%	21.1%
Statins	100%	89.5%
Beta Blockers	69.2%	69.3%
ACE Inhibitors	61.5%	58.5%
*p<0.05, †p=0.06		

Prevalence of Migraine in Patients with Patent Foramen Ovale

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Introduction: Migraine is a common neurological disorder with a prevalence of 11-12% in the general population and a great impact on the quality of life and on social activities. Patent foramen ovale (PFO) is an inter-atrial left-to-right shunt with a prevalence of 25% in the general population. Recent epidemiological data suggest a bidirectional link between PFO and migraine with aura. PFO closure might improve migraine symptoms and serves as an effective treatment modality for migraines. **Objectives:** To investigate the prevalence of migraine with and without aura in a consecutive unselected cohort of young patients with PFO. **Methods:** Patients with PFO between 18-65 years of age were retrieved from database of the echocardiography laboratories at the Meir and Soroka medical centers. Patients were interviewed by phone for headache and migraine using a standard migraine questionnaire and MIDAS questionnaire for quality of life. **Results:** One hundred and eighty-four patients with PFO were included. The prevalence of headache was 51%. Thirty-six percents fulfilled criteria for migraine compared to 12% in the general population ($p<0.001$). Fifty percents of the migraine sufferers had migraine with aura compared to 5-15% in the general population ($p<0.001$). **Conclusions:** Our findings confirm previous observations of higher incidence of migraine with aura in patients with PFO compared to the general population. Echocardiography study should be included in the workup of patients with migraine especially in migraine with aura.

High Frequency ECG – a Novel Tool for Improving the Diagnostic Accuracy of Exercise Testing in the Community Setting

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ECG based detection of exercise-induced myocardial ischemia relies on identifying ST changes, representing the repolarization phase. Recently, a new technology utilizing high-resolution ECG was reported to better identify stress-induced ischemia. This approach quantifies subtle ischemic-induced changes in the depolarization phase using analysis of high frequency QRS components (HFQRS). Our aim was to test the clinical applicability of this novel technique in a large patient population in three community cardiology centers.

Methods: High-resolution ECG was acquired (HyperQ™ System, BSP, Israel) during clinically indicated exercise test (ETT) in 1205 consecutive patients (age 57±9 yo, 64% men). The relative intensity change of HFQRS components (HyperQ™) during exercise was used as an index of ischemia. HFQRS data were evaluated automatically using computerized analysis. Patients with evidence of ischemia in exercise ECG or HFQRS data, or those with inconclusive test results were referred for follow-up imaging tests (FIT; stress echocardiography, SPECT perfusion imaging, CT angiography, or angiography, n=172). The follow-up imaging tests were used as the gold standard for presence of IHD.

Results: Based on FIT results, addition of HFQRS to ETT significantly improved specificity (74% combined vs. 51% for ETT alone, $p<0.005$) and enhanced accuracy (76% combined vs. 59% for ETT, $p<0.05$), although sensitivity was similar. Negative predictive value of HFQRS was > 93% irrespective of ETT result. The positive predictive value for patients with positive ETT and positive HFQRS was 86%. HFQRS was particularly useful in patients with inconclusive ETT.

Conclusions: This is the first large scale study to evaluate the utility of the HFQRS technique in a realistic clinical scenario. HFQRS analysis is complementary and additive to conventional ETT. Integrating HRQRS into the clinical decision process could markedly improve the standard of care and decrease unnecessary invasive procedures.

Ectatic Coronary Arteries are Associated with Peripheral Vascular Endothelial Dysfunction in Patients with Chest Pain

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Background: Endothelial dysfunction is an important prognostic factor in determining atherosclerosis. Prognosis, treatment, and etiology of coronary artery ectasia, abnormal enlargement of coronary arteries, remain unresolved. Current literature suggests that even without the presence of coronary stenosis, ectatic coronary arteries are subject to thrombus formation, vasospasm, and spontaneous dissection.

Objective: To evaluate the association of flow-mediated dilation (FMD), assessed by brachial artery vasoreactivity in patients with chest pain and ectatic coronary arteries.

***Methods and Results*:** FMD in 40 subjects with chest pain and ectatic coronaries [35 (88%) men, mean age 66±9 years, mean body mass index 28±5 kg/m^2] was compared to FMD in 40 age- and sex-matched patients with chest pain and normal coronaries. After overnight fasting and discontinuation of all medications for ≥12 hours, percent improvement in endothelium-dependent brachial artery FMD (%FMD) and endothelium-independent nitroglycerin (%NTG)-mediated vasodilatation were assessed using high resolution(15 MHz) linear array ultrasound (Table).

	Ectatic Coronaries (n=40)	**Normal Coronaries (n=40)**	**p-value**
Systolic BP (mmHg)	142±22	144±2	0.77
Diastolic BP (mmHg)	82±10	78±9	0.36
Resting heart rate (bpm)	63±9	65±10	0.76
Brachial artery diameter (mm)	6.25±0.93	5.24±0.98	<0.0001
%FMD	7.2±5.0	12.0±5.0	<0.001
%NTG	12.1±4.8	14.3±5.1	0.38

Values are expressed as mean±SD; BP=blood pressure; %FMD, %NTG=% change from baseline in brachial artery diameter caused by FMD and NTG, respectively.

Conclusions: Ectatic coronary arteries in patients with chest pain are associated with endothelial dyfunction, compared to normal coronary arteries, suggesting a potential mechanism whereby ectatic coronaries contribute to cardiovascular risk. Long-term follow-up is warranted to further elucidate our findings.

Dual Therapy with Statins and Antioxidants is Superior to Statins Alone in Decreasing the Cardiovascular Disease Risk of Individuals with Diabetes Mellitus and the Haptoglobin 2-2 Genotype

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Background. Oxidative stress is an important mediator of DM atherosclerosis. Paradoxically, antioxidants have not been found to provide CVD benefit to DM individuals. The Haptoglobin gene, an antioxidant protein, is polymorphic in man with two classes of alleles denoted 1 and 2. Diabetic individuals with the Haptoglobin 2-2 genotype, have increased CVD risk. These individuals have high oxidative stress and may benefit from antioxidant therapy. We sought to determine if antioxidant therapy could be demonstrated to provide benefit to Haptoglobin 2-2 DM individuals also taking statins which are currently recommended for all DM individuals.

Methods. The ICARE was a double blind prospective study in 1434 DM individuals with the Haptoglobin 2-2 genotype randomized to vitamin E or placebo. We showed a 50% decrease in CVD events (MI, stroke, CVD death) with Vitamin E treatment. We present here a secondary analysis of the CVD event rate in ICARE stratified by vitamin E and statin use.

Results. The event rate among individuals who did not receive antioxidants or statins was 6.1%. As expected we found that statins reduced the event rate in this population compared to individuals who did not take statins. However, unexpectedly we found that the addition of vitamins to statin treatment dramatically reduced the event rate (4.1% vs. 1.3%, $p<0.01$), significantly more than statin or vitamin E treatment alone.

Conclusions. Dual therapy with antioxidants and statins appears to provide superior cardiovascular protection to Hp 2-2 DM individuals as compared to statins alone.

Exercise ECG Testing: Low Tech, High Impact

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Background: Currently, reliance on noninvasive imaging tests and cardiac catheterization in diagnosing the etiology of chest pain (CP) raises questions about the role of exercise EGC testing (EET) in its evaluation. We assessed the impact of EET on the diagnosis and management of hospitalized pts with CP.

Methods: Pts hospitalized with CP without dynamic ECG changes and troponin elevation were referred to treadmill EET. Internal medicine physicians responsible for the pts completed a questionnaire pre and post EET which included a hypothetical question about the management of those pts if EET could not be performed.

Results: Physicians filled out the questionnaire for 57 pts, age 51 ± 10 years, 32/57 considered to be of low probability for ischemic heart disease and 25/57 pts of intermediate probability. Based on EET results, physicians confirmed their clinical diagnosis in 68%, modified their diagnosis in 28%, and EET was unhelpful in 4% of the pts. Level of physicians' confidence in their diagnosis at pre-test was 6 (from 1 to 10) and rose to 9 post-test. EET had major impact on the continuing management of the referred pts (Table1) by allowing physicians to discharge 61% (35/57) of the pts who otherwise would have remained hospitalized for additional diagnostic procedures. No major cardiac events were noted as a consequence of the EET study.

Conclusions: For many hospitalized pts with CP, EET is a safe procedure that helps physicians to increase their diagnostic rate and diagnostic level of confidence. EET renders significant benefit in the management of these pts by modifying diagnostic strategies, shortening hospitalization, and avoiding inappropriate discharge.

Table1

PRE-EET			**POST-EET. Discharged**
Candidate for	Cardiac catheterization	6	5
	Non invasive imaging test	15	12
	In hospital follow-up	9	8
	Discharged	27	26