

## **The Use of Drug Eluting Stents in Regular Clinical Practice did not Reduce the Clinical Restenosis Rate Compared to Bare Metal Stents.**

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**Background:** Compared to BMS ,DES reduce the angiographic restenosis rate post PCI significantly in patients with ACS or stable angina. The effect of DES implantation ,in the usual indications, on symptomatic restenosis rate was not elucidated yet.

**Hypothesis:** In patients post PCI there is no effect of DES on clinical restenosis rate compared to BMS.

**Methods and Results:** We compared two periods of nine months each ,before and after the approval of the DES in regular clinical practice base.

We inserted DES in 20 percents of patients in the second group according to the regular indications ,instent restenosis and long lesions.

Three hundreds fifty eight patients were included in the BMS only group. Re-PCI was performed in 56 patients who suffered from clinical restenosis (16 percent). The DES plus BMS group included 413 patients and 58 patients suffered from clinical restenosis (14 percent). There was no significant difference in clinical restenosis rate between the two groups (P=0.54 ,RR=1.07 ,CI:0.9-1.3).

**Conclusion :** Compared to BMS ,DES has no effect on the clinical restenosis rate post PCI .

## The Impact of Diabetes Mellitus on Drug Eluting Stents Outcomes at One-year Following Acute ST Elevation Acute Myocardial Infarction

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**Background:** Little is known about the late outcome of patients with diabetes mellitus (DM) who receive DES during the course of STEMI.

**Objective:** We investigated the clinical outcomes of diabetic (DM) versus non DM patients with ST elevation AMI treated using DES.

**Methods:** We used our clinical database consisting of all pts treated with DES in primary PCI for STEMI. Patients with cardiogenic shock were excluded. We compared the procedural and angiographic results and clinical outcome at 1-year in DM versus non-DM pts.

**Results:** Of 162 patients with AMI 38(23.5%) had DM, clinical characteristic, short and long-term outcome are summarized in the **Table**:

|   | <b>No DM<br/>N=124</b> | <b>DM<br/>N=38</b> | <b>P-value</b> |
|---|------------------------|--------------------|----------------|
| Age (years)                               | 58±12                  | 60±12              | 0.4            |
| Males (%)                                 | 90                     | 79                 | 0.06           |
| GFR (<60 mL/min/1.73 m <sup>2</sup> ) (%) | 8.9                    | 13                 | 0.002          |
| Killip class >1 (%)                       | 10                     | 8                  | 0.2            |
| Anterior MI (%)                           | 63                     | 66                 | 0.8            |
| 2/3-vessel disease (%)                    | 56                     | 71                 | 0.01           |
| Ejection fraction <40% (%)                | 41                     | 50                 | 0.4            |
| Successful PCI (%) <sup>†</sup>           | 95                     | 97                 | 0.7            |
| CADILAC risk score                        | 3.5±3                  | 4.6±3.4            | 0.07           |
| 1 year outcome                            |                        |                    |                |
| Death (%)                                 | 2.9                    | 5.4                | 0.5            |
| Re-AMI (%)                                | 0.8                    | 0                  | 0.5            |
| Target vessel revascularization (%)       | 7.7                    | 0                  | 0.08           |
| CABG (%)                                  | 2.9                    | 5.4                | 0.5            |
| Stent thrombosis (%)                      | 1                      | 0                  | 0.5            |
| MACE <sup>+</sup>                         | 12.5                   | 10.8               | 0.8            |

<sup>†</sup> TIMI 3 and residual stenosis <30%, <sup>+</sup>MACE= Death, re-AMI, TVR

**Conclusions:** DES implantation in STEMI in diabetic and non-diabetic appears safe with similar incidence of death, myocardial infarction and stent thrombosis up to 1 year although target vessel revascularization (TVR), albeit low, appears to be concentrated among diabetic patients implanted using DES.

## Urgent Coronary Catheterization in the Daily Practice: Indications and Changes Over 10 Years

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Increasing number of urgent coronary catheterizations (UCC) is performed over the last years. Primary percutaneous intervention (PPCI) for ST-elevation myocardial infarction (STEMI) is currently considered as the main indication for urgent catheterization.

**Objectives:** To assess the indications for UCC over the last 10 years.

**Methods:** Different rate of coronary intervention was noticed in two different periods: During January 1998 to December 1999 (old period) 587 PCI of 2414 cardiac catheterization (24%), and during November 2005 to October 2007 (new period) 1588 PCI of 3404 (47%) were performed.

**Results:**

UCC was performed in 72/2414 (3%) patients at the old period and in 241/3404 (7%) in the new period ( $p < 0.0001$ ). Patient's characteristics and the indications for UCC in both periods are presented in the following table:

|  | Old period<br>(n=72) | New period<br>(n=241) | P value |
|--|----------------------|-----------------------|---------|
| Mean age (years±SD)                            | 60.1±13.7            | 62.2±14.3             | <0.0001 |
| Women  | 22%                  | 19%                   | NS      |
| <u>Indications for urgent catheterization:</u> |                      |                       |         |
| - Primary PCI for STEMI (Killip 1-3)           | 49 (68%)             | 204 (85%)             | 0.0017  |
| - Cardiogenic shock                            | 12 (17%)             | 13 (5%)               | 0.002   |
| - Treatment of stent thrombosis                | 4 (6%)               | 20 (8%)               | NS      |
| - Other indications                            | 7(10%)               | 4(2%)                 | 0.001   |
| In-hospital major adverse cardiac events       | 9 (12%)              | 15 (6%)               | 0.08    |

**Conclusion:** The increasing number of urgent catheterizations in our institute over the recent years was due to primary PCI for STEMI and treatment of stent thrombosis.

## **Late Drug Eluting Stent Thrombosis: Clinical, Angiographic and Intravascular Ultrasound Characteristics**

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Late stent thrombosis (LAST) after drug-eluting stent (DES) implantation has been the focus of intense interest because of its attendant morbidity and mortality. Its cause remains unknown.

**Objectives:** To describe the clinical, angiographic and intravascular ultrasound (IVUS) characteristics of patients who presented with LAST after DES implantation.

**Methods:** We studied 6 patients who were admitted to our institute in the last 2 years with LAST after DES implantation. All patients underwent immediate percutaneous coronary intervention (PCI) of whom IVUS was performed to 4 patients.

**Results:** Four males and 2 females, mean age  $56.6 \pm 15.4$  years, 5/6 (83%) diabetic.

In 3 patients the DES was implanted after ST-elevation myocardial infarction (STEMI) and 3 patients for stable angina pectoris. All primary lesions were de-novo, 4/6 (67%) type C. Mean period from stent implantation to thrombosis was  $16.7 \pm 8.8$  months. Thrombosis had occurred after 2 days and more than 1 month after clopidogrel cessation, in 1 and 5 patients respectively. All patients were stable on aspirin monotherapy.

Clinical presentations were STEMI in 4(67%) and non-STEMI in 2 patients. All patients had total thrombotic occlusion of the stented area. IVUS data demonstrated: incomplete stent apposition in 2 patients, underexpansion of the stent in 1 patient and normal apposition and expansion in 1 patient. One patient died during hospitalization.

**Conclusion:** LAST may appear when patients are stable on aspirin monotherapy more than one year after DES implantation. Incomplete stent apposition and underexpansion may contribute to stent thrombosis.

**Management of Stable Coronary Disease Actual Practice and the Courage Trial**

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Background: The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial showed that coronary interventional procedures added little to optimal medical therapy with respect to the long-term outcome of patients with stable coronary disease when used as initial therapy.

Aim: To review the clinical and angiographic characteristics of patients undergoing elective cardiac catheterization in a large cohort of patients in Israel and to compare it to patients included in the Courage trial (C).

Methods: Catheter reports of patients undergoing elective cardiac catheterization at public and private hospitals were analyzed. Analysis was targeted to those patients having the "same" entry criteria as those (C).

Results: 1060 patients from private hospitals and 474 patients from public hospitals were included- Cohort

|         | Age<br>(years) | Males<br>(%) | Angina<br>(%) | Previous<br>PCI (%) | Previous<br>CABG<br>(%) | 1VD<br>(%) | Prox.<br>Lad<br>(%) |
|---------|----------------|--------------|---------------|---------------------|-------------------------|------------|---------------------|
| Cohort  | 63             | 86           | 72            | 40                  | 20                      | 36         | 23                  |
| Courage | 61             | 85           | 88            | 15                  | 11                      | 31         | 31                  |

Conclusions: 1. Asymptomatic patients are frequently catheterized. 2. Previously revascularized patients undergo a high rate of recatheterization. 3. Our patients have less severe coronary anatomy than in Courage.

Clinical implication: Many patients with stable coronary disease some asymptomatic are undergoing PCI as the first medical intervention, It is time to practice optimal medical therapy before referring stable patients to unnecessary and expensive invasive procedures.

## Nitroglycerin Administration into the Left Main Coronary Artery: Immediate Hemodynamic Effects and Mechanism

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**Background:** Nitroglycerin (NTG) is administered frequently intracoronary during coronary angiography. We studied the hemodynamic effects of NTG injection into the left main coronary artery (LMCA).

**Methods:** NTG 150 micrograms was given as bolus into LMCA, ascending aorta (AA), right ventricle (RV), femoral artery (FA) and femoral vein (FV). Pulse and blood pressure (BP) were continuously recorded at the RV/PA and aorta. Cardiac output (CO) and stroke volume (SV) were calculated by simultaneous echocardiogram.

**Results:** Injection of NTG into AA and LMCA induced a similar and significant drop in systemic BP that started within 1.54 and 1.2 sec and reached a trough low at 12.5 and 12.9 sec, respectively. Injection into RV and FV caused slower immediate (10.3 and 17.1 sec) and maximal (24.5 and 43.8 sec) response. Stroke volume decreased after injection to AA. CO and SV remained constant after injection to LMCA, FA and FV.

| Inj site                       | LMCA            |       | AA              |       | RV             |       |
|--------------------------------|-----------------|-------|-----------------|-------|----------------|-------|
|                                | Base            | NTG   | Base            | NTG   | Base           | NTG   |
| SYS BP AO (mmHg)               | 142.3           | 126.1 | 131.8           | 103.9 | 135.7          | 115.4 |
|                                | <i>P=0.0001</i> |       | <i>P=0.0001</i> |       |                |       |
| Time to start of BP drop (sec) |                 | 1.2   |                 | 1.54  |                | 10.3  |
| Time to trough (sec)           |                 | 12.5  |                 | 12.9  |                | 24.5  |
| SV (ml)                        | 65              | 65    | 70.7            | 63.3  | 67.1           | 63.7  |
|                                | <i>P=NS</i>     |       | <i>P=0.047</i>  |       | <i>P=0.154</i> |       |
| CO (l/min)                     | 4.07            | 4.01  | 3.98            | 3.76  | 4.38           | 4.12  |
|                                | <i>P=NS</i>     |       | <i>P=0.21</i>   |       | <i>P=0.14</i>  |       |

**Conclusions:** NTG injected into the AA and LMCA induced systemic BP reduction through different mechanisms. NTG injected into AA induced direct vasodilation and secondary (statistically significant) reduction in SV and (non-significant) reduction in CO. NTG administered into the LMCA induced immediate drop of BP that was not caused by either direct effect on systemic or pulmonary vascular bed, nor by decrease in SV and CO. A proposed mechanism might be reflex systemic vasodilation through coronary receptors.

## **A New Method for Femoral Sheath Withdrawal Using Elastic Bandage Compression**

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**Background:** Hemostasis of femoral puncture by manual or mechanical devices is painful, and is time and effort consuming. We present a simple method for femoral artery puncture site hemostasis used in our department during the last 13 years.

**Methods:**

**Femoral homeostasis:** Upon sheath withdrawal gauzes folded to a cone shape are compressed by elastic bandage (EB) applied from the patient's left lower back (for right femoral puncture) towards the right groin, surrounding the right thigh to the patient's belly and then to his right lower back in an 8 shape. Bandage tension is adjusted to maintain pressure while keeping palpable peripheral pulse.

**Method evaluation:** The EB was used in 100 consecutive patients who underwent diagnostic coronary angiography or angioplasty. Conventional manual or mechanical pressure was then used in another 100 consecutive patients (CM group). All patients underwent femoral Duplex on the day after procedure.

**Results:** Ninety five percent of the arterial sheaths were 6F and 5% were 8F diameter. Compression in group CM included manual in 85%, Compressar (AVD™) in 10%, and Femo-Pump in 5%. The median time needed was 90±35 seconds and 16±6 minutes in the EB and CM groups, respectively (p<0.001). On duplex, 1 patient in each group had small pseudo-aneurysm resolved with local compression. Three patients in the EB group had hematomas – one small and two medium size, neither needed blood transfusion. Four patients in group CM had hematomas and one needed blood transfusion.

**Conclusions:** EB compression can be used for femoral homeostasis following coronary angiography and angioplasty, with comparable outcome to conventional compression. EB saves medical staff time and effort and seems to cause less discomfort to the patient.

## Drug Eluting Stents in Diabetic Versus Non-diabetic Patients with Saphenous Venous Graft Occlusive Disease

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**Background:** The safety and efficacy of drug-eluting stent (DES) implantation for the treatment saphenous venous graft (SVG) lesions remains uncertain and the impact of diabetes mellitus (DM) on long-term outcomes is not well established

**Objective:** To evaluate clinical and angiographic outcomes of DES implantation in SVG lesions in diabetic versus non-diabetic patients.

**Methods:** Data from consecutive patients who underwent PCI of SVG were imputed into a dedicated clinical database. We compared the procedural and angiographic results and clinical outcome at 1-year in DM versus non- DM patients.

**Results:** Of 74 patients with SVG treated with DES 41 (55%) had DM, clinical characteristic, long-term outcome are summarized as follow:

|                                     | <b>No DM<br/>(N=33)</b> | <b>DM<br/>(N=41)</b> | <b>P-value</b> |
|-------------------------------------|-------------------------|----------------------|----------------|
| Age (years)                         | 72±8                    | 69±9                 | 0.01           |
| Males (%)                           | 91                      | 88                   | 0.7            |
| Acute coronary syndrome (%)         | 70                      | 75                   | 0.8            |
| Age of the grafts (years)           | 11.2±4.8                | 10±5.3               | 0.3            |
| Degenerated vein grafts (%)         | 31                      | 40                   | 0.4            |
| Slow/No- reflow (%)                 | 0                       | 7                    | 0.1            |
| Distal protection (%)               | 36                      | 43                   | 0.5            |
| <b>1 year outcome</b>               |                         |                      |                |
| Death (%)                           | 0                       | 0                    | 1              |
| Re-AMI (%)                          | 3                       | 4.9                  | 0.7            |
| Target vessel revascularization (%) | 6.3                     | 9.8                  | 0.7            |
| Acute stent thrombosis              | 2.6                     | 2                    | 0.7            |
| MACE <sup>+</sup>                   | 12.5                    | 12.8                 | 0.8            |

<sup>+</sup>MACE= Death, re-AMI, TVR

**Conclusions:** DES implantation in SVG lesions in diabetic and non-diabetic appears safe with similar incidence of death, myocardial infarction, target vessel revascularization and stent thrombosis up to one year.

## **Comparison of Late Versus Early Stent Thrombosis: 5-Year Experience from a Large Unselected Population**

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**Background:** It has been recently implicated that the risk for stent thrombosis (ST) extends for many months after stent implantation. We sought to investigate differences between early and late ST in a broad unselected population.

**Methods:** Data on all consecutive cases of angiographic ST from January 2003 to October 2007 was analyzed. During this period 8,849 stents (6,737 bare metal stents and 2,112 drug-eluting stents) were implanted in 5,141 patients. We compared early (0-30 days) versus late (>30 days) ST regarding the clinical attributes, angiographic findings, treatment and short-term outcome.

**Results:** Angiographic ST was reported in 63 patients (45 males, mean age  $66\pm 12$ ): 44 (70%) early and 19 (30%) late cases. The median time (25-75% interquartile range) from stent deployment was 6 (2-87) days, with the last cases occurring more the 3 years after stent implantation. The majority of patients presented as ST-elevation MI in both late and early cases (84% vs. 93%,  $p=0.36$ ), but late cases tended to be younger ( $62\pm 12$  vs.  $68\pm 11$ ,  $p=0.06$ ), and to be in a worse clinical condition (Killip class III-IV 26% vs. 16%,  $p=0.08$ ). Angiographically, in late cases the thrombosed stent tended to be more likely a drug-eluting stent (57% vs. 35%,  $p=0.14$ ), and to less likely occur in the left anterior descending artery (53% vs. 71%,  $p=0.09$ ). The need for additional stenting was much more frequent in early cases (42% vs. 5%,  $p=0.04$ ). A few in-hospital fatalities were observed in both groups (2 early and 1 late).

**Conclusions:** Early and late stent thrombosis might be associated with different clinical and angiographic profiles. More early cases needed treatment with additional stenting, implying for different mechanisms for stent thrombosis.

## One-Year Outcomes of Consecutive Patients Undergoing Percutaneous Coronary Intervention. Single Israeli center and European perspective- A Report from the PCI Registry, European Heart Survey

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**Background:** The European Percutaneous Coronary Intervention (PCI) registry is conducted to evaluate the current practice and outcomes of PCI for different indications in an unselected population in different centers and nations across the continent.

**Aim:** To compare the in-hospital and 1-year follow-up outcomes of patients undergoing PCI at Rambam medical to other participating European centers.

**Methods and results:** A total of 7894 consecutive patients underwent PCI in participating centers that provided 1-year follow up data. Of them, 7807 (99%) pts were discharged alive. Long term follow-up was available for 5666 (73%) patients. At Rambam medical center, the rate of follow-up was 90% (79/88 pts). Baseline characteristics, procedural data and one year follow up outcomes are presented in the table:

| Baseline characteristics and procedural data |                       |                | One year follow up    |                       |                |
|--|-----------------------|----------------|-----------------------|-----------------------|----------------|
|  | Rambam medical center | European sites |                       | Rambam medical center | European sites |
| Number of pts                                | 88                    | 12 307         | Number of pts         | 79                    | 5666           |
| Diabetes mellitus                            | 30%                   | 25%            |                       |                       |                |
| STEMI  | 27%                   | 24%            | Alive at 1-y          | 98.7%                 | 95.9%          |
| Acute coronary syndrome                      | 61%                   | 46%            | MACCE:                | 3.8%                  | 6.6%           |
|  |                       |                | Death                 | 1.3%                  | 4.1%           |
|  |                       |                | Non-fatal MI          | 2.5%                  | 1.8%           |
|  |                       |                | Non-fatal stroke      | 0%                    | 0.9%           |
| Drug eluting stent                           | 46%                   | 42%            | Hospital readmission  | 19.2%                 | 27.7%          |
| Free from periprocedural complications       | 94%                   | 94%            | CABG                  | 1.3%                  | 1.9%           |
| In hospital stent thrombosis                 | 1.1%                  | 0.6%           | PCI                   | 5.1%                  | 10.1%          |
| In hospital mortality                        | 0%                    | 1.5%           | Late stent thrombosis | 0%                    | 1.1%           |
| In hospital reinfarction                     | 2.3%                  | 1.8%           | NYHA III-IV           | 5.1%                  | 6.7%           |
|  |                       |                | Medication at 1-y     |                       |                |
|  |                       |                | Aspirin               | 89.6%                 | 91.7%          |
|  |                       |                | Clopidogrel           | 20.8%                 | 37.5%          |
|  |                       |                | Beta blockers         | 66.7%                 | 77.1%          |
|  |                       |                | ACE-I                 | 37.3%                 | 59.9%          |
|  |                       |                | Statins               | 81.8%                 | 85.4%          |

**Conclusions:** By applying current guidelines, patients selected for treatment by PCI for all clinical indications have very good in-hospital and post discharge 1-year outcomes. With the reported penetration of drug eluting stents, the rate of MACCE, recurrent PCI and stent thrombosis are low.

## Mechanical Facilitation of Primary Coronary Interventions – Is it Possible?

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**Background:** Primary coronary intervention is now the preferred strategy for the treatment of STEMI.

Given the pathophysiologic role of intra-coronary thrombus generation and occlusion, aspiration thrombectomy technique may be an attractive approach.

**Purpose:** To assess the mechanical yield of thrombus aspiration with the Pronto device in primary PCI.

**Patients and methods:** We reviewed the reports and digital data of all patients admitted to the cathlab with acute ST elevation coronary syndrome, who underwent urgent Primary PCI, with total occlusion of infarct related artery – TIMI 0 coronary flow on diagnostic coronary angiography. The use of aspiration thrombectomy (PRONTO technique) and implementation of different intravascular interventions such as balloon pre-dilatation as opposed to direct coronary intervention (direct stenting or PTCA-POBA), were investigated.

**Results:** Between June-November 2007, 66 patients with STEMI were treated.

Sixty four patients underwent primary coronary intervention, 2 were urgently transferred for surgery. 38 patients presented with total occlusion of the IRA with TIMI 0 coronary flow on diagnostic angiography. Aspiration thrombectomy was used in 24 cases (based on operator's discretion). In 21 cases aspiration was the first intravascular intervention performed – "Pronto-First" group. In 17 other cases aspiration was either not performed (14 cases) or was used later after another intravascular intervention had been performed (3 cases – all because distal embolization or non-reflow phenomenon) – "Non-Pronto" group.

In the Pronto-first group, pre-dilatation was performed in 7 (33.3%) cases and direct stenting became feasible in 14 (66.7%); in the "Non-Pronto" group, pre-dilatation was performed in 8 (47.1%) and direct stenting in 9 (52.9%) of cases.

Whenever aspiration technique was implemented – either as the first intervention or later during PCI, it resulted in mild improvement of TIMI flow, average from 0 to 1.7 in both groups. The resulting TIMI coronary flow was similar in both groups 2.86 in "Pronto-First" vs 2.78 in the second group.

**Conclusion:** The application of aspiration technique by Pronto in primary PCI, may reduce the need for balloon pre-dilatation, and may result in less intimal injury associated with the procedure.

## **Transient Rises in Serum Creatinine Following Coronary Angiography and the Risk of Long-Term Mortality**

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Current data regarding the long-term implications of transient serum creatinine (SCr) rises following coronary angiography are limited. We prospectively followed-up, during a median period of 4.9 years, 78 patients with chronic renal insufficiency who underwent coronary angiography with or without intervention. All patients received intravenous 0.45% saline (1ml/kg of body weight per hour) 12 hours prior to and after coronary angiography, and were further randomly assigned to either acetylcysteine (600 mg orally t.i.d.) or placebo. There was a transient increase of  $\geq 0.5$  mg/dL in SCr concentration or  $>25\%$  increase above baseline 48 hours after coronary angiography in 10 of the 78 patients (13%). All changes were no longer evident 7 days after coronary angiography. At 5 years of follow-up, the cumulative probability of death from any cause was significantly higher among patients who developed post-coronary angiography transient SCr rises (90%) as compared with those who did not (32%;  $p<0.001$ ). In multivariate analysis, an older age ( $\geq 70$  years: HR=2.68;  $p<0.001$ ), a lower ejection fraction ( $\leq 40\%$ : HR=2.38;  $p=0.001$ ), and transient SCr rises (HR=2.60;  $p<0.001$ ) were identified as independent predictors of long-term mortality, whereas administration of acetylcysteine at the time of coronary angiography was not associated with long-term outcome (HR=1.22;  $p=0.22$ ). In conclusion, our findings suggest that transient short-term reductions in renal function following coronary angiography in patients with renal insufficiency are independently associated with a significant increase in the risk of subsequent long-term mortality. Careful follow-up of postcoronary angiography SCr levels is warranted for risk assessment in this population.

## Initial TIMI 0-1 Flow is Associated with Worse 30-day Outcomes of Patients Undergoing Primary Percutaneous Coronary Intervention for Acute Myocardial Infarction

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**Background:** Previous studies have shown that closed culprit vessel (TIMI 0-1 flow) following administration of thrombolytic therapy was associated with worse outcomes that were improved by rescue percutaneous coronary intervention (PCI). Primary PCI is superior to thrombolytic therapy in acute myocardial infarction (AMI), and therefore it might have changed this association. However, the available data regarding this association at the PCI (with stents) and IIb/IIIa era are limited. We sought to evaluate the association of initial TIMI 0-1 flow with 30-day outcomes in 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 1<sup>st</sup> balloon inflation). Patients (n=1025) were allocated into 2 groups: 1<sup>st</sup> Group (n=646 pts) included those with initial TIMI 0-1 flow and 2<sup>nd</sup> Group (n=379 pts) included those with initial TIMI 2-3 flow. All patients were treated with stents. Patients' clinical and angiographic characteristics as well as 30-day outcomes are shown:

|   | Initial TIMI 0-1 Flow | Initial TIMI 2-3 Flow | P Value           |
|---|-----------------------|-----------------------|-------------------|
| <b>N</b>                                  | 646                   | 379                   |                   |
| <b>Age</b>                                | 60±13                 | 60±13                 | 0.99              |
| <b>Male (%)</b>                           | 82                    | 81                    | 0.7               |
| <b>Anterior AMI (%)</b>                   | 46                    | 50                    | 0.1               |
| <b>2-3 Vessel CAD (%)</b>                 | 55                    | 58                    | 0.5               |
| <b>DM (%)</b>                             | 24                    | 25                    | 0.9               |
| <b>CADILLAC score</b>                     | 4.4±3.5               | 3.7±3.6               | <b>0.002</b>      |
| <b>Distal embolization (%)</b>            | 14                    | 5                     | <b>&lt; 0.001</b> |
| <b>Anti GP 2B/3A (%)</b>                  | 78                    | 77                    | 0.7               |
| <b>No/Slow Reflow incl. transient (%)</b> | 8                     | 2                     | <b>&lt; 0.001</b> |
| <b>Myocardial Blush 3 (%)</b>             | 78                    | 90                    | <b>0.007</b>      |
| <b>Peak CK</b>                            | 2.5±2.1               | 1.4±1.6               | <b>&lt; 0.001</b> |
| <b>LVEF &lt; 40% (%)</b>                  | 47                    | 35                    | <b>&lt; 0.001</b> |
| <b>30-day outcomes</b>                    |                       |                       |                   |
| <b>Death (%)</b>                          | 4.3                   | 1.1                   | <b>0.001</b>      |
| <b>Re-MI (%)</b>                          | 3.7                   | 1.6                   | <b>0.05</b>       |
| <b>Stent thrombosis (%)</b>               | 2.6                   | 0.8                   | <b>0.04</b>       |
| <b>MACE (%)</b>                           | 9.6                   | 4.2                   | <b>0.002</b>      |

**Conclusion:** Initial TIMI 0-1 flow in patients undergoing primary PCI for AMI was associated with increased rates of distal embolization and no-reflow. It was also associated with increased infarct size and worse LV dysfunction, consequently resulted in worse 30-day outcomes.

## Percutaneous Transluminal Renal Angioplasty, the Cardiologist Experience

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**Background:** Percutaneous transluminal renal angioplasty (PTRA) is used widely to treat hypertensive patients resistant to drug therapy and to alleviate deteriorating renal function. We present our experience with PTRA during the last years.

**Methods:** Patients with renal artery stenosis were either diagnosed non-invasively by nephrologists, or during coronary procedures. We retrospectively analyzed data of all patients who underwent PTRA between 1999-2006.

**Results:** Forty patients who underwent PTRA were included; 25% were referred by nephrologists and 75% were diagnosed during coronary angiography. Patients who were diagnosed primarily by the cardiologist were referred to a nephrologist for further assessment before PTRA. The indication for PTRA was uncontrolled HTN in 67.5%, flash pulmonary edema in 20%, and unexplained renal failure in 12.5%.

Stents were implanted in all patients. Guidewires, 70% of the balloon catheters and 40% of the stents were coronary equipment. Procedural success rate was 100% with no procedural complications.

At follow-up of  $2.64 \pm 1.41$  years, the average number of antihypertensive medications was reduced, episodes of flash pulmonary edema did not recur, and average renal function remained stable (table 1). One patient had in-stent restenosis and underwent balloon re-dilation. Six patients died from unrelated diseases at an average of  $4.16 \pm 1.3$  years post PTRA.

**TABLE 1**

|             | CREATININE | UREA        | #ANTI HTN MEDS |
|-------------|------------|-------------|----------------|
| Before PTRA | 1.53±0.28  | 52.65±16.97 | 2.85±0.69      |
| At F/U      | 1.54±0.76  | 52.60±25.13 | 1.66±0.81      |
| P value     | NS         | NS          | P<0.001        |

**Conclusions:** PTRA was performed successfully in the coronary catheterization laboratory with reduction of antihypertensive medications, disappearance of flash pulmonary edema and maintaining renal function. The favorable outcome in this series may be attributed to cooperation between cardiologists and nephrologists and careful selection of patients.

## Beneficial 2-years Results of Drug-eluting Stents in Saphenous Vein Graft Lesions

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**Aims** There are conflicting data regarding clinical outcomes of drug-eluting stents (DES) in saphenous vein graft (SVG) lesions compared to bare metal stents (BMS). We compared the outcomes of DES in *de novo* SVG lesions versus BMS using contemporary percutaneous coronary intervention (PCI) techniques.

**Methods and Results** We compared the one and two years outcomes in 68 patients (72 grafts) who underwent PCI of SVG lesions using DES and a control BMS group composed of 43 patients (46 grafts) who underwent angioplasty in *de novo* SVG lesions. Major adverse cardiac events (MACE) included death, myocardial infarction (MI), target lesion revascularization (TLR), and target vessel revascularization (TVR).

Results are shown in Table:

|                   | BMS (Patients = 43)<br>(Grafts = 46) | SES (Patients = 68)<br>(Grafts = 72) | <i>P</i> value |
|-------------------|--------------------------------------|--------------------------------------|----------------|
| One year outcomes |                                      |                                      |                |
| Death / MI / TVR  | 4.7%/4.7%/23.3%                      | 0%/4.4%/10.3%                        | 0.1/0.9/0.1    |
| Overall MACE      | 3.2%                                 | 11.8%                                | 0.02           |
| 2 year outcomes   |                                      |                                      |                |
| Death / MI / TVR  | 4.7%/7%/32.6%                        | 2.9%/8.8%/14.7%                      | 0.6/0.9/0.03   |
| Overall MACE      | 41.9%                                | 20.6%                                | 0.02           |

Between one to two years after PCI, no cases of angiographic stent thrombosis were recorded in either group

**Conclusion** According to our experiences, DES implantation in SVG lesions was safe and had better overall clinical outcomes after two years.

## Side Branch Restenosis: Comparative Analysis of “T” Versus “Crush” Stent Techniques.

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**Background:** PCI treatment of coronary bifurcation lesions remains challenging. Although stent placement with dedicated techniques has been suggested to be a useful therapeutic modality for bifurcation lesions, restenosis of the side branch after drug eluting stent [DES] remain a problem. To overcome this limitation, the “Crush” technique has been proposed to provide optimal lesion coverage.

**Objective:** We compared clinical outcomes of the "Crush" versus the "T" technique in bifurcation lesions with drug eluting stents [82% using Cypher].

**Methods & Results:** We prospectively followed all patients who underwent PCI for symptomatic true bifurcation lesions at our center. Patients treated with two stents were included. Two techniques were used according to the operator's discretion:

|                           | <b>T technique<br/>(N=38)</b> | <b>Crush<br/>(N=26)</b> | <b>P-value</b> |
|---------------------------|-------------------------------|-------------------------|----------------|
| Age (years)               | 62±14                         | 64±11                   | 0.2            |
| Male                      | 84%                           | 85%                     | 0.9            |
| Diabetes mellitus         | 26%                           | 42%                     | 0.1            |
| ACS presentation          | 66%                           | 61%                     | 0.8            |
| LAD/DIAGONAL              | 55%                           | 81%                     | 0.1            |
| Final Kissing Balloon     | 90%                           | 92%                     | 0.7            |
| Anti GP 2b/3a             | 84%                           | 80%                     | 0.5            |
| 6 month death             | 0%                            | 0%                      | 1.0            |
| 6 month Stent thrombosis  | 0%                            | 0%                      | 1.0            |
| 6 month TVR               | 0%                            | 7.7%                    | 0.1            |
| 6 month MACE              | 0                             | 7.7%                    | 0.1            |
| 12 month death            | 2.6%                          | 0%                      | 0.8            |
| 12 month Stent thrombosis | 0%                            | 0%                      | 1.0            |
| 12 month MI               | 0%                            | 3.9%                    | 0.4            |
| 12 month TVR              | 0%                            | 11.5%                   | 0.4            |
| 12 month CABG             | 2.6%                          | 3.8%                    | 1.0            |
| 12 month MACE             | 5.3%                          | 11.5%                   | 0.4            |

**Conclusions:** Our results show that for the treatment of true bifurcation lesions with two stents, the use of DES (predominantly Cypher) is associated with improved one year patency regardless of whether "Crush" or "T" techniques were used. Restenosis of the side branch was not eliminated with the “Crush” technique.

## **Comparative Analysis of 1-year Outcome between Direct and Conventional Stent Implantation in Patients with ST Elevation Myocardial Infarction**

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**Background:** In selected patients presented with ST elevation myocardial infarction (STEMI), direct stenting is associated with reduce procedural complications, duration and costs without compromising short-term outcome. Whether these short-term advantages are also sustained for 1-year has not been fully elucidated.

**Methods:** We compared procedural results, 30-day and 1-year outcomes between patients with non-cardiogenic shock STEMI who underwent primary percutaneous coronary intervention (PCI) within 12 hours of chest pains, using direct (n=233) versus conventional stenting (n=733) approaches.

**Results:** Patients who underwent direct stenting were younger ( $57\pm 12$  vs  $61\pm 13$ ,  $p=0.0001$ ), had more frequently single vessel disease (53% vs. 41%,  $p=0.003$ , admission TIMI 2/3 flow (63% vs 29%,  $p=0.0001$ ), and less often calcified (5.6% vs. 16%,  $p=0.005$ ) and bifurcation lesions (8.2% vs. 16%,  $p=0.005$ ). CADILLAC score was also lower among patients who underwent direct stenting ( $3.2\pm 3.4$  vs.  $4.4\pm 3.5$ ,  $p=0.0001$ ). Plavix loading (46% vs. 46%,  $p=1.0$ ) and use of IIB/IIIa antagonists (76% vs 79%,  $p=0.4$ ) were similar between groups. Fluoroscopy time ( $10\pm 8$  vs  $16\pm 11$  min,  $p=0.001$ ), volume of contrast ( $150\pm 63$  vs  $180\pm 70$ ,  $p=0.0001$ ) and need for a second stent (15% vs. 31%,  $p=0.01$ ) were lower in the direct stenting group. Post procedure TIMI III flow (98.7% vs. 96.2%,  $p=0.2$ ) and blush 2/3 scores (83% vs. 83%,  $p=1.0$ ) were similarly high although no-reflow rates (2.6% vs. 6.6%,  $p=0.01$ ) were lower. 1-year MACE (death, MI, TVR-PCI, CABG, stent thrombosis) were similar between groups (19.9% vs. 22.2%,  $p=0.5$ ) and no differences were noted in each of the individual endpoints.

**Conclusions:** Direct stenting is feasible and safe to perform in ~20-25% of *carefully* selected STEAMI patients, providing a reduction in procedural complications and costs, with similar clinical outcomes. Further studies to assess whether such approach is applicable to larger STEMI population are warranted.

## Primary Percutaneous Coronary Interventions in Acute Myocardial Infarction in Diabetic Versus Non-diabetic Patients

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**Background:** Diabetes mellitus (DM) is an independent predictor of outcome after primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI).

**Objective:** To compare the short and long term clinical outcome of AMI patients with DM to those without DM undergoing primary PCI.

**Methods:** We used our clinical database consisting of all patients treated using primary PCI for AMI between 1/2001-7/2007. Patients with cardiogenic shock were excluded. We compared the procedural and angiographic results and clinical outcome up to one-year in diabetic and non-diabetic patients.

**Results:** Of 1092 patients with AMI 273(25%) had DM, clinical characteristic, short and long-term outcome are summarized:

|   | <b>No DM<br/>N=819</b> | <b>DM<br/>N=273</b> | <b>P-value</b> |
|---|------------------------|---------------------|----------------|
| Age (years)                               | 60±13                  | 64±11               | 0.0001         |
| Males (%)                                 | 84                     | 71                  | 0.0001         |
| GFR (<60 mL/min/1.73 m <sup>2</sup> ) (%) | 10.5                   | 23                  | 0.001          |
| Killip class >1 (%)                       | 15                     | 16                  | 0.3            |
| Anterior MI (%)                           | 46                     | 52                  | 0.3            |
| 2/3-vessel disease (%)                    | 54                     | 66                  | 0.007          |
| Ejection fraction <40% (%)                | 43                     | 43                  | 0.8            |
| Successful PCI (%) <sup>‡</sup>           | 95                     | 96                  | 0.5            |
| CADILAC risk score                        | 4±3.4                  | 5.1±3.9             | 0.0001         |
| <b>One year outcome</b>                   |                        |                     |                |
|   | <b>N=706</b>           | <b>N=259</b>        |                |
| Death (%)                                 | 6.4                    | 10.4                | 0.03           |
| Re-AMI (%)                                | 6.2                    | 11.1                | 0.01           |
| Target vessel revascularization (%)       | 12.6                   | 17.7                | 0.04           |
| Stent thrombosis (%)                      | 3.4                    | 4.6                 | 0.4            |
| CABG (%)                                  | 4.7                    | 8.9                 | 0.01           |
| MACE <sup>+</sup>                         | 20.5                   | 33                  | 0.005          |

<sup>‡</sup> TIMI 3 and residual stenosis <30%, <sup>+</sup>MACE= Death, re-AMI, TVR

Multivariate logistic regression analysis identified CADILAC risk score (OR 1.4, CI 1.3-1.5, P = 0.001) and DM (OR 1.2, CI 0.7-2.2, P = 0.5) associated with one-year mortality

**Conclusions:** At one year following STEMI there were higher mortality and recurrent ischemic events among diabetic patients as compared to non diabetics.

## **Clinical Characteristics and Outcomes of DES Related ‘Failures’: A Comprehensive Single-Center Analysis**

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**Background:** Limited data are available on drug eluting stent (DES) failure (i.e. characteristics and outcome management). We aimed to characterize the pattern, treatment and outcomes of DES in stent restenosis (ISR) in a large consecutive group of patients (pts) treated at our hospital.

**Methods:** We determined the incidence and major adverse clinical events (MACE) in 79 consecutive pts with DES failure: 71 pts had DES restenosis while 8 pts had DES thrombosis between the period of 1/2004 and 2/2007. We analyzed the clinical data, procedural parameters and outcomes of DES restenosis. ISR pattern was classified according to ‘Mehran classification’ as follow: focal (I), proliferative/diffuse (II/III) or occlusive (IV).

**Results:** DES failure was presented in 2.9% of treated patients (71 DES ISR patients out of 2473 DES implanted: cypher N= 1808, Endeavor N=421, Taxsus N= 319 treated patients). Mean age was 65±11 years, 75% were male. 68% of patients had diabetes mellitus (20% needed insulin treatment) and chronic renal failure (Creat. ≥1.5 mg/dl) was encountered in 18% of pts. MV disease was presented in 80% of patients 44% had previous myocardial infarction and 41% had previously CABG. Unstable angina was the clinical presentation in 52 (73%) of patients. Lesion location were mostly in the LAD (35%) followed by LCX (21%) RCA (20%) and bypass grafts (14%). Cypher stents were implanted in 53 pts while 10 pts had Endeavor stents and 8 pts had Taxus stent deployed. The index procedure stent length was 23.3±7.6 and stent diameter was 3.0±0.4. The mean time to restenosis was 11.3±9.9 months. One patient (1.4%) was previously treated using brachytherapy and 22% had prior ISR events. Six month clinical outcome were available in all patients. Three pts developed myocardial infarction (4.2%) of which stent thrombosis was the presentation in one pts (1.4%), restenosis at follow up were diagnosed in 8 pts (11.3%) the overall MACE was 18.3% (13 pts) and two pts died (2.8%).

**Conclusions:** According to our experience, DES related ISR is relatively infrequent but when encountered it remains a major clinical challenge. DES related restenosis is more frequently encountered in complex patients and lesions subsets (e.g. diabetics, patients with renal dysfunction and/or long lesions) but nonetheless the overall intermediate-term prognosis following repeat percutaneous treatment is favorable.

## Results of Unprotected Left Main Coronary Stenting Distinguished by Drug Eluting vs. Bare Metal Stenting: A Single Center Clinical Outcome Analysis

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**Background:** Unprotected left main coronary artery (ULMCA) disease is considered a surgical indication in most centers. However, in some cases prohibited from surgery, there is a need for percutaneous coronary intervention (PCI) in ULMCA disease scenarios. Our study aimed at assessing the clinical outcomes among patients undergoing stent-based ULMCA angioplasty at our institution and compared the results of drug eluting stents (DES) vs. bare metal stents (BMS) utilization.

**Methods:** We identified 59 consecutive patients who underwent PCI in ULMCA between 1/2003 and 5/2007. Procedural and angiographic data and clinical outcomes were obtained for all patients (excluding infarction-related cardiogenic shock) and distinguished between DES vs. BMS groups. Clinical follow-up was obtained for all patients at 6 months following PCI.

**Results:** In the DES group, stent utilization included Cypher in 68%, Taxus in 9% and Endeavor in 24% of treated patients. Baseline characteristics and results of ULMCA stenting distinguished by stent group are shown in **Table**:

|                           | BMS (n=25) | DES (n=34) |
|---------------------------|------------|------------|
| Age (yrs)                 | 76±14      | 74±11      |
| Male (%)                  | 60         | 65         |
| Diabetes (%)              | 20         | 38         |
| LVEF >40% (%)             | 71         | 62         |
| Hemodynamic unstable (%)  | 8          | 15         |
| Distal LM bifurcation (%) | 24         | 47         |
| EuroScore*                | 8.2±3.1    | 6.6±3.9    |
| <b>6 month outcomes</b>   |            |            |
| Death (%)                 | 20         | 3.0        |
| CABG (%)                  | 8.0        | 3.0        |
| TVR (%)                   | 12.0       | 3.0        |
| MACE (overall) *          | 28.0       | 9.0        |

\* Statistical significant difference ( $p \leq 0.05$ )

The six-month mortality rate [univariate] was correlated with the following parameters: DES utilization ( $r=0.3$ ;  $p=0.03$ ), EuroScore ( $r=0.5$ ;  $p=0.004$ ).

**Conclusion:** According to our experiences, overall clinical results of unprotected left main stenting are improved using DES.

## **Stepwise Combined Approach in Primary Percutaneous Intervention: Extensive Clot Extraction, IVUS Guided Focused Forced Predilatation, Stenting and Provisional Post Dilatation**

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Israel*

**Background:** Distal embolization and "no reflow" are common complications during primary PCI.

**Aim:** The aim of the study was to assess the impact of stepwise lesion preparation on acute angiographic and long term clinical outcomes in patients undergoing primary PCI.

**Methods and results:** A total of 30 consecutive patients (43 treated lesions) with acute STEMI scheduled for primary PCI were included in the analysis. All patients were systematically treated by extensive thrombus extraction (aspiration of 125±47 cc of blood), focused predilatation with a scoring balloon prior to stent insertion and finally, provisional post dilatation with a non compliant balloon. IVUS (grayscale and virtual histology) was essential to assess the culprit lesion and the adjacent vessel before predilatation and for result optimization.

Baseline and angiographic characteristics were as follow:

| <b>Patient baseline characteristics(n=30)</b> |       | <b>Lesion characteristics</b>                   |         |
|---|-------|---|---------|
| <b>Age (mean±SD)</b>                          | 69±16 | <b>In-stent occlusion</b>                       | 7%      |
| <b>Male</b>                                   | 66%   | <b>SVG occlusion</b>                            | 3%      |
| <b>Diabetes mellitus</b>                      | 31%   | <b>Vessel diameter</b>                          | 2.9±0.6 |
| <b>History of MI</b>                          | 43%   | <b>Moderate or severe Calcification by IVUS</b> | 38%     |
| <b>History of PCI</b>                         | 28%   | <b>Initial TIMI-0 flow</b>                      | 57%     |
| <b>History of CABG</b>                        | 3%    |   |         |

Angioplasty and stenting were successfully performed with final TIMI-3 flow and without angiographic evidence of distal embolization in all 30 patients.

At 30-days, the rate of MACE (Death/reinfarction/TLR) was 3% (1/30) due to stent thrombosis in a patient with resistance to clopidogrel. At 6 months follow-up (97% of pts), the rate of MACE was 13% (4/30), one side branch occlusion and restenosis in two cases.

**Conclusions:** A systematic stepwise approach with extensive clot aspiration and lesion preparation by focused forced angioplasty during primary PCI is safe and associated with a very good short and long term clinical results. It is associated with a reduced rate of distal embolization or "no reflow". IVUS guidance is essential for accurate lesion coverage and optimal stent expansion. This approach should be tested in a randomized trial.

## **Treatment of In-Stent Restenosis: are Drug Eluting Stents Really the Best Solution?**

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**Background:** In-stent restenosis (ISR) remains a serious challenge after stent implantation. Existing data support the use of drug eluting stents (DES) in these cases. However, few data exist comparing DES with other modalities of treatment.

**Aim:** To compare the clinical efficacy of DES and bare metal stents (BMS) in the treatment of ISR.

**Methods:** Retrospective analysis of 160 patients with ISR detected in the setting of clinically-driven coronary angiography between 04/2004 and 10/2006. We compared 129 pts treated with DES (mean age  $65\pm 12$  y.) and 31 pts treated with BMS (mean age  $65\pm 11$  y,  $p=ns$ ). The patients were followed over a median period of 588 days. Clinical and angiographic characteristics on admission, technical details of PCI and clinical events including all-cause mortality, myocardial infarction (MI), stroke and repeat angioplasty, as well as combined end point were compared. Data were obtained from computerized databases.

**Results:** Baseline demographic and clinical characteristics, including diabetes mellitus, left ventricular function and number of diseased vessels were similar in both groups. During angioplasty, the reference vessel diameter was smaller in the DES group ( $3\pm 0.4$  mm vs.  $3.2\pm 0.6$  mm,  $p=0.02$ ). The stent diameter was smaller ( $3\pm 0.4$  mm vs.  $3.2\pm 0.6$  mm;  $p=0.04$ ) and stent length longer ( $28\pm 14$  mm vs.  $18\pm 11$ ;  $p=0.01$ ) in the DES group. The angiographic success rate was 98% in both groups. The event rate for the DES and BMS groups was similar: All-cause mortality (8% vs. 13%), MI (8% vs. 10%); Stroke (5% vs. 0%) and repeat PCI (19% vs. 16%). A combined end point of all events was observed in 37% of DES pts and 35% of BMS pts ( $p=ns$ ).

**Conclusions:** During long term follow up, instent restenosis is associated with an adverse clinical outcome. In this study, DES did not demonstrate superiority over BMS in the treatment of instent restenosis.

## **Angiographic Results and Patient Risk-factor Differences between Indian-Jews and non Indians on First Time Coronary Angiography.**

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**Background:** Asian Indian ethnicity is known to be associated with higher rates of metabolic syndrome, diabetes and coronary artery disease (CAD). It is unclear whether Jews who emigrated from India also have a higher prevalence of CAD compared to the non-Indians population in Israel.

**Objectives:** To compare the demographic, clinical and angiographic results of Jewish Indian and non-Indian patients referred for a first time coronary angiography (CA) for suspected CAD.

**Methods:** A retrospective analysis of registry data from a cardiac catheterization lab in a tertiary hospital between January 2000 to December 2006. Patients referred for catheterization for indications other than suspected CAD, as well as patients who had a previous catheterization were excluded from the study.

**Results:** Between January 2000 to December 2006, 8886 consecutive patients aged 18 to 96 years (248 of Indian Jewish origin and 8638 of non-Indian origin) performed a first time ever CA in our hospital. The Indian Jews compared to non-Indians, were younger (average age  $57.9 \pm 10.9$  vs.  $62 \pm 12.5$  years respectively,  $p < 0.0001$ ), had more diabetes (42.3% vs. 34%  $p = 0.008$ ) and had a trend towards a higher prevalence of any CAD (91.9 % vs. 88.4%). There was a non-significant trend towards a higher prevalence of multivessel disease in Indian Jews patients below age 40 and in males, but not in females. In a multivariate analysis age, gender, diabetes and Indian ethnicity were independent risk factors for the presence of CAD on angiography. (OR for male sex, diabetes and Indian ethnicity were 4.5, 2.8, and 1.9 respectively).

**Conclusions:** Indian Jews referred for a first-time CA are younger and have a higher prevalence of diabetes and angiographic CAD compared to non-Indians patients. Although the possibility of a bias in referral pattern of this patient population cannot be excluded, our results suggest the need for a more intensive preventive strategy for diabetes and CAD in Indian Jews

## Coronary Artery Disease in an Asymptomatic Population Undergoing a Multidetector Computed Tomography Coronary Angiography

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**Background:** Non-invasive coronary imaging using multidetector computed tomography (MDCT) has emerged as a diagnostic tool that permits assessment of the coronary lumen and coronary plaques. Few data on coronary artery disease in asymptomatic patients who are at risk for coronary atherosclerosis are available.

**Objective:** To assess the prevalence of Coronary Artery Disease (CAD) using MDCT coronary angiography in asymptomatic subjects and its relationships to demographic and clinical risk factors.

**Methods:** A consecutive asymptomatic volunteers with no evidence of ischemic heart disease underwent MDCT at our institute for the early detection of CAD. Data regarding demographic, cardiovascular risk factors, drug treatment, and previous cardiac investigations were collected from all subjects. For each subject the number of diseased coronary segments, segments with obstruction lesions; defined as significant (diameter stenosis  $\geq 50\%$ ) and non-significant (diameter stenosis  $\leq 50\%$ ), and the number of each type of plaque (soft, calcified, or mixed) was determined. All MDCT findings were correlated with demographic and risk factors.

**Results:** A total of 2820 coronary segments were analyzed in 188 asymptomatic subjects including 150 males and 38 females aged  $54.4 \pm 7.4$  years. One hundred twenty eight (68%) demonstrated MDCT findings compatible with CAD; of these 111 (86.7%) had non-significant and 17 (13.3%) had significant CAD. The total number of coronary segments with atherosclerotic plaques was 454 (16.5%); of which 147 (32.4%) had calcified, 123 (27.1%) had soft and 184 (40.5%) had mixed morphology. Compared with older subjects (mean age  $56 \pm 8$  years), younger subjects had a lower prevalence of MDCT findings of CAD 55.5% vs. 12.5%, respectively ( $P < 0.001$ ), regardless of risk factors. Males had more CAD (mostly non-significant) compared with females (109 [72.7%] vs. 19 [50.3%], respectively;  $P = 0.007$ ). Subjects with  $\geq 2$  risk factors had a higher prevalence of CAD in general and significant CAD in particular ( $P < 0.001$ ).

**Conclusions:** CAD in asymptomatic population seems to be not uncommon. Using MDCT coronary angiography a high prevalence of non-significant and low prevalence of significant CAD was discovered in middle age asymptomatic population. CAD was related to older age and number of risk factors.

## **Cost-utility Analysis of a National Project to Reduce Hypertension in Israel**

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**Background:** This study aims to calculate the health effects and costs of a proposed national hypertension prevention and control program.

**Methods:** Interventions are based on experience from our two programs: 10-year period of Ashkelon Hypertension Detection and Control Program (AHDC Program) and the Israel Blood Pressure Control (IBPC) program. The costs of a nationwide program were calculated based on economic data, training staff levels, course frequency and unit costs.

**Results:** Over the next 20 years, the program should decrease the risk in one-half of the treated hypertensive cases of the following ailments:-cardiovascular events such as Acute Myocardial Infarction (AMI) and Unstable Angina Pectoris (UAP) by 16.0%, stroke by 41.2%, End stage renal disease (ESRD) by 50.0% and peripheral vascular disease (PVD) by 42.6%. This translates into a decrease in incidence of 8749 fewer AMIs (543 fewer deaths), 6765 fewer UAPs (145), 8074 fewer strokes

(1,114), 2316 fewer ESRD (440) & 8134 fewer PVD. In total, around 2,242 lives, 35,117 years of life or 24,433 disability adjusted life years will be saved due to decreased mortality. Program costs amount to \$352.7 million. However savings (\$537.6 million), from reduced medical treatment (\$444.3 million) and reduced pharmaceutical use (\$93.3 million) as a result of morbidity decreases, exceed costs by \$185.0 million.

**Conclusions:** our study shows that a national health education program is likely to save over two thousand lives, improve the quality of life in many more people and at the same time actually save \$185.0 million in health care resources alone.

## **The Cost Burden of Drug Therapy in Cardiology**

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**Background** Patients hospitalized in Cardiology Departments often suffer from complex medical conditions. They are discharged with many drugs targeting the cardiac disease itself, the risk factors and the associated pathologies.

**Purpose of the study** To evaluate prospectively the financial burden associated with drug prescription.

**Methods** We evaluated 83 consecutive patients discharged from the Department of Cardiology who gave informed consent. We calculated the monthly cost of the treatment prescribed in the discharge letter. Medication cost was calculated according to the price published on the Internet by one of the major Kupoth Holim (highest cost). The cost was also calculated according to the discounts given by the Kupoth Holim according to the National Health Law (lowest cost).

**Results** There were 73 men and 10 women. Mean age was  $60.1 \pm 12.8$  years. The admission was through the Emergency department in 48 subjects and elective in 35.

Mean number of drugs prescribed per patient was  $6.4 \pm 2.7$ . The monthly cost of drugs was  $679.4 \pm 357.4$  NIS per patient (highest cost) and  $137.2 \pm 61.0$  NIS (lowest cost). We assume that many patients would be recognized as having a chronic disease, in which case the maximum monthly cost to the patient could not exceed 240 NIS (according to the National Health Law). Using the lowest estimate, 10 patients had monthly payment  $>240$  NIS.

Of the 83 patients, 41 were living on pensions and 38 were still working. Four refused to answer the question. Monthly income for people living on pension alone can be as low as 1373 NIS/month and would be for example 3230 NIS (minus 322 NIS for health insurance) for a couple receiving a Social Security pension of the elderly.

**Conclusion** Although most patients receive substantial discounts, the cost-burden of medications is important considering that many patients subsist on very low incomes.

**Prevalence of the Metabolic Syndrome in Individuals  
with Normal Concentrations of Liver Enzymes.  
An Additional Step Towards Early Recognition of Dysmetabolism**

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**Objective:** Metabolic syndrome (MetS) is frequently characterized by the appearance of elevated liver enzymes and especially gamma-glutamic transferase (GGT). We have presently addressed the question of the prevalence of the MetS in a cohort of apparently healthy individuals and within normal limits liver enzymes.

**Methods:** A cross sectional study in a group of apparently healthy individuals with within normal limits liver enzymes values and following exclusion of diseases and medications that may effect the concentration of liver enzymes.

**Results:** We have presently analyzed a cohort of 3,361 men and 1,690 women at a mean+SD age of 44+11 years. The most remarkable finding was observed in relation to GGT where the prevalence of MetS increased from 2.9% in the first quintile to 13.8% in the fourth one, all the five quintiles being in the normal range for this enzyme. A logistic regression analysis for the presence of MetS in relation to the quintile of this liver enzyme showed an odds of 5.3 and 3.9 between the first (GGT <9 and <6) to the fourth (16<GGT<20 and 11<GGT<14) in men and women respectively.

**Conclusions:** A relatively high prevalence of the MetS can be noted in a cohort of apparently healthy individuals who have within normal limits concentration of liver enzymes. A practical consequence might be therefore the follow-up of these enzymes as continuous variables and to take into consideration that even relatively small changes within the normal range might reflect the presence of dysmetabolism.

## **Resting Heart Rate Is Significantly Associated With the Metabolic Syndrome - an Additional Connection Between Resting Heart Rate and Cardiovascular Disease**

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**Objective:** To explore the possibility that increased resting heart rate (RHR) is associated with the prevalence of the metabolic syndrome (MetS) in a cohort of apparently healthy individuals and those with atherothrombotic risk.

**Methods:** A cross-sectional analysis in a relatively large cohort of apparently healthy individuals who attended a general health screening program.

**Results:** In a cohort of 3907 men and 1980 women, the multi-adjusted odds for the presence of the MetS increased gradually from an arbitrary defined figure of 1.0 in the lowest RHR quintile (<60 beats per minute (BPM) in men and <64 BPM in women) to 4.45 and 4.31 in men and women respectively in the highest one ( $\geq 80$  BPM in men and  $\geq 82$  BPM in women).

**Conclusion:** Raised resting heart rate is significantly associated with the presence of MetS in a group of apparently healthy individuals and those with an atherothrombotic risk. The strength of this association supports the potential presence of one or more shared pathophysiological mechanisms for both RHR and the MetS.

## Cardiovascular Disease Characteristics among Elderly in a Consultant Outpatient Cardiac Clinic.

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Cardiovascular diseases (CVD) are increasing with age. Therefore elderly patient visits are becoming more frequent in outpatient cardiac clinic.

Aim: to report cardiovascular (CV) pathologic characteristics among elderly > 70 year , visiting in outpatient cardiac clinic.

Patients and Methods. We report CV pathologies, risk factors and medications in consecutive new patients over a two months period.

Results. Two hundred and ninety patients were included: 139 (47,9 %) were older than 70 years. The CV pathologies are summarized in the table.

|                      | > 70 y<br>N. Pts 139<br>(%) | < 70 y<br>N. Pts 151<br>(%) |        |
|----------------------|-----------------------------|-----------------------------|--------|
| Aortic Stenosis      | 14 (10)                     | 2 (1.3)                     | 0.001  |
| Mitral Valve disease | 8 (5.7)                     | 12(7.9)                     | n.s    |
| S/P AVR              | 6 (4.3)                     | 2 (1.3)                     | ns     |
| S/P CABG             | 26 (18.7)                   | 8 (5.3)                     | 0.0004 |
| S/P Myoc. Infarct.   | 35 (25.2)                   | 26(17.2)                    | ns     |
| Angina Pectoris      | 36 (25.9)                   | 16(10.6)                    | 0.0003 |
| Cong. Heart Failure  | 21 (15.1)                   | 4( 2.6)                     | 0.0002 |
| Chronic Atr. Fibril. | 14 (10.1)                   | 4( 2.6)                     | 0.001  |
| Parox. Atr. Fibril.  | 24(17.3)                    | 8(5.3)                      | 0.0003 |
| Hypertension         | 102(73.4)                   | 50(33)                      | 0.0001 |

The mean number of medications was 3.5 in the elderly and 2 in the younger patients.

Beta blockers were the most frequent used cardiovascular drug both in the elderly (57,7%) and in the younger patients (43%) ( p=0.004).

Conclusions. Patients  $\geq 70$  years represent about half of the visits in out patient clinic. The multiple CV pathologies and their therapeutic related needs in this group raise the issue of developing geriatric cardiology service.

## **Has Abdominal Obesity any Clinical Significance in Patients with Active Coronary Artery Disease?**

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**Background** - In the past 20 years, obesity and diabetes have overtaken cigarette smoking, dislipidemia, and hypertension as risk factors for coronary heart disease. Overweight and obesity increase the risk for hospitalization and death from cardiovascular disease and diabetes at all levels of risk and independently of other risk factors. Abdominal obesity, assessed indirectly by measuring waist circumference (WCi), is associated with clustering of cardiovascular and metabolic risk factors known as the metabolic syndrome. Patients with even minimal abnormalities in any 3 of the 5 risk factors for the metabolic syndrome are at heightened risk for CVD or diabetes. Obesity is also associated with coronary artery calcification, a marker of the presence and extent of subclinical coronary atherosclerosis. Similarly, physical fitness and several exercise related indices are associated with prognosis in CAD patients.

**Aim** – To assess the association of abdominal obesity with exercise parameters which are related to prognosis in patients with active coronary artery disease (CAD).

**Methods** – The association between WCi and heart rate reserve (HRR), Recovery heart rate (RecHR), VO<sub>2</sub>max, Mets, exercise duration (EXd), peak oxygen pulse (OP), rest & peak exercise HR, BP, Borg Scale, and functional class (F.C.) has been evaluated in 91 consecutive patients participating in a 12 week cardiac rehabilitation training program.

**Results** – No correlation was found between WCi and HRR, RecHR, VO<sub>2</sub>max, Mets, EXd, peak exercise HR & BP, or F.C.

Correlation was found only with rest HR ( $r = 0.85$ ,  $p < 0.05$ ) and with diabetes and hypertriglyceridemia ( $r = 0.89$ ,  $0.81$ ,  $p < 0.01$ , &  $< 0.01$  respectively).

**Conclusions** – Assessment of abdominal obesity by waist circumference in patients with chronic IHD provides no complementary value to most of the exercise indices which are related to prognosis in patients with CAD.

## **Elevated White Blood Cell Count Before Coronary Angiography is Associated with Poor Outcome after Coronary Artery Bypass Surgery**

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**Background:** Previous studies demonstrated that elevated White Blood Cell (WBC) count is associated with higher morbidity and mortality following coronary artery bypass surgery (CABG). It has not been established if elevated WBC count prior to coronary angiography influences outcome of patients undergoing CABG.

**Methods:** Preoperative data of 401 consecutive patients that underwent coronary angiography and referred to surgery in our institution were prospectively collected. WBC count was analyzed before cardiac catheterization. Patients were followed-up intraoperatively and postoperatively during hospitalization for surgery. Elevated white blood cell count was defined as higher than  $14 \times 10^3/\text{mm}^3$ . Prolonged ICU stay was defined as longer than 72 hours and prolonged hospital length of stay was defined as longer than 10 days.

**Results:** Patients with elevated WBC count prior to coronary angiography had an increased mortality rate (17% vs. 3%,  $p=0.003$ ), prolonged ICU stay (22% vs. 6%,  $p=0.01$ ) as well as prolonged hospital length of stay (13% vs. 3%,  $p=0.04$ ). Patients with elevated WBC count that were operated within 24 hours from coronary angiography had a significantly higher mortality rate (28% vs. 4%,  $p<0.001$ ) even when adjusted to other confounding factors.

**Conclusions:** Elevated WBC count before coronary angiography is an important marker of poor outcome for coronary artery bypass operations, especially if surgery was performed within 24 hours from angiography. If possible, surgery should be delayed for more than 24 hours or until a decrease in the white blood cell count.

## **Endoscopic Versus Open Vein Harvesting for Coronary Artery Bypass Grafting**

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**OBJECTIVE:** Conventional open saphenous vein harvesting (OVH) with long operative incision can be associated with significant wound pain and serious morbidity in some patients with a resultant extended treatment period. Endoscopic vein harvesting (EVH) with one or two small 3 cm incisions, in theory should alleviate wound pain, reduced leg wound infection and lead to greater patient satisfaction. This study aims to compare the two techniques on this basis and determine whether EVH is a viable technique within normal operative time. Also we sought to compare infection complications of greater saphenous veins removed during coronary artery bypass grafting with the endoscopic vein harvesting vs. open vein harvesting techniques.

**METHODS:** During 2001 – 2006 years, 2576 patients undergoing coronary artery bypass grafting. From these patients 578 underwent endoscopic vein harvesting. All performed by three surgeons with the Clearglide endoscopic vein harvest system (CardioVaition Johnson and Johnson Inc). End points were impaired wound healing and postoperative pain. Follow-up was scheduled at 1 month. Leg wound healing was evaluated at discharge and 1 month late for evidence of complications.

**RESULTS:** The groups were well matched. Leg wound complications were significantly lower in the endoscopic vein harvest group (2.3% vs. 8.1%). Patients in the EVH group had lower postoperative pain. On multivariable analysis, endoscopic vein harvesting associated with lower leg wound complications. The new procedure did not prolong the overall operative time.

**CONCLUSION:** These data clearly demonstrate that endoscopic vein harvest results in significantly reduced post-operative pain, better impaired wound healing, allows earlier ambulation and does not prolong the operative time significantly with no compromise in vein quality.

## **Alcohol Use in Donors is a Protective Factor on Recipients' Outcome after Heart Transplantation**

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**Objective:** Outcome of heart transplantation is highly influenced by good donor selection. Since history of alcoholism is prevalent among potential heart donors, we sought to explore the effect of alcohol use in donors on the outcome of heart transplantation in the recipient.

**Method:** 437 consecutive patients underwent heart transplantation, from January 2002 through September 2005. Patients' files were retrospectively studied. Mean follow-up period was 3.14±1.9 years (range, 3 days to 6.5 years). The cohort was divided into two subgroups. Alcoholic donor group (ADG) include 98/421 patients and non-alcoholic donor group (NADG) with 323/421 patients. Mean age, 35.3±11.4 (Range, 18 to 66) for the ADG and 33±12.2 years (range, 18 to 62) for NADG.

**Results:** Mortality rate among the ADG was 7/98 (7.1%), NADG was 55/323 (17.1%) (p=0.015). The mean interval time between transplant and mortality was at ADG 27.7±20.6 months (range, 0.07 to 51), NADG 16.4 ±19.6 months (range, 0.14 to 73) (p= 0.031). Survival rate was significantly higher among the ADG 72.8±1.9 months compare with NADG: 66.2±1.5 months (p=0.019). Rejection rate was 22/421 (5.2%), in NADG 17/323 (5.2%) and 5/98 (5.1%) in ADG. Rejection free survival was 74.6±0.85 with no significant difference between the two groups (p=0.85).

**Conclusion:** Donor's chronic alcoholism found to be a protective factor regarding the outcome after heart transplantation. Significant differences were found in mortality rate and survival after heart transplantation between the ADG and NADG. This data supports the fact that it is safe to use donors' hearts regardless of a history of alcoholism.

## **Trans Esophageal Echocardiography - a Priceless Tool in Providing Surgical Excellence**

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**Introduction:** Post operative evaluation of the adequacy of surgical repair of congenital heart defects is of utmost importance. Trans Esophageal Echocardiography (TEE) has become the standard of care in providing real time information and in assessing the operative success, and has great influence on cardiac surgical decision making. For the last decade TEE is routinely performed at our institution following congenital heart surgery. We herein present our experience and clinical impact of the use of TEE in the operating room.

### **Materials and Methods:**

Retrospective review of all intra-operative TEE studies performed in the operating room in the years 2004 to 2007.

**Results:** 1000 TEE studies were performed in the operating room following congenital heart surgery in the years 2004 to 2007. In 5.5% of the cases (55 Pts) a second bypass run was needed in order to achieve optimal results due to residual RVOTO (51%, mostly TOF), residual LVOTO (7%), Valve dysfunction (18%), Ventricular dysfunction (5%) and Unexpected surgical errors (5%). In all 55 patients residual lesions were corrected.

**Conclusion:** TEE is a priceless tool in providing surgical excellence. Close collaboration between the cardiologist and the cardiac surgeon leads to a team approach, enabling the surgeon to safely walk the thin ice by precisely tailoring his surgical repair, knowing that TEE will guide him through in achieving an the optimal result for the benefit of the patient.

## **Risk Factors for Failed "Fast-tracking" after Cardiac Surgery in Patients Older than 70 Years**

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**INTRODUCTION** In recent years, the number of elderly people has grown at twice the rate of the general population. Cardiac surgery is one of the most often performed procedures in this age group. "Fast-track" pathway after cardiac surgery was introduced to expedite recovery and thus to make more efficient use of limited facilities and resources. The present study sought to identify the determinants of failure of "Fast-track" pathway in elderly patients.

**MATERIALS AND METHODS** We performed a retrospective observational study of all patients aged 70 years or more who underwent cardiac surgery between January 2004 and June 2007.

**RESULTS** During the study period 2272 patients underwent cardiac surgery. Of them 860 (37.9%) were 70 years old or older. The septuagenarian group included 576 patients and the octogenarian group, 284. "Fast-track" pathway was successful in 54.5% and 37.3%, respectively. On multiple logistic regression analysis, stroke, renal failure, and procedures other than first isolated CABG were independently associated with failed early extubation, delayed intensive care unit discharge and delayed hospital discharge in both groups. Infections and atrial fibrillation were independent risk factors for delayed hospital discharge in both groups and delayed intensive care unit discharge in the octogenarians. In the octogenarians, congestive heart failure was an independent risk factor for failed early extubation, delayed intensive care unit discharge and delayed hospital discharge.

**CONCLUSION** "Fast-track" pathway may be safely applied in selected septuagenarians and octogenarians. Age alone should not exclude otherwise qualified candidates from consideration for "Fast-track" pathway.

## **Pericardial Window Through Left Vertical Minithoracotomy for Thick Pericardium with Massive Effusion**

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**Background:** There are two main approaches (transthoracic and subxiphoid) for creation of pericardial window. In recent years thoracoscopy has also yielded positive results. Some controversies still exist regarding the efficacy of such operations in for thick pericardium. We retrospectively reviewed our 5-year experience with left minithoracotomy through parasternal vertical approach in patients with massive pericardial effusion.

**Patients and methods:** Between September 2001 and October 2006, 14 patients (men-8, women-6; mean age 62 years) with recurrent massive pericardial effusion underwent minithoracotomy in the 4th intercostals space through a left vertical parasternal skin incision.

**Results:** Large pericardial windows were created. Mean operating time was 35 min. Thick pericardium (3-4 mm) and fibrin collections were found in 13 cases. Pathologic findings were compatible with: acute or chronic pericarditis (9), metastatic carcinoma (3), mesothelioma (1) and tuberculosis (1). There were no postoperative complications and no recurrent pericardial effusions. Seven patients died due to the progress of their main disease (renal failure – 3, malignancy-3, cirrhosis –1).

**Conclusions:** Minithoracotomy through a left parasternal vertical incision in the 4th intercostal space is suitable for creation of the window even in complicated cases, where the pericardium is thick. It gives optimal conditions for surgeon and provides excellent material for a pathological diagnosis, with good functional and cosmetic results.

## **Permanent Left Ventricular Assist Device (Destination Therapy), One Year Follow-Up; the Cardiologist Perspective**

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**Background:** Left ventricular assist devices (LVADs) were recently approved for “destination therapy“, namely a permanent mechanical solution for patients with end-stage heart failure who are not eligible for heart transplantation. We present our one year follow-up in a patient with HeartMate II LVAD.

**Case presentation:** A 67 year old man who suffered from HF for 7 years was admitted with acute decompensated heart failure (HF) and hemodynamic manifestations of cardiogenic shock. After he remained dependent on an intra aortic balloon pump and positive inotrops, a HeartMate II (Thoratec Corporation) LVAD was implanted as destination therapy. During one year follow-up, the patient remained free of HF symptoms and was able to perform daily activities with no significant limitations including traveling out of town for family gathering meeting. The patient was followed closely by the cardiology heart failure team on a basis of two visits per month. Speed adjustments of the device were done based on clinical and echocardiogram measurements. There were no significant technical problems of the device and the patient was able to replace batteries independently. During one year of follow-up we needed to take care of several issues; epistaxis which required local treatments and anti-coagulation therapy adjustment, cable exit wound infection and bacteremia which required intra-venous course of antibiotics.

**Conclusion:** The LVAD as a destination therapy, both prolonged our heart failure patient's life and significantly improved its quality. It is however prudent to keep the patients in a close surveillance as medical complications are not un-common.

## Wireless Acoustic Miniature Pulmonary Pressure Sensor in Patients with Congestive Heart Failure (CHF)

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**BACKGROUND:** Decompensation is frequent in patients with CHF despite improved medical therapy. Heart catheterization is the most accurate way to define hemodynamic state, but its invasive nature limits its use to patients with severe decompensation. Therefore, the noninvasive detection of hemodynamic abnormalities before clinical deterioration occurs might be helpful to improve care.

**AIMS:** This study describes a new wireless pulmonary artery (PA) pressure measurement system comprising a miniature PA device implant using right heart catheterization.

**METHODS:** 10 pts (aged  $71 \pm 10$  y, 8 males, 7 CAD, 8 LVEF  $< 35\%$ ) underwent right heart catheterization. A miniature device was implanted in 6 pts (the anatomy of the PA was not suitable for implantation in 4 pts.). Safety of implantation and functionality of the device - The ability to obtain PA pressure from the implant using wireless acoustic communication in clinic and during daily measurement at home was examined.

**RESULTS:** The device was successfully implanted in the PA using right heart catheterization in 6 pts. Patients were discharged 1 day after the procedure. No device or implantation related complications occurred during the following 3 months.

Pressure measurements were successfully and repeatedly obtained from all implants. Compared to measurement at implantation accuracy of the implant was checked [mean  $\pm$  SD (mmHg):  $22 \pm 6$  versus  $19 \pm 5$ ,  $p=ns$ ]. Five patients used the home unit to obtain daily measurement of their PA pressure. Altogether  $>500$  PA tracings were obtained from these patients. Trends of change in PA pressure over time were obtained. In one patient medical therapy was changed based on these measurement. None of the patients had a decompensation event during the monitoring period.

**CONCLUSIONS:** This study demonstrated that wireless communication with a miniature PA pressure sensor is feasible. Repeated, high-quality PA tracings were easily obtained that might be helpful to improve management of patients with CHF.

## **Prevalence and Hemodynamic Consequences of Sleep Apnea in Advanced Systolic Heart Failure Patients using Novel Cardiovascular Sleep Markers**

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**Background:** Sleep apnea is associated with poor prognosis in heart failure (HF) patients although its prevalence and implications are still debatable. With the aim of assessing the incidence of sleep apnea in advanced systolic HF and its hemodynamic consequences, home sleep studies of 60 patients, routinely treated in a HF clinic, were conducted and analyzed using standard and novel sleep markers.

**Methods:** 60 patients (52 males, 8 females, age 65±13 years) with advanced systolic HF were included. Mean New York Heart Association Classification was 3; left ventricle ejection fraction per echocardiogram was 25±8%; ischemic cardiomyopathy was the HF etiology in 38 (63%) patients. Beta blockers were used in 56 (93%) patients.

Each patient was home sleep monitored (Somte ambulatory polysomnograph and Mortara H12 scribe Holter) for a full night. WideMed's Morpheus system was used for scoring and analysis (including novel cardiovascular apnea markers) and the results were manually validated.

**Results:** Total sleeping time was 5±1 hours. Apnea-hypopnea index was 35±19 episodes per hour; Cheyne-Stokes breathing was present in 57 (95%) patients.

We define cardiovascular response to an apnea by ≥3% desaturation, increase of at least 10% in heart rate, and peripheral (finger) vasoconstriction of at least 75%. Out of 55 patients with complete Holter recordings, 40 (73%) patients had at least 10% of their apneas resulting in a complete response; 6 (11%) showed only heart rate response; 5 (9%) showed only vasoconstriction response, and the remaining 4 (7%) were below the thresholds.

### **Conclusions:**

Assessment of the prevalence and hemodynamic consequences of sleep apnea in advanced systolic HF resulted in the following:

1. The prevalence of apnea as well as Cheyne-Stokes breathing is much higher than had been previously reported: both were observed in almost all the studied patients. This may be attributed to the severity of HF condition in this study.
2. Novel sleep parameters were used to assess hemodynamic consequences of sleep apnea: episodes of sleep apnea are associated with desaturation, increased heart rate and peripheral vasoconstriction. These repeated hemodynamic events related to sympathetic reactivation may provide a basis for using sleep apnea as a prognostic marker in HF patients.

## **Trend in Admission Rate and One Year Mortality of Heart Failure Patients Admitted to Clalit Hospitals, 2002-2005**

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**Aim:** The study aim was to evaluate the admissions time trend, 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 consecutive patients were included into the study cohort. Average age was 76 years, 48% male patients, 61% of ischemic origin. A significant decline in rate of first admission from 250 to 170 cases per month was noted during the study period. Seasonality in admission rate was associated with a two-fold difference between summer and winter.

Hospital mortality rate was 5.7%. One year mortality rate 28.7%. A small decline in one year mortality from 31% to 27% was noted during the study period. One year mortality and was associated with patients' age, co-morbid conditions, routine admission laboratory results and pre-admission medications in Cox regression survival analysis. ACEI/ARBs, statins and beta-blockers were protective, while spironolactone and diuretics were associated with increased mortality risk.

**Conclusions:** This observational, quasi-national study demonstrated some significant time trends in admission rate and outcome of heart failure patients. Changes in drug management prior to admission could have contributed to both the decline in rate of admission and the one year mortality of these patients.

## Predictors of 1-Year Mortality in Elderly Hospitalized Patients with Acute Heart Failure

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**Background:** Heart failure (HF) is associated with high mortality, particularly in elderly patients. However, the difference between prognostic risk factors in older and younger HF patients is unclear.

**Objectives:** To identify and compare predictors of 1-year mortality in patients older and younger than 75 years hospitalized with acute HF.

**Methods:** We analyzed the data of 2336 patients with acute HF, who were hospitalized during a 2-month prospective national survey in all public hospitals in Israel (HFSIS 2003). Patients were divided into 2 groups: >75 years (elderly), and ≤75 years (younger). Independent predictors of 1-year mortality and their significance were analyzed in each group.

**Results:** The elderly group included 1182 (47% males), and the younger group 1154 (63% males) patients. Strong independent predictors of 1-year mortality in the younger group included low left ventricle ejection fraction (LVEF), renal failure, hyponatremia and anemia. In the elderly group, admission systolic blood pressure (SBP) <115 mmHG, renal failure and NYHA functional class were strong predictors of mortality (Table). The relationship between admission SBP and mortality in the younger group took a reversed 'J-shape' curve, while in the elderly group a reversed steep linear curve was noted.

**Conclusions:** In hospitalized patients with HF younger than 75 years 1-year mortality risk is strongly associated with low LVEF, while in older patients mortality risk was inversely related to admission SBP, including the hypertensive range. These findings suggest different mechanisms of outcome in young and older patients with HF.

| Independent Predictors of 1-Year Mortality |                         |           |                        |           |
|--|-------------------------|-----------|------------------------|-----------|
|  | Age ≤ 75 years (n=1154) |           | Age >75 years (n=1182) |           |
|  | Hazard Ratio            | 95% CI    | Hazard Ratio           | 95% CI    |
| LVEF<30% vs. LVEF ≥ 50%                    | 2.22                    | 1.44-3.42 | 1.3                    | .95-1.86  |
| Admission SBP <115 mmHG                    | 1.46                    | 1.04-2.04 | 2.00                   | 1.51-2.65 |
| GFR <30 ml/min                             | 1.81                    | 1.01-3.24 | 1.91                   | 1.01-3.59 |
| NYHA III/IV                                | 1.57                    | 1.15-2.13 | 1.70                   | 1.31-2.21 |
| Sodium <136 meq/dL                         | 1.65                    | 1.20-2.25 | 1.17                   | .89-1.55  |
| Hemoglobin < 12g/dL                        | 1.56                    | 1.13-2.17 | 1.3                    | 1.00-1.69 |

## **Factors Associated with One-year Mortality among Patients with Acute Myocardial Infarction in Israel from 1994 to 2004: Data from ACSIS**

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**BACKGROUND:** Mortality from coronary artery disease (CAD) has declined substantially in the last decade. However, studies focusing on the relative impact of the factors contributing to this decline are scarce.

**METHODS:** Data on use of medications and procedures and one-year mortality following AMI were derived from six Acute Coronary Syndrome Israeli Surveys (AC SIS) performed between 1994-2004. The survey population included 7,383 patients hospitalized with AMI in 25 Intensive Care Units (ICCU) in Israel. Logistic regression models were used in order to evaluate the effect of various in-hospital treatments on mortality trends.

**RESULTS:** One-year mortality following AMI declined from 19.0% in 1994 to 12.1% in 2004 (a decrease of 33%). Logistic models adjusted for baseline characteristics and severity of the disease (Killip class >2) demonstrated that the use of each of the medications (aspirin,  $\beta$ -blockers, ACE Inhibitors and lipid lowering drugs), as well as the use of coronary angiography during the index hospitalization, was associated with a reduction in one-year mortality. Rates of survival increased with each additional medication given. Age and severity of disease were associated with an increase in mortality, however gender did not influence the outcome.

**CONCLUSION:** ACSIS surveys have demonstrated that adherence to treatment guidelines for AMI has been associated with mortality decline from coronary heart disease in Israel.

## Impact of Elevated Admission White Blood Cell Count on Outcomes of ST-Elevation Acute Coronary Syndrome Patients Treated with Primary Percutaneous Intervention.

Avital Porter, Ran Kornowski, Zaza Yakobishvilli, Tamir Ben-Tal, David Brosh, Hana Vaknin-Assa, David Hasdai, Shmuel Fuchs, Alexander Battler, Abid Assali

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**Background:** Elevated white blood cell (WBC) count on admission in pts with ST-elevation acute coronary syndrome (STE-ACS) has been associated with adverse prognosis. Little data are available on the relationship of WBC count to outcome in STEMI patients treated by primary percutaneous intervention (PPCI).

**Aims:** To examine the association of WBC counts on admission with clinical outcomes after PPCI in STEMI.

**Methods and Results:** We analyzed consecutive STE-ACS pts without cardiogenic shock after PPCI. The 1027 pts were divided into 3 groups according to WBC count determined on admission: 1) < 10,000, n=319 (31%) pts; 2) 10,000-20,000, n=651 (63%) pts; 3) > 20,000, n=57 (6%) pts. Pts with elevated WBC were more often smokers, without previous history of myocardial infarction. They presented more often with anterior STEMI location, and higher Killip class. Peak CK and the left ventricular dysfunction as well as the Cadillac score, denoting increased risk, were significantly higher in pts with elevated WBC. There was no difference in prevalence of other risk factors, extent of coronary disease, and procedural success.

Outcomes:

| <i>Variable</i>          | <i>&lt;10,000</i> | <i>10-20, 000</i> | <i>&gt;20,000</i> | <i>P value</i> |
|--------------------------|-------------------|-------------------|-------------------|----------------|
| MACE*                    | 6.8%              | 8.6%              | 13.5%             | 0.02           |
| <b>30-days mortality</b> | <b>0.9%</b>       | <b>3.5%</b>       | <b>14%</b>        | <b>0.000</b>   |
| Stent thrombosis         | 2.5%              | 2%                | 1.8%              | 0.8            |

\* Composite of mortality, re-infarction and re-PCI

In multivariate analysis adjusted to the Cadillac risk score, pts in groups 2-3 had almost four-fold greater risk of mortality, as compared with group 1 (OR 3.8; CI 1.9-7.5, p=0.0001).

**Conclusion** - Baseline leukocytosis [simple and easy obtained measure] is an independent correlate of increased mortality after PPCI in STEMI. Our findings suggest that the WBC count should be considered an important prognostic factor in patients with STEMI treated by PPCI.

## **Intra-Aortic Balloon Pump Counter-Pulsation Improves Coronary Flow and Recovery of Left Ventricular Systolic Function after Primary Angioplasty in Patients with Suboptimal Microcirculation**

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Coronary artery Doppler velocities reflect coronary flow and their patterns correlate with function of the microcirculation and may allow assessment of pumping efficacy after intra-aortic balloon pump counter-pulsation (IABP) after primary angioplasty. Aim: Evaluation of the effects of IABP on left anterior descending coronary artery (LAD) velocities and recovery of left ventricular ejection fraction (LVEF) in patients with acute anterior ST-elevation myocardial infarction (STEMI) after primary angioplasty and suboptimal flow. Methods: twenty eight patients with acute anterior STEMI who had primary angioplasty and suboptimal flow were evaluated. In eleven IABP was applied. Results: Transthoracic Doppler sampling of LAD velocities was feasible and diastolic LAD deceleration time was less than 600 msec in all. Diastolic LAD peak velocities of pumped beats,  $73 \pm 28$  cm/sec were higher than those of non-pumped beats,  $34 \pm 11$  cm/sec,  $p=0.00075$ . Diastolic time velocity integrals of pumped beats  $14.7 \pm 6.5$  cm were higher than non-pumped beats,  $7.3 \pm 3.1$  cm,  $p=0.0047$ . Diastolic LAD flows of pumped beats  $60 \pm 47$  ml/min were higher than without pumping,  $28 \pm 19$  ml/min,  $p=0.05$ . Baseline LVEF in subjects with IABP  $29.4 \pm 5.7\%$  was less than that in those without,  $36.4 \pm 7\%$ ,  $p=0.05$ . One week after angioplasty, LVEF in IABP patients,  $34 \pm 7\%$ , was similar to LVEF in those without,  $36.4 \pm 6.8\%$ . In 6 (54.6%) patients with IABP LVEF increased more than 5% while only in 4 (23.5%) in those without,  $p<0.05$  Conclusions: IABP increases LAD flow, as detected by transthoracic Doppler, and promotes recovery of left ventricular systolic function in patients with suboptimal microcirculation after primary angioplasty for acute anterior myocardial infarction.

## Mortality Outcome of ACS Patients Treated with Bare Metal vs. Drug Eluting Stents: Insights from the National ACSIS-2004 Registry

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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 long-term mortality data are still awaited.

**Methods:** We identified 163 patients enrolled in the ACSIS-2004 (Acute Coronary Syndrome Israeli Survey) registry who underwent PCI using DES during or soon following the course of ACS (e.g. unstable angina, non-STEMI and STEMI) and compared the clinical characteristics and mortality outcomes to 812 corresponding ACS patients treated using bare metal stents (BMS). Baseline characteristics and mortality outcomes data were obtained for all patients up to one year.

**Results:** The main demographic and mortality results are shown in the **Table** as follow:

|                                 | DES (n=163) | BMS (n=812) |
|---------------------------------|-------------|-------------|
| <b>Men</b>                      | 77          | 78          |
| <b>Age (yrs) *</b>              | 63.6±12     | 61.3±12     |
| <b>Diabetes (%)</b>             | 31          | 27          |
| <b>MV disease (%)</b>           | 64          | 59          |
| <b>STEMI (%) *</b>              | 39          | 64          |
| <b>Non-STEMI (%) *</b>          | 61          | 36          |
| <b>Killip Class ≥2 (%)</b>      | 16          | 16          |
| <b>PCI following lytics (%)</b> | 29          | 19          |
| <b>Mortality data</b>           |             |             |
| <b>30 day (%)</b>               | 1.2         | 3.5         |
| <b>180 day (%)</b>              | 3.1         | 4.8         |
| <b>360 day (%)</b>              | 3.7         | 5.8         |

\* Statistical significant difference ( $p < 0.05$ )

Using a logistic regression analysis model, the patients age (by 10 years increment: odds ratio=2.17 and confidence limits = 1.69-2.83;  $p < 0.001$ ) was the most powerful independent predictor for one year mortality following ACS and regardless of stent category being utilized (i.e. DES vs. BMS).

**Conclusion:** PCI indicated for ACS is associated with comparable mortality outcomes up to one year in ACSIS-2004 cohort despite heterogeneous baseline variables which is primarily due to age at ACS onset and STEMI clinical presentation.

## The Ratio of Contrast Load to Glomerular Filtration Rate (GFR) as a Predictor for Renal Dysfunction and Subsequent Mortality Following Emergent PCI for STEMI

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**Background:** The ratio of contrast load utilized during PCI to baseline glomerular filtration rate (GFR) has been proposed as a surrogate marker for the development of contrast induced nephropathy post elective PCI. We sought to use the ratio in order to predict the renal and cardiac prognosis among patients with STEMI who were treated using emergent primary PCI.

**Methods:** Data from consecutive patients who underwent PCI for STEMI at our hospital were imputed into a dedicated clinical database. We compared the clinical outcome (death, re-MI, TVR, MACE) at 6 month in patients distinguished by the ratio of contrast load utilized during PCI to baseline GFR prior to PCI.

**Results:** Results of 871 consecutive (non-shock) patients with STEMI are summarized as follow:

| Contrast Volume / GFR Ratio   | 0.14-1.5<br>(N=290) | 1.5-2.35<br>(N=290) | >2.35<br>(N=290) |
|---|---------------------|---------------------|------------------|
| Age (years)   | 62±10               | 63±12               | 63±11            |
| Males (%) <sup>+</sup>  | 83                  | 86                  | 76               |
| Diabetes Mellitus (%)   | 24                  | 23                  | 28               |
| Anterior MI (%) <sup>+</sup>  | 37                  | 46                  | 56               |
| Multivessel Disease (%) <sup>+</sup>                                  | 46                  | 56                  | 70               |
| Killip>1 (%) <sup>+</sup>   | 11                  | 10                  | 22               |
| Successful PCI (%)  | 98                  | 98                  | 92               |
| Multivessel PCI (%) <sup>+</sup>                                      | 2.4                 | 8.6                 | 13.8             |
| EF<40% (%) <sup>+</sup>   | 31                  | 38                  | 53               |
| GFR<60 ml/min <sup>+</sup>  | 0.7                 | 4.8                 | 33               |
| <b>In-hospital renal dysfunction (on top of baseline)<sup>+</sup></b> |                     |                     |                  |
|   | 0.7                 | 3.8                 | 20.3             |
| <b>6 months outcome</b>   |                     |                     |                  |
| Death (%) <sup>+</sup>  | 1.8                 | 3.1                 | 9.6              |
| Re-AMI (%)  | 4.9                 | 4.5                 | 5.5              |
| Target vessel revascularization (%)                                   | 8.5                 | 8.4                 | 8.3              |
| MACE (death, re-AMI, TVR) (%) <sup>++</sup>                           | 12.3                | 15.3                | 19.6             |

<sup>+</sup>p<0.05 (statistically significance) ; <sup>++</sup>p=0.06

**Conclusions:** Our results show: 1) the ratio of contrast load utilized during PCI to baseline GFR would predict the likelihood of in-hospital renal deterioration and/or dysfunction, 2) higher contrast volume to GFR ration is associated with increased subsequent total mortality. Thus, such ratio should be utilized in order to optimize the contrast utilization adjusted for GFR during emergent PCI

## On-Admission Serum Phosphate Level and Long Term Outcome in Patients with Acute Myocardial Infarction

Robert Dragu, Michael Kapeliovich, Haim Hammerman

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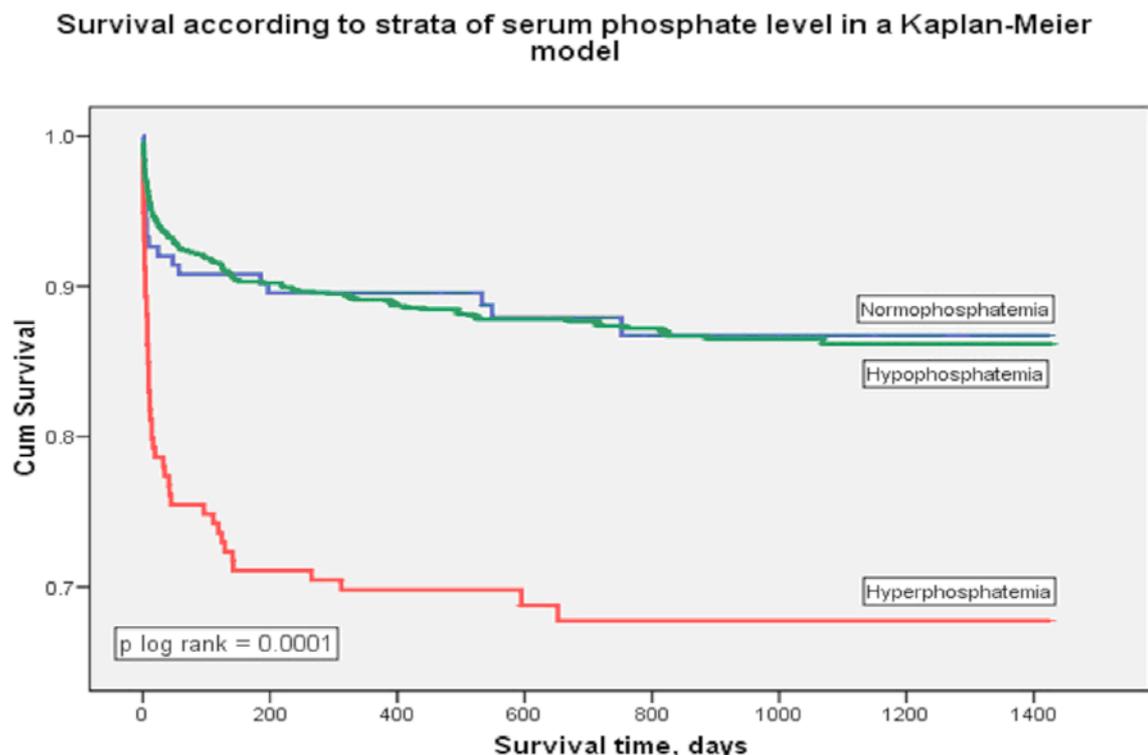
**Aim:** To study the prevalence and the long term prognostic significance of changes in serum phosphate in patients with acute myocardial infarction (AMI).

**Methods:** We prospectively studied 1746 consecutive patients admitted with AMI. Serum phosphate levels were tested 12-24 hours from admission. Mean follow-up was 24 months. Logistic regression models were used to assess the relationship between the serum phosphate levels and long term survival.

**Results:** On-admission 1367 (78.3%) of patients had normal serum phosphate levels, 192 (11.0%) had hypophosphatemia (<2.5 mg/dl), and 187 (10.7%) had hyperphosphatemia (>4.5 mg/dl). The overall mortality was 11.7%, 12.0% and 32.6% in normal, hypo and hyperphosphatemia, respectively ( $p < 0.0001$ ). After adjusting for age, gender, diabetes mellitus, ST-elevation AMI, anterior wall involvement, creatinine clearance and serum calcium levels, the odds ratio for mortality were: 0.80 (95% confidence interval [CI], 0.42-1.52) in patients with hypophosphatemia and 2.16 (95%CI, 1.35-3.48) in patients with hyperphosphatemia, as compared to those with normal levels. Figure 1 depicts the survival in the different groups in a Kaplan-Meier model.

**Conclusion:** Hyper but not hypophosphatemia in patients with AMI is strongly correlated to increased long term mortality. Further investigations regarding the impact of rapid correction of high serum phosphate levels on mortality are necessary.

Figure 1



## The Impact of Changes in Serum Albumin Levels during Hospitalization on Long Term Mortality in Patients with Acute Myocardial Infarction

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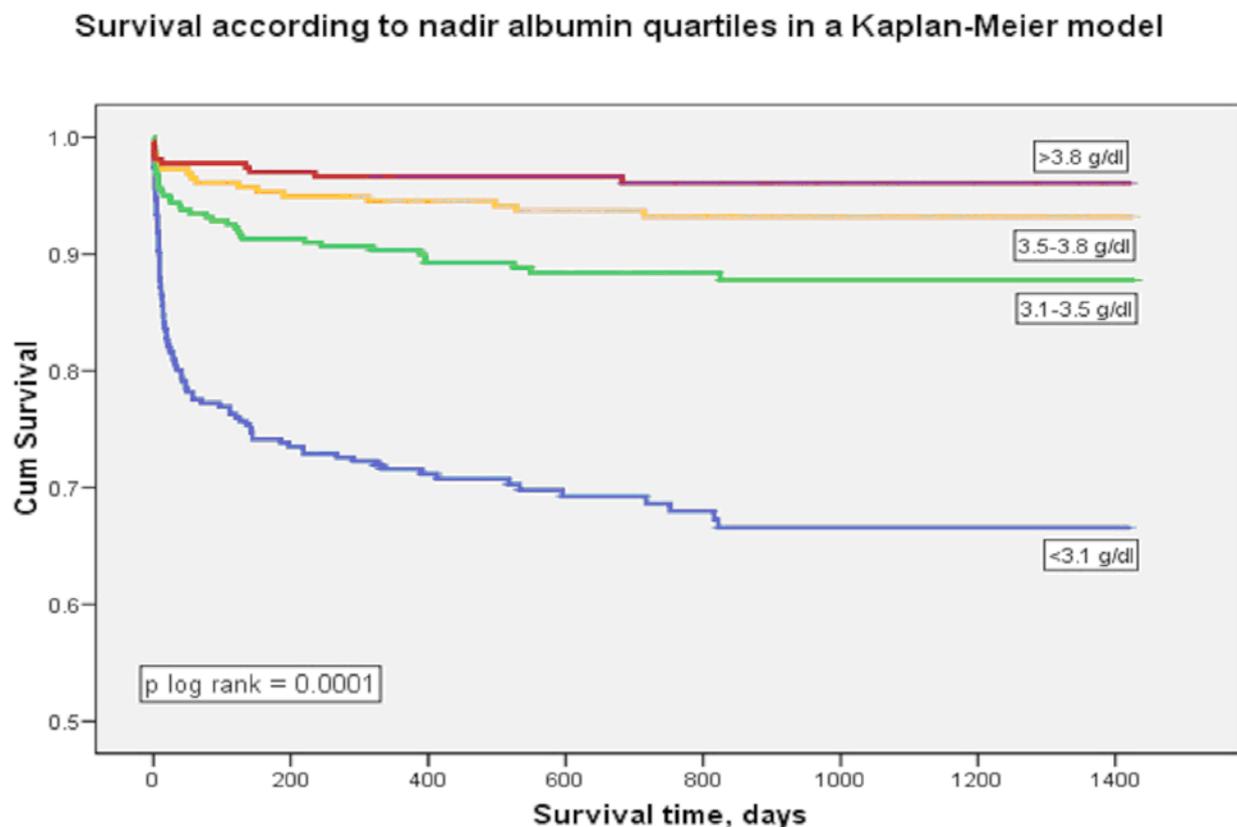
**Aim:** To assess the prevalence and long term prognostic significance of changes in serum albumin levels during hospitalization in patients with acute myocardial infarction (AMI).

**Methods:** We prospectively studied 1460 consecutive patients admitted with AMI and normal synthetic liver function. Serum albumin concentration was tested daily during hospitalization. The mean follow-up period was 24 months. Multivariate Cox models were used to assess the relationship between nadir albumin level and long term survival.

**Results:** During hospitalization 54.5% of study population developed hypoalbuminemia (<3.5 g/dl). The mean nadir albumin was  $3.38 \pm 0.58$  g/dl (median 3.5, IQR 3.1-3.8), 0.31 g/dl lower than admission levels ( $p < 0.0001$ ). Low nadir albumin was strongly associated with high mortality (Fig. 1). After adjusting for age, gender, diabetes mellitus, hypertension, ST-elevation AMI, anterior wall involvement, left ventricular systolic function and creatinine clearance, the nadir albumin in the lower quartile (<3.1 g/dl) remained a strong predictor for mortality (HR 3.54, 95% confidence interval 1.06-11.80).

**Conclusion:** The development of hypoalbuminemia is frequent during hospitalization of patients with AMI and is strongly related to an increased long term mortality.

Fig.1



## Detection of Acute Myocardial Ischemia using High-Frequency QRS Analysis

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**Background:** Myocardial ischemia causes changes in the depolarization phase of the ECG which can be quantified by analyzing the high-frequency mid-QRS components (HFQRS). Our aim was to test this technique in detecting supply ischemia caused by prolonged intra-coronary balloon occlusions and assess the feasibility of HFQRS detection of acute ischemia using a single, unreferenced measurement.

**Methods:** High resolution 12-lead ECG was recorded prior to and during prolonged intra-coronary balloon occlusion in 104 patients (60±11 yo, 65 men) undergoing elective PTCA (STAFF3 database). The HyperQ™ System (BSP Ltd, Israel) was used to derive HFQRS data and ST segment levels. Indices of HFQRS based on i) relative intensity reduction and ii) ischemia-specific signal morphology without a reference measurement were examined. The area under the receiver operating characteristics (AUROC) curve was used to assess the diagnostic value of each index and to derive optimal cutoff values. ST changes were examined according to ESC/ACCF/AHA guidelines.

**Results:** Balloon occlusions lasted 4.4±1.3 min. HFQRS intensity index was available in 87 pts, morphological index in 64 pts and ST analysis in 99 pts. Both HFQRS indices were more sensitive than ST analysis (Table), with similar specificity for the HFQRS intensity index and ST analysis.

| Index               | Sensitivity | Specificity | Accuracy | AUROC |
|---------------------|-------------|-------------|----------|-------|
| HFQRS intensity     | 95%*        | 96%         | 96%*     | 0.99  |
| HFQRS morphology    | 84%*        | 80%         | 82%*     | 0.88  |
| ST segment analysis | 55%         | 95%         | 75%      | NA    |

\* p<0.001 vs. ST analysis

**Conclusion:** HFQRS analysis provided high diagnostic performance in detecting acute supply ischemia. In particular, HFQRS morphology index achieved high accuracy without using a baseline measurement. Thus, HFQRS analysis may aid in detecting both transient ischemic episodes and conditions of acute myocardial ischemia/infarction.

## Time to Fibrinogen in Acute Coronary Syndromes

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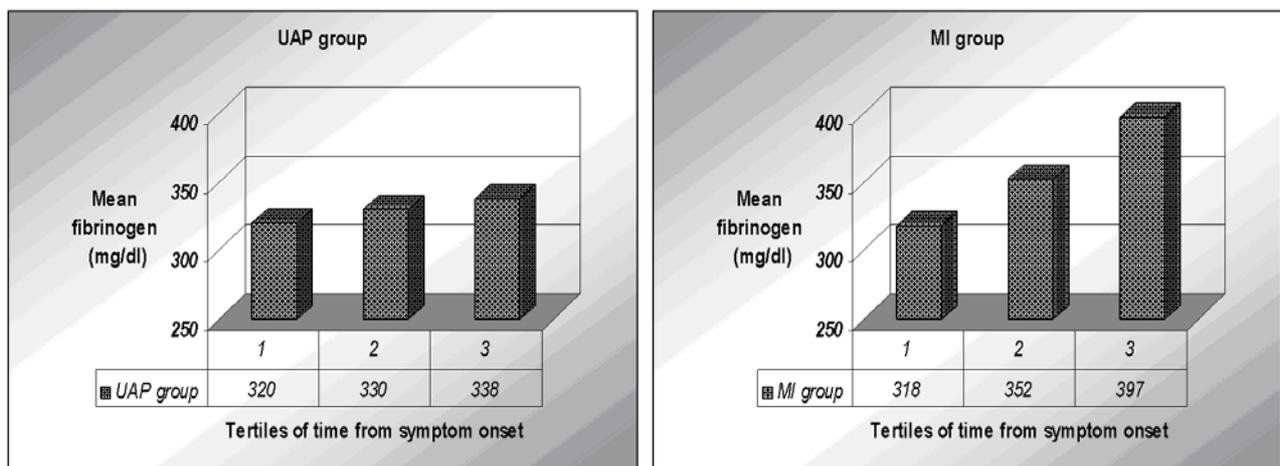
**Background:** Elevated fibrinogen concentrations correlate with poor prognosis in acute coronary syndromes (ACS). We presently explored the correlation between fibrinogen concentrations and the time from symptom onset to angiography.

**Methods:** We enrolled ACS patients during coronary angiography. Linear regression models were fitted for fibrinogen as the dependant variable and adjusted to cardiovascular risk factors and relevant medications. Anova and Kruskal Wallis tests were used to determine differences between time tertiles from symptom onset.

**Results:** Included were 540 patients, 316 with unstable angina (UAP group), and 224 with non-ST and ST-elevation myocardial infarction (MI group). In the MI group the mean fibrinogen was 356 mg/dl and the mean time to angiography from symptom onset was 66 hours. There was a significant difference between the tertiles of time from onset of pain ( $p < 0.001$ ) and the time from onset of pain entered as a strong predictor for fibrinogen ( $r = 0.395$ ;  $p < 0.001$ ). In the UAP group the mean fibrinogen was 330 and the mean time from onset of pain to angiography was 126 hours. No significant contribution of time from onset of pain on the baseline fibrinogen concentration was noted for the UAP group.

**Conclusion:** Time to angiography is an independent predictor of fibrinogen concentration in MI patients. Increased fibrinogen concentrations, probably part of the acute phase response, could be detrimental in terms of increased viscosity and microcirculatory dysfunction.

### Mean Fibrinogen in tertiles of time from symptom onset



## **Single Center Experience with Mild Therapeutic Hypothermia in ICCU**

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**Aim:** To assess the impact of mild therapeutic hypothermia in patients admitted to ICCU after cardiac arrest and successful out-of-hospital CPR.

**Methods:** We prospectively studied 33 consecutive patients admitted to our institution ICCU after cardiac arrest due to VF, VT, asystole or other tachy-brady arrhythmias, and who were treated by mild hypothermia together with standard intensive care treatment according to guidelines. Hypothermia was defined as a body temperature of 32-34 °C, and achieved with the use of an external cooling device. Patients were followed-up during hospitalization.

**Results:** The rhythm abnormalities observed at arrival of resuscitation team were: 63.6% VF, 9% VT, 12.1% asystole and 15.3% other associated arrhythmias. Out of 33 patients studied, 14 (42.4%) patients survived the index event. Mean time duration from collapse to start of advanced life support was 9.0±5.3 minutes, with 9.4±6.0 minutes and 8.5±4.4 minutes in the deceased and discharge from hospital groups respectively. The total resuscitation duration was 36.1±10.9 minutes, with 39.9±11.0 minutes and 31.5±9.4 minutes in the deceased and discharge from hospital groups respectively. Cooling time in the group of patients who died during hospitalization was 801.1±535.4 minutes, while in the discharge from hospital group was 1011.0±560.2 minutes. The hospitalization period was 12.9±12.5 days in the succumbed patients and 16.1±5.8 days in survivors.

The most common complication observed after re-warming was pneumonia.

**Conclusions:** Mild therapeutic hypothermia in patients who survived out-of-hospital CPR, was effective for all causes of cardiac arrest without major complications. Our results are in line with previous reported studies.

## **Clinical Characteristics and Angiographic Findings of Patients with Acute Myocardial Infarction and Spontaneous Reperfusion and Comparison with STEMI Patients who Underwent Primary PCI**

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**Background:** Spontaneous reperfusion (SR) is a well recognized phenomenon in myocardial infarction but the best approach to treating these patients has not yet been determined.

**Objectives:** To describe the clinical and angiographic features and prognosis of STEMI patients with SR versus STEMI patients.

**Methods:** Retrospective analysis of 86 patients admitted between April 1998 and December 2006 with the diagnosis of STEMI and SR and compared their baseline, event and outcome features with patients with STEMI without SR.

**Results:** Of the total number of STEMI patients (2756) there were 86 who met criteria of SR (group I). All patients were catheterized within 48 hours. Group II consisted of 86 consecutive patients with STEMI admitted between April and October 2006. Baseline characteristics were similar except for lower incidence of diabetes in group I (15% vs. 28% p0.037). Median time from symptom onset to ER admission tended to be shorter in group I ( $108 \pm 87$  vs.  $180 \pm 27$  min p0.076). More patients in group I had been treated with chewable aspirin (89% vs. 64% p<0.01). Infarct related artery was patent with pre-PCI TIMI flow 3 in 95% of patients in SR group vs. 14% in group II (p <0.01). SR patients developed less myocardial damage: normal LV Function was detected in 60% of patients in group I vs. 27% in group II ( p<0.01) and there was significant survival benefit in SR group at 30 days ( mortality 3.5% vs. 11.6% p=0.043).

### **Conclusions:**

1. There was excellent correlation between clinical and ECG markers of spontaneous reperfusion and patent infarct related artery with TIMI flow 3.
2. Acute aspirin treatment was an important predisposing factor for SR.
3. SR is less frequent in diabetic patients.
4. SR in STEMI is associated with smaller infarct size and a better clinical outcome at 30 days.

## Emergency PCI Therapy in 1336 Consecutive Patients with STEMI: Mortality Insights from the a Large Single-center Registry

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*Cardiology, Rabin Medical Center, PetachTikva, Israel*

**Background and Aims:** Because cumulative evidence has demonstrated that rapid primary percutaneous coronary intervention (PCI) is the most effective reperfusion strategy for acute STEMI, the development of integrated system providing full time coverage for primary PCI is suggested. Some of the large and high volume hospitals implemented full time coverage for emergency PCI. In this study we report our experience in implementing “around the clock” coverage for primary PCI in a 1336 consecutive pts with STEMI.

**Methods:** We used our clinical database consisting of all pts treated using emergent PCI for AMI between 1/2001 and 10/2007. Clinical, procedural and angiographic results and 30 days mortality were analyzed.

**Results:** 1336 pts with STEMI mean age 61±13 years [range 24-101] were included. PCI was successful in 94% of non-shock pts and in 84% of shock pts. Mortality results distinguished by the categories are shown in the Table as follow:

| Mortality  | One month   | Six months  | One year    |
|--|-------------|-------------|-------------|
| Non cardiogenic shock [n=1224]                     | 3.5%        | 5.9%        | 7.7%        |
| Cardiogenic shock [n=112]                          | 55%         | 60%         | 64%         |
| Non cardiogenic shock                              |             |             |             |
| Age>75years [n;207/1017]                           | 8.2%/2.3%*  | 16.2%/3.8%* | 19.4%/8.8%* |
| Female/Male [n; 242/982]                           | 6.2%/2.9%*  | 10%/4.9%*   | 13.2%/6.2%* |
| Rescue PCI [n;47/1177]                             | 4.3%/3.5%   | 4.3%/6%     | 6.4%/7.7%   |
| Anterior AMI [N=584]                               | 4.6%        | 7.7%        | 10%         |
| Right ventricular AMI [N=117]                      | 7.7%        | 10.6%       | 11.5%       |
| GFR (<60 mL/min/1.73 m <sup>2</sup> ) [n; 173/995] | 9.8%/2.3%*  | 16.3%/3.8%* | 19.6%/5.1%* |
| Day/Night [n;713/497]                              | 4.4%/3.0%   | 7.4%/4.9%   | 9.3%/6.6%   |
| Weekend [n;321/903]                                | 5.3%/2.9%*  | 7.8%/5.3%   | 10.2%/6.7%* |
| Failed PCI [n;75/1149]                             | 17.3%/2.6%* | 21%/5%*     | 24%/6.6%*   |

\* p<0.05

### Conclusions:

1. Cardiogenic shock still remains an important cause of mortality in STEMI with most mortality occurs in the first month.
2. Female gender, MI location, renal function, “off-hours” admission, and failure to restore normal coronary flow 3 are important prognostic factors.

## Impact Sub-clinical Renal Dysfunction on One Month Mortality of Patients with STEMI with Cardiogenic Shock Undergoing Primary Angioplasty

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**Background:** Acute myocardial infarction complicated by cardiogenic shock is associated with an exceedingly high mortality, even if patients are treated with early reperfusion therapy. Risk stratification of these patients before undergoing primary angioplasty is important in order to predict outcomes and to delineate targeted therapeutic strategies. Current knowledge of predictors of death is limited.

**Aims:** The aim of this study was to evaluate the impact of sub-clinical renal failure on one month mortality of a cohort of consecutive patients with cardiogenic shock treated with primary percutaneous coronary intervention (PCI).

**Methods:** We used our database of consecutive patients treated by primary PCI for AMI performed between 1/2000–10/2007. A total of 1336 procedures were registered, of these 112 (8.4%) were performed in patients with cardiogenic shock. In this analysis we included pts with normal serum creatinine [ $<1.5\text{mg}\%$ ]. Pts were stratified according to GFR values at admission:  $\text{GFR} < 60 \text{ mL}/\text{min}/1.73 \text{ m}^2$ .

### Results:

|                       | GFR $>60$<br>mL/min/1.73<br>m <sup>2</sup> )<br>N=46 | GFR $\leq 60$<br>mL/min/1.73<br>m <sup>2</sup> )<br>N=13 | P     |
|-----------------------|--|--|-------|
| Age (yrs)             | 64 $\pm$ 12  | 77 $\pm$ 8   | 0.001 |
| Male                  | 74%  | 31%  | 0.004 |
| Anterior AMI          | 48%  | 54%  | .7    |
| DM                    | 26%  | 38%  | 0.4   |
| 2 or 3 vessel disease | 67%  | 77%  | 0.4   |
| SBP [mmHg]            | 89 $\pm$ 22  | 83 $\pm$ 23  | 0.4   |
| Anti GP 2B/3A use     | 33%  | 54%  | 0.2   |
| Post PCI TIMI 3       | 87%  | 100%   | 0.4   |
| Mortality             |  |  |       |
| 1 month mortality     | 28%  | 77%  | 0.001 |
| Six months mortality  | 31%  | 92%  | 0.009 |

In a multivariate analysis adjusted for age and gender,  $\text{GFR} \leq 60 \text{ mL}/\text{min}/1.73 \text{ m}^2$ ) [OR=1.8, 95% CI=1.04-3.0, P=0.03] was a significant independent predictors of one month mortality.

**Conclusion:** Sub-clinical renal failure even with “normal” serum creatinine is an important risk factor for mortality in patients undergoing emergency PCI for acute myocardial infarction in the presence of cardiogenic shock.

## Trends in Management and Outcome of Women and Men with STEMI in Israel in the New Millenium

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**Background:** Major modifications in therapies have been introduced in the management of patients with STEMI in the last decade, leading to a decline in mortality.

**Aim:** To evaluate trends in management and their impact on outcome of women (W) and men (M) with STEMI, in the new millenium.

**Methods:** 840 W and 2868 M with STEMI hospitalized in 26 CCU's in Israel during the biannual ACSIS 2000-2006 surveys were assessed.

**Results:** W comprised 21-25% of cohorts, mean age 69-72 vs. 59-61 yrs in M.

| Year                        | Women (n=840) |                     |                     |                     |         | p-for trend | Men (n=2868) |                     |                     |                     |         |
|-----------------------------|---------------|---------------------|---------------------|---------------------|---------|-------------|--------------|---------------------|---------------------|---------------------|---------|
|                             | 2000          | 2002                | 2004                | 2006                |         |             | 2000         | 2002                | 2004                | 2006                |         |
| No. of pts                  | 219           | 211                 | 229                 | 181                 |         |             | 727          | 744                 | 703                 | 694                 |         |
| Ac. Reperfusion (%)         | 51            | 52                  | 56                  | 54                  | 0.36    |             | 62           | 63                  | 66                  | 57                  | 0.13    |
| TLx /PPCI (%)               | 78/22         | 58/42               | 31/69               | 22/75               | <0.0001 |             | 83/18        | 56/44               | 34/66               | 23/73               | <0.0001 |
| Angiography (%)             | 49            | 60                  | 73                  | 81                  | <0.0001 |             | 56           | 74                  | 86                  | 91                  | <0.0001 |
| PCI (%) of angiography      | 70            | 84                  | 86                  | 89                  | <0.0001 |             | 75           | 83                  | 85                  | 88                  | <0.0001 |
| <b>Medications @48h:</b>    |               |                     |                     |                     |         |             |              |                     |                     |                     |         |
| Aspirin (%)                 | 94            | 91                  | 98                  | 97                  | 0.007   |             | 97           | 96                  | 98                  | 98                  | 0.014   |
| b-blockers (%)              | 59            | 71                  | 80                  | 78                  | <0.0001 |             | 66           | 76                  | 85                  | 84                  | <0.0001 |
| ACE-I/ARBs (%)              | 57            | 65                  | 71                  | 76                  | <0.0001 |             | 57           | 66                  | 75                  | 80                  | <0.0001 |
| Statin (%)                  | 29            | 47                  | 74                  | 91                  | <0.0001 |             | 31           | 60                  | 78                  | 95                  | <0.0001 |
| Clopidogrel (%)             | 14            | 44                  | 71                  | 78                  | <0.0001 |             | 19           | 52                  | 80                  | 87                  | <0.0001 |
| *SCORE (4,5)                | 18            | 46                  | 73                  | 83                  | <0.0001 |             | 22           | 56                  | 79                  | 89                  | <0.0001 |
| <b>30-day Mortality (%)</b> | 20.5          | 13.7                | 12.2                | 8.3                 | 0.0004  |             | 8.7          | 5.2                 | 5.5                 | 4.9                 | 0.003   |
| OR <sub>adj</sub> (95% CI)† | 1.0           | 0.55<br>(0.39-0.24) | 0.40<br>(0.22-0.71) | 0.23<br>(0.11-0.46) |         |             | 1.0          | 0.39<br>(0.24-0.64) | 0.56<br>(0.34-0.89) | 0.51<br>(0.30-0.84) |         |

\*SCORE (4,5) management with  $\geq 4$  evidence-based medications (either aspirin, b-blockers, ACE-I/ARB, statins, or clopidogrel).

† Adjusted for: age, Killip (admission)  $\geq$  II, Anterior MI, heart-rate  $> 100$  bpm, SBP  $< 100$  mmHg, history of diabetes, hypertension, angina, renal failure, year performed.

**Conclusions:** In both sexes the management of pts with STEMI changed substantially during the last years. The high degree of implementation and adherence to recommended guidelines was associated with a significant decline in early mortality.

## Patients with Diagnosis of ST-elevation Myocardial Infarction not Treated with Reperfusion: Clinical Characteristics, Causes, and Short-term Outcome

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**Background.** According to registries and surveys about 30% of patients with diagnosis of ST-elevation myocardial infarction (STEMI) do not receive reperfusion therapy (RRx), neither primary PCI nor thrombolysis. The reasons for this phenomenon ("reperfusion paradox") are ill-defined.

**Aim.** To study clinical characteristics, reasons for omitting RRx and outcome of STEMI patients who did not receive RRx.

**Patients.** Source of data: Rambam Intensive Cardiac Care (RICCa) database.

Study period: 01.01 – 31.12.2004.

**Results.** During the study period 327 patients were hospitalized with diagnosis of STEMI. We identified 80 (24%) patients who did not receive RRx; mean age  $65 \pm 13$ . In-hospital mortality in entire cohort was 16%. Patient's characteristics presented in the table 1; reasons for not receiving RRx and outcome – in table 2.

Table 1.

|                                | Number of patients (%) |
|--------------------------------|------------------------|
| Female gender                  | 22 (28)                |
| Diabetes mellitus              | 24 (30)                |
| Previous MI                    | 13 (16)                |
| Previous PCI                   | 8 (10)                 |
| Previous CABG                  | 3 (4)                  |
| Cardiogenic shock on admission | 12 (15)                |

Table 2.

| Reason for not receiving RRx        | Number of pts (%) | In-hospital mortality (%) |
|-------------------------------------|-------------------|---------------------------|
| Late admission (>12 hrs)            | 41 (51)           | 9                         |
| Early ST-elevation resolution       | 16 (20)           | 0                         |
| Very elderly ( $\geq 90$ years old) | 3 (4)             | 0                         |
| Death before RRx                    | 4 (5)             | 100 (by definition)       |

**Conclusions.** Late admission is the main reason for not receiving RRx. After exclusion of patients who died shortly after admission, patients with early ST-segment resolution and late comers, the proportion of patients in whom omitting RRx seems inappropriate is small (6%).

## Enhanced Basal and Exertional Isometric Diastolic Function in Resistance Training Athletes

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**Background:** It is widely accepted that individuals involved in sports characterized by intense resistance training present with an increased absolute left ventricular (LV) wall thickness and mass and show a good systolic response to isometric exercise. Despite these well-established characteristics, there is no consensus regarding the diastolic features; rest diastolic function was described to be either normal, improved, or even diminished. Moreover, no information is available regarding diastolic function in athletes during isometric exertion itself. Therefore, our aim is twofold: 1) to assess the basal diastolic left ventricular function in athletes engaged in resistance training, and, 2) to evaluate the exercise-induced modifications in diastolic function while performing isometric exercise in these athletes, as compared with healthy untrained individuals.

**Patients and Methods:** The population consisted of 96 men (mean age 29±7 years): 48 weightlifters (W) who trained 15-20 hours/week and 48 sedentary (S), not engaged in any kind of routine training. All weightlifters had been active for >6 years, including the 6 months prior to the study. Ultrasound was performed using a commercially available echocardiographic Doppler system. Isometric exercise was performed in the supine position using a standard 2-hand bar dynamometer, i.e. a telescopic bar designed to be stretched simultaneously by both hands, determining the force in kilograms on a linear scale.

**Results:** End-diastolic volume at rest was 97±6 ml in S and 101±5 in W, augmenting to 100±6 and 118±11 at exercise (p=0.06 and p<0.01, respectively). End-systolic volumes at rest were similar in both groups, showing a significantly greater reduction during exercise in the weightlifters. Absolute LV mass was 167±30 g in S and 202±32 in W (p<0.0001). Stroke volume increased from 65±7 to 86±7 ml in S and from 70±6 to 107±11 in W (intergroup significance p=0.05 and p<0.01, respectively). A similar pattern of response was documented for ejection fraction, i.e. a significantly greater increase during exercise for the W group. Doppler diastolic indexes were peak early velocity (PEV, cm/s), peak atrial velocity (PAV, cm/s), early-to-atrial velocity ratio (EAR), acceleration time (AT, ms), acceleration rate (AR, cm/s/s), isovolumic relaxation time (IRT, ms), deceleration time (DT, ms) and deceleration rate (DR, cm/s/s). Out of these indexes, in the W group rest PEV was 68±7, EAR 1.8±0.2, AR 1242±176 and DR 414±44. All these values were significantly higher than those in the S group, with further increase during exercise (p<0.0001). Rest PAV in W group was 37±6, AT 55±4, IVR 63±3, and DT 164±4; these values were lower than in S group (p<0.0001 for all).

**Conclusions:** These data demonstrate that despite their markedly increased LV mass, diastolic function in resistance athletes remains normal and even better than in healthy sedentary men. Whilst rest systolic function was similar in both groups and presented only weak differences at exercise, athletes' LV diastolic function at rest and while exercising exhibited significant quantitative differences, noticeably distinguishing them from their sedentary counterparts.

## **Attenuation of the Expression of Matrix Metalloproteinases (MMPs) in Coronary Thin Cap Fibroatheromas (TCFAs) by Valsartan Alone or in Combination with Simvastatin**

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**Background:** We investigated the effect of Valsartan (V) alone or in combination with Simvastatin (S), on the gene expression of MMP-2 and -9, as well as their tissue inhibitors (TIMP-1 and -2) in coronary atherosclerotic plaques.

**Methods:** 12 streptozotocin-induced diabetic, hyperlipidemic swine were allocated into 3 treatment groups: placebo (P, n=4), V (n=4), and VS (n=4) and followed-up for 30 weeks. Coronary arteries (n=31) were harvested at the end of this period and 156 subsegments of interest were identified, cryosectioned, analyzed for the expression of MMP- 2, -9, and TIMP-1, -2 by real-time PCR, and examined by histology and immunohistochemistry. Intima/media ratio, minimum fibrous cap thickness, lipid deposition and inflammation were quantified, and lesions were histopathologically classified into minimal, intermediate, or TCFAs. The MMP-2/TIMP-2 and MMP-9/TIMP-1 ratio were assessed as measures of matrix degrading activity.

**Results:** Blood pressure, serum cholesterol and glucose were similar between the treatment groups. Compared to P, VS significantly reduced the levels of MMP-2 (Fig A), and the MMP-2/TIMP-2 ratio (Fig B) in TCFA. MMP-9 levels were reduced in both treatment groups (V, VS) but not significantly. These effects were regardless of the lipid lowering effects of S.

**Conclusion:** Treatment with VS significantly reduces the expression of MMP-2 (Fig A), in TCFAs, thereby suggesting it may have a role in attenuating the matrix degrading activity.

## Correlated Expression of D-Dimer Concentrations with Thrombotic Burden in Acute Pulmonary Embolism

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**Objective:** Thrombotic burden might have an influence on the concentration of D-Dimer in patients with acute pulmonary embolism (PE). The correlations of the concentrations of D-Dimer with the pulmonary artery occlusion score (PAOS) in a cohort of patients with acute PE was assessed in this study.

**Methods:** We have studied the correlation between the concentrations of D-Dimer and the PAOS in a group of 75 patients who presented to the Department of Emergency Medicine with a clinical picture suggestive for acute PE and had a positive pulmonary CT angiography.

**Results:** A significant ( $P < 0.001$ ) correlation ( $r = 0.42$ ) was noted between the concentration of D-Dimer and the PAOS in this group of 75 patients with acute PE. We have further divided the cohort into those who had a score below the median of 18 ( $n = 37$ ) and those who had a score above the median ( $n = 38$ ), the corresponding mean concentrations of D-Dimer being 364 and 814 ng/ml as opposed to a concentration of 285 ng/ml that was observed in the group of controls ( $n = 73$ ). In addition, in the ROC curves that were performed in order to differentiate between the presence or absence of PE, those who had the low score turned to be non significant (area under the curve 0.595 as opposed to 0.835 [ $p < 0.001$ ] for the group with the high score).

**Conclusions:** Patients with acute small PE might present with relatively low concentrations of D-Dimer. These findings might have implications regarding the diagnostic yield of D-Dimer in patients who are suspected of having acute PE.

## **Calcification of the Thoracic Aorta as Detected by Spiral Computed Tomography among Stable Angina Pectoris Patients: Association with Cardiovascular Events and Death**

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**Background:** Calcification of the thoracic aorta is associated with atherosclerotic risk factors, yet its pathogenesis and clinical implications are not yet elucidated. The goal of the present study was to assess whether thoracic aorta calcification is associated with an increased risk of cardiovascular events and death, in patients with stable angina pectoris.

**Methods:** A prospective cohort of 361 stable angina pectoris patients (307 men and 54 female, age ranged 37-83 years) underwent chest spiral computed tomography and were evaluated for aortic calcification. We recorded the prevalence of cardiovascular events and death during a 4.5-6 year follow-up.

**Results:** Aortic calcification was documented in 253 patients (70% of patients, 213 men, 40 women, mean age  $65 \pm 7$ ). Patients with aortic calcification were older ( $p < 0.001$ ) and fewer were classified as smokers (13% vs. 26%,  $p = 0.014$ ) in comparison to patients without aortic calcification. Significant correlation was found between patients with aortic calcification to those without for the presence of aortic valve calcification (28% vs. 11%,  $p < 0.001$ ), mitral annulus calcification (29% vs. 4%,  $p < 0.001$ ) and coronary calcification, as expressed by coronary calcium score ( $p < 0.001$ ). During a 4.5-6 years of follow-up, 19 patients have died, all of which were in the aortic calcification group. Age adjusted O.R. for total events, cardiovascular events and for acute MI, by aortic calcification, were 3.19 (95% C.I. 1.60-6.36), 2.82 (95% C.I. 1.30-6.11) and 5.62 (95% C.I. 1.73-18.27) respectively. Multivariate adjusted odds ratio for all events in patients with aortic calcification as compared to no calcification was 1.73 (95% C.I. 0.64-4.67,  $p = 0.27$ ), 3.74 (95% C.I. 1.71-8.18,  $p = 0.001$ ) and 3.22 (95% C.I. 1.50-6.90,  $p = 0.003$ ) for calcification of ascending aorta, descending aorta and both respectively.

**Conclusions:** Calcification of the thoracic aorta is age related and associated with coronary calcification as well as valvular calcification. Thoracic aortic calcification is associated with an increased risk of death and cardiovascular disease.

## **Timing of C-Reactive Protein Increment in Acute Traumatic Stress. Relevance for CRP Determinations in Acute Cardiovascular Events**

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**Objective:** To evaluate whether acute stress of few hours duration is capable to increase the concentration of C-reactive protein (CRP), a valuable biomarker in patients with acute myocardial infarction or stroke.

**Methods:** We measured the concentration of CRP in patients who presented with an acute fracture and in whom we can assume that the CRP concentrations prior to the event were within the normal limits.

**Results:** There were 20 patients with bone fractures and 20 gender and body mass index (BMI) matched controls at the respective mean+SD age of 52+27 and 51+21 years. The patients were examined at a mean+SD of 3.2+2.5 hours from their actual trauma and presented a modestly elevated concentrations of CRP (2.7+2.1 mg/l) as compared to the controls (2+2.2 mg/l). No difference was noted in the CRP concentration of 10 patients who presented earlier than the median of 2.5 hours (2.8+2.1 mg/l) and in those who presented later than that (2.8+2.1 mg/l). At the same time, the expected increment in the white blood cell count was noted in the patients ( $12.4+3 \times 10^3/\mu\text{L}$ ) as opposed to the controls (7.1+1.9).

**Conclusions:** We conclude that the expected increment in CRP within few hours from the onset of acute traumatic stress is modest. The findings are relevant for stressful conditions of acute myocardial infarction and stroke who present within few hours and in whom elevated CRP levels might represent the causative inflammation and are not necessarily a results of the acute stress/infarction per se.

## **Erythrocyte Aggregation is Associated with Erectile Dysfunction in Men with Ischemic Heart Disease**

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**Introduction:** Endothelial dysfunction and atherosclerosis have a significant role in the pathophysiology of erectile dysfunction (ED) and ischemic heart disease (IHD). Erythrocyte aggregation is one of the main factors affecting blood viscosity. However, the role of enhanced erythrocyte aggregation in the pathophysiology of ED and IHD has never been studied.

**Methods:** A total of 119 men underwent coronary angiography and filled the Sexual Health Inventory for Males questionnaire (SHIM). Excluded were men with acute coronary syndromes and men with recent or chronic inflammation. Erythrocyte aggregation was evaluated by a computer filming slides of blood smear and calculating the erythrocyte percentage (EP), i.e. the field that was covered by erythrocytes. High EP represented low erythrocyte aggregation. SHIM scores 21 or less represented ED.

**Results:** Included were 62 men, mean ages  $61.0 \pm 11.9$  years. Mean SHIM scores were  $15.5 \pm 8.1$  and the mean EP was  $70.9 \pm 14.7\%$ . EP was associated with SHIM scores ( $r=0.4$ ;  $p=0.001$ ) for the whole cohort. After dividing the cohort into four groups: men with no ED and no IHD ( $n=6$ ), men with ED but no IHD ( $n=9$ ), men with both IHD and ED ( $n=40$ ), and men with IHD but no ED ( $n=7$ ), EP was significantly higher in the last group compared with the other ( $69.7 \pm 8.7\%$ ,  $68.6 \pm 16.6\%$ ,  $69.0 \pm 14.6\%$ , and  $86.4 \pm 7.1\%$ , respectively;  $p=0.02$ ).

**Conclusions:** Increased erythrocyte aggregation is associated with ED. Men with IHD and normal erections have decreased erythrocytes aggregation. This finding may be the first step in establishing therapeutic intervention in order to prevent ED in men with IHD.

## Spatial Relation of QRS-T Vectorcardiogram is a Good Predictor of Coronary Disease in Patients with Normal Rest 12-Leads ECG

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**Background:** Many people with normal rest 12-leads ECG (NE) have underlying significant coronary disease (CAD). We describe a new method to detect CAD in this population.

**Methods:** 101 patients with NE underwent coronary angiography due to routine indications. Prior to angiography a computerized simultaneous multi-leads ECG was recorded and using a new dedicated algorithm for 3D electrical activity reconstruction we plotted the horizontal vectorcardiogram (VCG) of the whole ECG cycle. We defined two configurations of spatial relation for the QRS and T VCG loops: 1) T inside QRS (T in), 2) T outside or overlapping QRS (T out). Following angiography patients were categorized as having normal coronary arteries (NC), or coronary disease (CD) if >50% lumen diameter narrowing was found in one of the arteries.

**Results:**

|    | Number | T in | T out |
|----|--------|------|-------|
| NC | 31     | 20   | 11    |
| CD | 70     | 7    | 63    |

The positive predictive value of “T outside QRS” to reveal CD is 85% and the negative predictive value is 74% with 90% sensitivity and 65% specificity,  $p < 0.0001$ .

**Conclusions:** Using a regular simultaneous multi-leads ECG, we found a very high predictive value to reveal coronary disease in cases where the T VCG is outside the QRS VCG among patients with NE. This new feature can serve as a simple, low cost, easy to perform tool with no side effects for a global screening of coronary disease.

## **Weak Magnetic Field is Cardio Protective Following Chronic Coronary Occlusion but Not Following Reperfusion**

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**Background:** Previous study has shown that pre exposure the heart to weak magnetic field (WMF) reduces infarct size shortly after induction of myocardial ischemia. **Aim:** To further investigate the role of WMF on left ventricular remodeling following chronic coronary occlusion and short episode of ischemia reperfusion (I/R). **Methods:** The study was conducted on rats using two sets of experiments: (1) acute myocardial infarction (AMI) followed by a 4 week recovery period, and (2) 60 minutes of ischemia followed by 120 minutes reperfusion. Half of each group was subjected to WMF comprising of 15.95Hz and 80nT. Left ventricular function was measured with echocardiography before AMI or I/ R and while sacrificed. In the I/ R model, infarct size was determined as a percentage of the area at risk using triphenyltetrazolium chloride (TTC) staining. **Results:** AMI resulted in a significant 13.4%±1.7% reduction in SF compared with 6.1%±2.8% decrease in animals exposed to WMF (p<0.04). Exposing the heart to WMF prior to reperfusion did not show any preservation neither on SF (17.4%±6.7 decrease in SF in the treated group vs. 18.6 ±6.7% reduction in the non treated group, p=NS) nor on the infarct size. **Conclusion:** WMF was cardiac protective in the AMI model but not in the I/ R model. The mechanisms underlying cardiac protection following chronic injury is currently under investigation.

## **Short-term Exercise Training Induces Cardiac Protection Through Molecular Stimulation of the Remodeled Left Ventricle**

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**Background:** We have previously shown that long-term exercise training induces favorable morphological changes that play a major role in the deteriorated left ventricle following acute myocardial infarction (AMI). **Aim:** To investigate the effect of prior exercise training and duration on the molecular and gene expression alterations and their relation to cardiac repair during remodeling. **Methods:** SD male rats (n=188) underwent 3 or 7 weeks of swimming exercise training (90 min, 5 days/wk), or remained sedentary, and then subjected to AMI, followed by a 4-week sedentary period. At sacrifice, hearts were harvested, weighted, dissected the viable left ventricle, and flashed frozen for RNA extraction. Biotin-labeled cRNA were hybridized to a high-density oligonucleotide array (Affymetrix) and analyzed. **Results:** Based on a hierarchy of expression similarity, global analysis of all the expressed genes distinguished the experimental groups according to AMI (p<0.05): 486 and 533 genes from the 3 vs. 7 weeks, respectively. Criterion of 2 fold change in the average difference for each probe set divided to up/down regulated genes in 3 vs. 7 weeks, respectively (up: 33 vs. 160 genes; down: 93 vs. 41 genes). Bioinformatics web tools enabled to identify 45 genes that fall in functional categories of angiogenic, antiapoptotic, antifibrotic, and metabolic role in the injured heart, which were significantly altered by 7 weeks and even by 3 weeks of exercise prior to AMI. **Conclusion:** Short-term exercise training conducted prior to AMI induces sufficient cardiac protection of the remodeled myocardium through variety of gene family expression and alteration.

## **Transmyocardial Revascularization Does Not Increase the Efficacy of Endothelial Cell Transplantation**

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### **Background:**

We have reported that transmyocardial revascularization (TMR) of infarcted hearts prior to bone marrow cell (BMC) transplantation increases BMC survival and angiogenesis.

### **Hypothesis:**

We hypothesized that endothelial cell (EC) transplantation would supply the optimal cell population to enhance TMR-induced angiogenesis.

### **Methods:**

Female rats underwent LAD ligation 3 weeks before TMR (2 groups: EC+TMR and TMR), or no TMR (2 groups: EC and CONTROL), followed **after 15 minutes** by transplantation of  $3 \times 10^6$  male EC, or medium. After 2 and 4 weeks, we evaluated regional perfusion by microspheres, vascular densities by histology, cell survival by PCR, and LVEF by echocardiography.

### **Results:**

At both timepoints, vascular densities were increased by EC transplantation and by TMR ( $p < 0.05$ ), but TMR prior to EC transplantation had **no** additive effect.

At 2 weeks, regional perfusion was lowest in the control, intermediate in EC+TMR and TMR, and greatest in the EC group ( $p < 0.05$ ).

Fewer than 5% of EC survived to 2 and 4 weeks, and survival was not increased by prior TMR.

At 4 weeks, LVEF was increased by EC transplantation ( $57 \pm 4\%$  to  $65 \pm 4\%$  in EC+TMR and  $57 \pm 5\%$  to  $63 \pm 3\%$  in EC, both  $p < 0.05$ ), but was not improved by TMR alone or in controls.

### **Conclusions:**

While TMR increases the survival and angiogenic effect of BMC transplantation, this effect is cell-type specific, as no such effect is seen with EC. Combined TMR and cell transplantation may enhance treatment effects in infarcted hearts, but further studies defining optimal cell type and time interval between therapies are mandatory.

## **Human Serum Corin Level as a Predictor of Major Adverse Cardiovascular Events Post Percutaneous Coronary Intervention**

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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).

**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.

## Plaque Rupture: Look Out to the Other Side

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**Back ground:** Rupture of atherosclerotic plaque occurs when it cannot withstand the strain induced by the pulsating blood. Increase in circumferential strain will increase the risk of rupture.

**Aim:** To study the strain of the normal looking coronary artery arc (CA) opposing eccentric plaque.

**Methods:** We used Intravascular ultrasound to measured the ratio between the systolic and diastolic length of the normal arc of non culprit left main CA. Arteries were divided according to the atherosclerotic plaque arc: none,  $90^0\pm 30^0$ ,  $180^0\pm 30^0$  and  $270^0\pm 30^0$ . We used Young's modulus to describe tissue semi-compliance.

**Results:** In an artery with a plaque occupying  $270^0\pm 30^0$  of CA, a significant systolic distension, was found between the plaque ( $0.960\pm 0.049$ ) and normal arcs ( $1.04\pm 0.101$ ),  $p<0.00001$ . Such finding was not documented for an artery with a plaque occupying  $90^0\pm 30^0$  of CA. We calculated the Young's modulus; the higher the value, the stiffer the artery is. A significant difference was found between the stiffness of the free arc of a CA with a plaque of  $270^0\pm 30^0$  ( $1.35\pm 1.75$ ) and that of CA with a plaque of  $90^0\pm 30^0$  ( $3.78\pm 3.11$ ),  $p<0.0002$ , or with no plaque at all ( $5.25\pm 3.77$ )  $p<0.0001$ , suggesting that the larger the occupied arc, the less stiffer the normal part is.

**Conclusion:** The normal looking arc of eccentric plaque becomes more distensible as the arc becomes smaller. This enables on hand to allow sufficient cross-sectional area to maintain flow, but on the other hand increases the strain on the cap shoulder, rendering it for plaque rupture.

## Caloric Restriction Attenuates Cardiac Injury after Ischemia-Reperfusion Injury in Mice.

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**Background:** Caloric restriction (CR) is currently the only therapeutic intervention that delays age-related diseases and extends longevity in mammals. Our goal is to investigate whether CR can confer cardioprotection against ischemia-reperfusion (I/R) injury inflicted in murine models *in vitro* (isolated heart preparation) and *in vivo* (left anterior descending coronary artery -LAD- ligation).

**Methods & Results:** Wild type (WT) mice fed *ad libitum* were compared to life-time calorically restricted transgenic mice. Mice underwent LAD ligation at the age of 4 (young) or 18 (old) months (n=5-9 in each experimental group). Echocardiography conducted before and one week after ligation indicated that after ligation the fractional shortening was significantly higher in all calorically restricted mice (46±1.2% vs. 39±5.2% for young; 48±0.4% vs. 37±0.2% for old; p<0.05). In addition, hearts excised from young mice (n=5 in each group) were subjected to global ischemia followed by reperfusion (30 min each). Cardiac analyses showed that the calorically restricted mice exhibited smaller infarct sizes compared to WT (11±1.6% vs. 16±1.8%, p<0.05), superior left ventricular pressure recovery (56±4.5% vs. 42±5%, p<0.05), and lower leakage of creatine kinase into the coronary effluent.

**Conclusions:** Collectively, these results indicate increased resistance to I/R injury in the calorically restricted mice, and suggest that the CR regimen could enhance clinical interventions for patients with myocardial infarction.

## **Early Cardiac Remodeling is Associated with Increased Myocardial Angiotensin II Expression in Normotensive Type I Diabetic Rats**

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**Purpose of the Study:** Cardiac remodeling is a major component of both diabetic and hypertensive heart disease. Local angiotensin II plays a key role in cardiac remodeling. Its tissue levels are regulated by angiotensin converting enzymes (ACE and ACE2). We characterized myocardial changes in an animal model of hypertension and DM, with emphasis on the local renin-angiotensin system.

**Methods:** The male Sabra rat model (SBH/y) of salt induced hypertension was used. Control non-diabetic (C), diabetic (D) (induced by streptozotocin), and D or C rats fed with salt (DS or CS) were sacrificed after 6 weeks.

**Results:** Systolic BP increased in diabetic and nondiabetic rats on high-salt diets (CS and DS), and decreased in D, beginning at the third week of the experiment. Heart weight to body weight ratio was increased in CS, D and DS. Beta myosin heavy chain ( $\beta$ -MHC), atrial natriuretic peptide (ANP) and skeletal  $\alpha$ -actin expression were significantly increased in D and DS compared to C and CS. A similar pattern was seen for type III collagen and TGF- $\beta$  mRNA levels. Myocardial ACE mRNA levels were increased, while ACE2 mRNA levels were decreased in both D and DS groups. Cardiac AT1 receptor protein levels were unchanged but the levels of phosphorylated (p-) ERK were increased in D and DS.

**Conclusion:** an early cardiac remodeling phenotype is seen in normotensive DM. The increase in ACE, the decrease in ACE2 and the increase in cardiac pERK suggest a BP independent increase in free angiotensin II cardiac levels and signaling in DM.

## **Natural History and Clinical Significance of Tricuspid Regurgitation in Patients with Mitral Valve Prolapse and Significant Mitral Regurgitation**

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**Objectives** The purpose of this study was to evaluate the prevalence, clinical importance and the progression of tricuspid regurgitation (TR) in patients with mitral valve prolapse (MVP).

**Background** Little information is currently available on the echocardiographic progression of TR in patients with MVP and significant MR.

**Methods** We studied 477 patients (mean age 65±15 years; 34% females) with MVP and at least moderate MR. 233 (mean age 64±15 years) of 477 patients had 2D echocardiogram with ≥1 year follow-up interval. The mean follow up was 4.04±2.4 years (range 1 to 11).

**Results** At entry, 85% of 477 patients had non-significant TR and only 4% had significant TR. Tricuspid valve prolapse was uncommon and found in only 4%. Over the follow-up period 200 patients (85%) had no change in TR grade. There were only 2 patients (0.85%) who had non-significant TR and developed severe TR. Twenty four patients (10 %) that had a non-significant grade TR at baseline. developed moderate or more severe TR. Overall, 14% (32) of the study patients had an increase of at least 2 levels in the severity of TR over the follow-up period.

**Conclusions** The study encompasses the largest reported patient group studied by echocardiography with relatively long-term follow-up. Significant TR is uncommon (4%) in patients with MVP and significant MR and the majority (85%) does not progress during follow-up.

## **The Impact of Tricuspid Valve Surgery on Right Ventricular Function – a single Center Experience**

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**Background:** Severe tricuspid regurgitation (STR), either organic or functional, is associated with increased morbidity and mortality. A major consideration in fixing STR is to prevent RV dysfunction. This study sought to assess whether surgical repair of STR had indeed a positive impact on RV function.

**Methods:** Our database was queried for patients who underwent surgery for STR between 2004 and 2007. Data included demographic, clinical (NYHA functional class) and echocardiographic information. The diagnosis of STR and RV dysfunction were made by echocardiography. Patients must have had an echocardiographic study both before surgery and during follow-up at our center.

**Results:** The study included 16 patients (mean age  $64\pm 14$  years, 9 females). Six patients (37%) had valve replacement and 10 (63%) had valve repair. The follow-up period was  $13\pm 17$  months (range: 0.5-48 months). A single patient suffered from STR postoperatively (6%). However, the prevalence of RV dysfunction did not change significantly (12% before surgery vs. 25% after surgery). Data regarding functional class were available only in seven patients. Improvement was noticed in three patients (change of a single grade) but the average change for the entire group was insignificant ( $2.4\pm 0.5$  vs.  $1.9\pm 0.7$ ,  $p=0.11$ ). One patient died 1 month after surgery.

**Conclusions:** Surgical therapy of STR was associated with significant amelioration of regurgitation. However, this was not translated into a significant improvement in RV function. The long-term impact of these opposite trends on functional class and prognosis need to be determined. Earlier surgical referral with emphasis on subtle changes in RV function, and better patient selection are advocated.

## Venflon for Radial Artery Access (VERAA study)

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Transradial approach is an excellent alternative to the usual transfemoral route for both diagnostic and coronary interventions. Most operators use standard dedicated kits for port of accesses entry whereas in the literature there are few reports about other radial artery (RA) puncture techniques.

The aim of our study was to compare effectiveness and safety of much more chipper technique using simple Venflon and ordinary femoral sheath 5-6Fr (10\$) compared to the standard trans radial kits (30\$).

**Methods:** 913 pts (65.1% males, mean age 60, mean BMI 31.7) enrolled to our prospective, open label comparative study. In 61(7%) the RA was accessed by simple Venflon (17 GA) using ordinary 0.35" J-wire and 5-6Fr femoral sheath (1<sup>st</sup> group) and in others by standard trans radial kits (2<sup>nd</sup> group). There was a trend for more women in the 1<sup>st</sup> group, significantly more pts with peripheral vascular disease in the 1<sup>st</sup> group, without significant differences between two groups in other baseline characteristics.

**Results:**

| Characteristics  | 1 <sup>st</sup> group (Venflon)<br>61 pts | 2 <sup>nd</sup> group (Standard Kit)<br>852 pts | P<br>value |
|--|---|---|------------|
| Left RA puncture (%)                                   | 55.7                                      | 26.9%   | <0.001     |
| Failure of puncture (%)                                | 4.5                                       | 4.7   | ns         |
| Crossover to brachial A. (%)                           | 3.3                                       | 1.8   | ns         |
| Crossover to femoral A. (%)                            | 3.3                                       | 4.5   | ns         |
| Crossover to ulnar or RA on<br>2 <sup>nd</sup> arm (%) | 0   | 1.2   | ns         |
| PTCA (%)   | 31.7                                      | 44.7  | <0.01      |
| Multivessel PTCA (%)                                   | 6.7                                       | 12.1  | 0.2        |
| Radiation time (min)                                   | 7.9                                       | 10.8  | 0.079      |
| No of nights to discharge                              | 1.09                                      | 1.32  | 0.1        |
| RA thrombosis (pts)                                    | 0   | 2   | ns         |

**Conclusions:** Trans radial catheterization using Venflon technique for port of access entry is comparable, effective, safety and chipper alternative to the standard radial kit technique.

## **Comparison of Three Dimensional and Two Dimensional Coronary Angiography: Preliminary Results**

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**Background:** Three-dimensional (3-D) coronary angiography was introduced recently as a promising technique in the coronary catheterization laboratories.

**Aim:** Comparison of three dimensional and two-dimensional (2-D) coronary angiography.

**Methods:** 10 consecutive patients were evaluated by 3-D angiography and were compared to 38 consecutive patients studied by the conventional technique by fluoroscopy time, radiation dose and the amount of contrast used.

**Results:** 3-D was superior to 2-D angiography in reducing volume of contrast agent used, 63.9+ 17.7 ml vs. 110+ 41.4 ml,  $p < 0.008$ . We don't observed a significant difference in the fluoroscopy time (minutes), 4.77+ 1.45 for 3-D vs. 5.18+ 3.12 for 2-D angiography,  $p = \text{ns}$ , and radiation dose(mGy), 652.5+ 216.5 for 3-D vs. 739.2+ 267.2 for 2-D angiography,  $p = \text{ns}$ .

**Conclusions:** 3-D angiography is superior to 2-D angiography by significant reduction in the volume of contrast agent used, but a significant reduction in fluoroscopy time and radiation dose was not observed.

## Safety and Feasibility of Transradial Primary Coronary Intervention in Patients with Acute Myocardial Infarction

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Intense anticoagulation or antiplatelet therapy potentially increases the risk of bleeding complications during primary percutaneous coronary intervention (PCI) in patients with acute myocardial infarction (AMI). The transradial approach to coronary interventions is associated with a lower incidence of vascular access site complications, although it is more demanding.

**Objectives:** To assess the efficacy and safety of radial versus femoral coronary catheterization in primary PCI for patients with AMI.

**Methods:** We studied 232 consecutive patients who underwent primary PCI for AMI in Killip class 1-3.

### Results:

|   | Radial group<br>(n=34) | Femoral group<br>(n=198) | P value |
|---|------------------------|--------------------------|---------|
| Mean age  | 59.3±10.6              | 60.2±14.3                | NS      |
| Women   | 26%                    | 18%                      | NS      |
| Diabetes mellitus   | 36%                    | 24%                      | NS      |
| Body mass index   | 31.9±7.3               | 26.6±5.6                 | <0.0001 |
| Significant peripheral vascular disease                     | 21%                    | 6%                       | 0.005   |
| <u>Medical treatment before and during catheterization:</u> |                        |                          |         |
| - Aspirin and clopidogrel                                   | 94%                    | 97%                      | NS      |
| - Heparin   | 97%                    | 96%                      | NS      |
| - IIb/IIIa GP antagonist                                    | 84%                    | 78%                      | NS      |
| <u>Procedural results:</u>                                  |                        |                          |         |
| Crossover to alternative entry site                         | 3%                     | 1%                       | NS      |
| Aspiration device   | 38%                    | 29%                      | NS      |
| Intra-aortic balloon pump                                   | 6%                     | 7%                       | NS      |
| Cannulation time (minutes)                                  | 1.9±0.6                | 1.7±0.7                  | NS      |
| Total procedure time (minutes)                              | 64±26                  | 61±23                    | NS      |
| Success rate  | 97%                    | 98.5%                    | NS      |
| <u>In-hospital outcome and complications:</u>               |                        |                          |         |
| MACE  | 6%                     | 5%                       | NS      |
| Significant access site complications                       | 0%                     | 2.5%                     | <0.0001 |
| Blood transfusion   | 0%                     | 1.5%                     | <0.0001 |

**Conclusion:** Transradial primary PCI is a safe and feasible with similar results to those with transfemoral approach, but with less vascular complications.

## **Angiographic Approach to Bifurcation Lesions in Patients with STEMI Undergoing Primary PCI**

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**Background:** PCI to bifurcation lesions is technically challenging. This is particularly the case in patients with STEMI due to culprit lesion pathology and the time factor limitation. We compared different technical approaches for bifurcation lesions during 1° PCI and evaluated clinical outcomes.

**Methods & Results:** We analyzed our primary PCI database (1.2005 – 11.2007) for culprit bifurcation lesions with branch width  $\geq 2$  mm. Of 387 cases during 78 (20 %) culprit bifurcations were detected (52 LAD, 18 RCA, and 8 LCx). Double wire technique was used in 62 patients. All patients underwent stenting of the main vessel (4 DES), 63% had branch vessel balloon angioplasty and in 17% a stent was implanted. The patients were divided into two groups: A - PCI to main vessel only, B – PCI to both vessels. Angiographic analysis revealed significantly reduced branch patency in group A (90 vs. 17%,  $p < 0.01$ ). Mortality (mean 14 months) in patients with bifurcation culprit lesions was 2.1% as compared with 4.2% in the general primary PCI cohort. There were no differences in mortality between group A and group B.

**Conclusions:** Culprit bifurcation lesions during primary PCI are not associated with increased risk for mortality. Double branch treatment is associated with better final angiographic result that is not translated in our small series into clinical difference.

## Drug Eluting Stents Restenosis Failures: Comparison between Cypher and Endeavor Stents

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**Objective:** We determined the different pattern and outcomes of limus-based DESs restenosis 'failures' according to stent type: e.g. Cypher vs. Endeavor stents.

**Methods:** We have identified all episodes of restenosis in 63 patients following Cypher (n=53) or Endeavor (n=10) stenting in our institution between 1/2004 and 2/2007. Restenosis pattern was classified as focal, diffuse or proliferative.

**Results:** Cypher failure was observed in 53 pts: (age 64±11 years, 79% male) with 57 lesions, referred for coronary angiography mostly (77%) due to acute coronary syndrome. Ten patients had Endeavor failure (age 72±8.7 years, 80% male). Retenotic patients were often characterized as 'high-risk' in both group with diabetes (73.5% versus 80%), HTN (83% versus 100%), and dyslipidemia (89% versus 90%). Cypher stents length were 24±8mm vs. 19±6 mm for Endeavor stent (p=0.07) with stent diameter averaging 3.0±0.4mm (Cypher) vs. 3.2±0.5mm (Endeavor) respectively (p=0.1). Mean time to target vessel revascularization (TVR) was 12.5±10.6 mos for Cypher and 5.2±2.7 mos for Endeavor (p<0.05). The vast majority of restenotic lesions (71%) were focal in the Cypher group vs. diffuse (80%) in the Endeavor group (p=0.004). Accordingly, the incidence of diffuse restenosis was significantly higher in Endeavor compared to Cypher stent (12% vs. 80%, p<0.0002). The treatment of ISR in both groups is shown in **Table**:

| Treatment of DES ISR   | Cypher | Endeavor | P values |
|------------------------|--------|----------|----------|
| Re-stenting using DES  | 63%    | 60%      | NS       |
| POBA / Cutting balloon | 26%    | 0%       | p=0.05   |
| CABG                   | 7.5%   | 30%      | NS       |
| Conservative           | 3.5%   | 10%      | NS       |

At six month follow up the overall MACE (death, MI, TVR) was 11.3% in the Cypher group and 50% in the Endeavor group (p=0.01).

**Conclusions:** Based on our experiences and compared to Cypher stent, Endeavor DES failure showed: 1) more diffuse restenotic pattern, 2) shorter time to restenosis, and 3) worse overall intermediate-term clinical outcome.

## **PRO-Kinetic: Results from an “All Comers” Clinical Registry**

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**Background:** The PRO-Kinetic stent combines the properties of Cobalt Chromium metal alloy with state-of-the-art design to deliver enhanced performances in all procedures. PRO-Kinetic's thin struts, low profile, exceptional deliverability and silicon carbide PROBIO® passive coating may ensure optimal clinical outcomes

**Purpose:** To conduct a retrospective registry of consecutive “real world” patients treated using PRO-Kinetic stents at Rabin Medical Center between January 2006 and March 2007.

**Methods:** With 40% DES utilization at our center, the PRO-Kinetic stent has been used in a wide variety of patients and clinical scenarios. Our study included 254 consecutive patients treated for 264 lesions. Patients were carefully followed by our Database team and all events were documented and adjudicated. We had 100% f/u rate by 6 months. Plavix administration was indicated for 3 months in stable patients and for 6 months or more following acute coronary syndrome events.

**Results:** The patients' characteristics are noted for 46% rate of diabetics and 18% renal insufficiency. Indications for angioplasty included patients with either stable or unstable clinical scenarios. 45% of lesions were of class B2/C and 23% of patients had reduced TIMI flow prior to interventions. The vast majority of these patients had acute or recent MI. The mean RVD was 2.8mm and lesions length was 10.4 mm prior to PCI and with angiographic success in all consecutively treated patients. The six month clinical outcome data were as follow: MACE rate of 5.5%, with 2.4% total mortality, 0.4% of any MI and TVR rate of 3.1% per treated patient and 3.4% per treated lesion and not a single case of stent thrombosis.

**Conclusions:** 1) The PRO-Kinetic clinical data shows excellent results on a group of coronary patients, treated consecutively. 2) The data should emphasize the remaining role of 'state of the art' non DES platforms for patients with a wide variety of characteristics and/or clinical syndromes.

## Cypher Stenting: Focal Restenosis Pattern Treatment and Outcome

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**Background:** The preferred treatment strategy for drug eluting stent (DES) restenosis (balloon angioplasty vs. re-stenting) is yet unknown.

**Objective:** We aimed to compare those different treatment strategies with patients outcomes following focal ISR within Cypher stents.

**Methods:** We identified all episodes of Cypher restenosis in 53 consecutive patients with 57 lesions. Patients' demographics according to angiographic restenotic pattern (e.g. focal and diffuse) were obtained. Focal restenosis was investigated in term of treatment type: re-stenting, balloon/cutting (POBA) angioplasty, bypass surgery or conservative treatment. This cohort was followed for 6 month for major adverse cardiac event rate (MACE) according to the treatment strategy.

**Results:** Cypher failure was observed in 53 pts; 42 (79%) patients had focal in stent restenosis (age 65±11 years, 69% male) and 11 (21%) patients had diffuse restenosis (age 62±12 years, 82% male). The prevalence of diabetes (focal vs. diffuse) was 69% vs. 82%, respectively, hypertension (79% vs. 82%), and dyslipidemia (81% vs. 82%) and hronic renal failure was encountered in 12% vs. 36% of pts (p=0.07). Focal restenosis was observed in 42 pts with 45 lesions, 31 (69%) lesions were treated using stent deployment and in 12 (27%) lesions POBA (±cutting) was the preferred treatment option. Outcome of patients according to treatment types is shown in **Table**:

| <b>Pts N=42</b> | <b>Re-Stenting</b> | <b>POBA</b> | <b>CABG</b> |    |
|-----------------|--------------------|-------------|-------------|----|
| <b>F/U pts</b>  | <b>N=28</b>        | <b>N=11</b> | <b>N=2</b>  |    |
| Death           | 0                  | 0           | 0           | NS |
| MI              | 3.6%               | 0           | 0           | NS |
| ST              | 3.6%               | 0           | 0           | NS |
| TVR             | 16.7%              | 0           | 0           | NS |
| MACE            | 18.0%              | 0           | 0           | NS |

At six month follow up, no death was encountered in any patient. One patient had stent thrombosis presented as AMI in the re-stented group.

**Conclusion:** Our experience showed that *focal* in stent restenosis pattern within Cypher stents had a tendency towards better clinical outcomes and especially when treated using POBA (±cutting) as compared to re-stenting sterategy.

## Comparison of Drug Eluting Stents with Bare Metal Stents in Daily Practice for Bifurcation Lesions: One Year Results of Simple One Stent Strategy

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**Background:** The optimal stenting strategy in coronary artery bifurcation lesions is unknown. A simple approach, stenting of the main branch with provisional stenting of the side branch is currently implemented in the majority of cases when bare metal stenting [BMS] is used. Drug-eluting stents [DES] decreased the TVR rate in most lesions. The one year results of “simple approach” to these lesions comparing DES and BMS is not well documented.

**Objective:** compare the one year results of the “simple approach” using BMS versus DES in “real world” practice.

**Methods & Results:** The study included 192 patients with bifurcation lesions treated by single stent in the main branch.

|                  | BMS [n=89] | DES [n=103] | P-value |
|------------------|------------|-------------|---------|
| Age [year]       | 64±12      | 63±12       | 0.5     |
| Male             | 81%        | 74%         | 0.3     |
| ACS              | 52%        | 49%         | 0.7     |
| DM               | 31%        | 33%         | 0.8     |
| Renal failure    | 13%        | 10%         | 0.6     |
| LAD/DIAG         | 44%        | 64%         | 0.002   |
| RVD [mm]         | 2.9±0.4    | 2.9±.5      | 0.6     |
| One year         |            |             |         |
| Death            | 8%         | 1%          | 0.03    |
| MI               | 9%         | 5.8%        | 0.4     |
| Stent thrombosis | 5.6%       | 2.9%        | 0.5     |
| TVR              | 22.5%      | 8.7%        | 0.01    |
| CABG             | 4.6%       | 4.9%        | 1.0     |
| MACE             | 28%        | 15%         | 0.03    |

By multi-variate analysis the age, renal function and clinical presentation were significant independent predictors of one year mortality while DES use was not.

**Conclusions:** Our results would indicate that with “simple approach” of treating bifurcation lesion the use of DES is not associated with increased thrombotic complication. The TVR rate is significantly decreased.

## The Impact of Culprit Lesions Morphology on Clinical Outcomes in Urgent Primary PCI for STEMI

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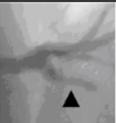
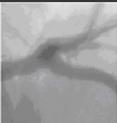
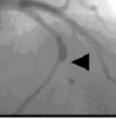
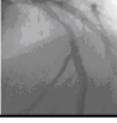
**Background:** Primary percutaneous coronary intervention (PCI) during STEMI is targeted at the culprit lesion. However, there are no studies classifying the different morphologic characteristics of culprit lesions on angiography or evaluating their possible prognostic significance.

**Objectives:** The aim of the study was to classify culprit lesions during primary PCI and to evaluate the long-term clinical results accordingly.

**Methods:** Images from 80 patients (81% men, mean age 62±13 years) undergoing primary PCI were evaluated. Culprit lesions were classified into morphologic subgroups according to their geometric characteristics. Findings were compared between 30 patients with major adverse-events up to one year (death, re-infarction or need for repeated revascularization) and a control group of 50 patients with no such adverse-events during follow-up.

**Results:** On long-term clinical evaluation, two morphologic types were significantly associated with adverse events ( $p < 0.05$ ). A slow tapering-down ("bird-beak") culprits were detected in 7 patients (23%) from the adverse-events group while in only 3 patients (6%) from the control group. Culprit lesions in the vicinity of a bifurcation were detected in 14 patients (47%) from the adverse-events group while in only 12 patients (24%) from the control group. The "cut-off" morphology, which was most prevalent in both groups, was less associated with the adverse-events group, although with a trend that did not reach statistical significance.

**Conclusions:** The culprit morphology during primary PCI might have a prognostic significance. The "bird-beak" morphology and near-bifurcation culprits are significantly associated with worse clinical outcomes and patients with such lesions should be regarded at higher prognostic risk.

| culprit     | before PCI  | after PCI   | adverse-events* group (n=30) | control group (n=50) | <i>P</i> |
|-------------|---|---|------------------------------|----------------------|----------|
| "bird-beak" |  |  | 23%                          | 6%                   | 0.02     |
| "cut-off"   |  |  | 50%                          | 70%                  | 0.07     |
| bifurcation |  |  | 47%                          | 24%                  | 0.04     |

\* defined as death, re-infarction or need for repeat revascularization at 1 year follow-up.

## **Results of Urgent Percutaneous Coronary Intervention in Patients with Acute Myocardial Infarction and Significant Aortic Stenosis**

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**Background:** Percutaneous coronary intervention (PCI) is associated with increased risk in the presence of severe aortic stenosis (AS). However, recently published data indicate that elective PCI is relatively safe in a subset group of severe AS patients with single-vessel coronary disease and good functional class. We sought to determine the safety of urgent PCI in patients with significant (at least moderate) AS.

**Methods:** We analyzed 18 consecutive patients with AS, who underwent urgent PCI (17 primary 1 rescue) for acute myocardial infarction at our medical center between 2001 and 2007. Data included demographic, clinical, angiographic and echocardiographic information. Aortic stenosis and ventricular function were graded by echocardiography criteria. The follow-up duration for post-procedure events was 6 months.

**Results:** The study group included 18 patients (12 males, mean age  $75\pm 8$  years) with aortic stenosis (61% moderate, 39% severe, mean BSA indexed aortic valve area:  $0.5\pm 0.1$  cm<sup>2</sup>/m<sup>2</sup>). All patients had AMI (17 had STEMI) with mean Killip score  $1.4\pm 0.9$  (72% in Killip I). The mean CADILLAC score of the group was  $8.5\pm 4.1$ . Complete reperfusion (TIMI flow 3) was achieved in 13 patients (72%). There were no events of acute stent thrombosis and zero TVR rate at 1 and 6 months after PCI. Mortality rate was 22% (all during the first month but none during the procedure). Of the 4 deaths: 3 were females and  $>75$  years old, respectively. Two patients had acute renal failure at the first month and one patient had CVA diagnosed at 6 months after PCI.

**Conclusions:** Urgent PCI in patients with significant AS and acute myocardial infarction is problematic from the standpoint of hemodynamic stability but if indicated it was shown to be feasible and relatively safe even in patients with concomitant LV dysfunction and significant co-morbidities.

## Sirolimus - Versus Paclitaxel-Eluting Stents: Long-Term Clinical Results in Acute Myocardial Infarction

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**Background:** Recent trials indicate that drug-eluting stents (DESs) can be used in primary percutaneous coronary intervention (PCI). However, the efficacy of the two most common DESs, the sirolimus-eluting stent and the paclitaxel-eluting stent, has not been compared in this setting.

**Objectives:** The aim of the study was to investigate the clinical outcome of patients treated with primary PCI using a DES and to compare the efficacy of the sirolimus- and paclitaxel-eluting stents.

**Methods:** Primary PCI with a DES was performed in 151 patients: 82 treated with sirolimus-eluting stents and 69 with paclitaxel-eluting stents. The sirolimus-eluting stent group was characterized by higher rates of anterior myocardial infarction and ejection fraction lower than 40% (Table). Death, reinfarction, and need for repeated revascularization were assessed.

**Results:** The rate of major adverse cardiac events in the whole cohort was 11.2%. There was a trend towards higher mortality at 6 months in the paclitaxel-eluting stent group, but that trend decreased on longer follow-up. Patients treated with sirolimus-eluting stents needed more revascularizations, but the difference between the groups was not statistically significant.

**Conclusions:** The use of a DES in primary PCI yields excellent clinical results. Outcome appears to be equally good for treatment with sirolimus- or paclitaxel-eluting stents, though the latter may be associated with a small trend towards higher mortality.

|                       | Sirolimus-Eluted Stents (n=82) |          | Paclitaxel-Eluted Stents (n=69) |          |
|-----------------------|--------------------------------|----------|---------------------------------|----------|
| Age (yrs)             | 58±12                          |          | 60±10                           |          |
| Male                  | 85%                            |          | 90%                             |          |
| Anterior AMI          | 76%*                           |          | 52%*                            |          |
| Diabetes mellitus     | 26%                            |          | 22%                             |          |
| 2/3-vessel disease    | 62%                            |          | 58%                             |          |
| Post-PCI TIMI 3       | 94%                            |          | 97%                             |          |
| EF < 40%              | 51%*                           |          | 34%*                            |          |
| Follow-up             | 6-month                        | 12-month | 6-month                         | 12-month |
| Death                 | 0% <sup>†</sup>                | 2.4%     | 2.9% <sup>†</sup>               | 6.4%     |
| Re-AMI                | 0%                             | 0%       | 0%                              | 0%       |
| TVR                   | 4.9%                           | 7.3%     | 1.5%                            | 2.1%     |
| CABG                  | 2.4%                           | 3.7%     | 1.5%                            | 2.1%     |
| MACE                  | 7.3%                           | 12.2%    | 5.9%                            | 10.4%    |
| *p<0.05, †p=0.05-0.10 |                                |          |                                 |          |

## **Transradial Access for Coronary Procedures in a Moderate Volume Hospital: a Potential for Eliminating Serious Access Site Complications?**

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**Background:** Numerous studies have demonstrated the feasibility and increased safety of transradial approach (TRA) over transfemoral approach (TFA) for coronary iprocedures in carefully selected patients. However the penetration of TRA in routine practice is still low. We sought to compare TRA with TFA for elective and emergency procedures in unselected patients in a hospital with moderate procedure volume.

**Methods:** We studied 100 consecutive patients who underwent cardiac catheterization iin October-November 2007. The patients were randomly assigned to TRA or TFA iaccording to the day of the week on which the procedure was performed. There were no exclusion criteria. Patients in TRA group with prior CABG or ischemic Allen test in the right hand underwent catheterization from the left radial access. The primary iend point was the incidence of access site complications (hematoma >10cm, pseudoaneurysm, arterio-venous fistula, need for blood transfusion or surgery).

**Results:** There were 52 patients in TFA group and 48 patients in TRA group. Coronary angioplasty (PCI) was performed in 25/52 (48%) patients in TFA group and 35/48 (73%) patients in TRA group ( $P < 0.05$ ). The access failure rate was 1/52 (2%) and 4/48 (8%) in TFA and TRA group respectively ( $P = NS$ ). The PCI was successful in all patients in TFA group and in 34/35 (97%) patients in TRA group ( $P = NS$ ). The mean ( $\pm SD$ ) contrast use and fluoro time in patients who underwent PCI was  $259 \pm 85$  cc and  $13.5 \pm 8.8$  min versus  $223 \pm 88$  cc and  $13.6 \pm 7$  min for TFA and TRA group respectively ( $P = NS$ ). 6/52 (11.5%) patients in TFA group and 0/48 (0%) patient in TRA group had at least one vascular complication ( $P < 0.05$ ). The rate of complications excluding hematomas was 3/52 (5.8%) and 0/48 (0%) in TFA and TRA group respectively ( $P = NS$ ).

**Conclusions:** The TRA for coronary procedures is a safe alternative to TFA in unselected patients in a moderate volume hospital. The routine implementation of TRA has a potential to reduce or even eliminate serious access site complications.

## Drug Eluting Stents – Pattern of Restenosis and Outcome Impact

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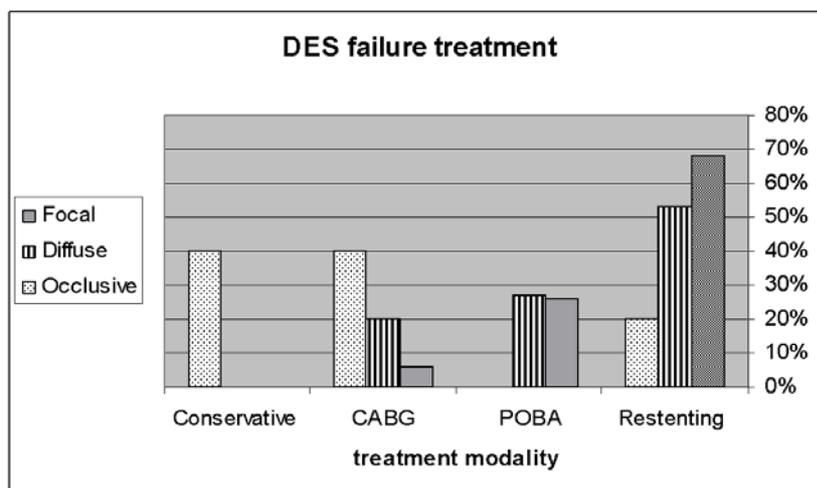
**Objective-** We sought to identify the Drug eluting stent (DES) restenosis pattern and outcome at six month

**Background** – The in stent restenosis (ISR) pattern (according to Mehran classification) in bare metal stent (BMS) is known as prognostic factor. Little is known whether this remains in DES.

**Methods** – Between January 2004 and February 2007 we identified 71 patients with DES related ISR: 75% Cypher stent, 14% Endeavor stent and 11% Taxus stent.

ISR pattern was classified according to Mehran classification as: Focal, Diffuse or Occlusive. Major adverse cardiac events were obtained at Six month follow up.

**Results** – During the study period, DES failure was presented in 2.9% of treated patients. Mean age was 65±11 years, 75%-male. 68%-DM (20% Insulin treated), 41%-after CABG, and chronic renal failure (Create.  $\geq 1.5$  mg/dl) was encountered in 18% of pts. Multi-vessel disease was presented in 80%, and 44% had previous MI. Unstable angina was the clinical presentation in 52 (73%) of patients. Focal ISR was found in 71%, diffuse-ISR in 22% and 7% presented with stent occlusion. Restenting was more often used for focal and diffuse pattern (68% & 53% respectively) followed by POBA (26% & 27% respectively) as compared to CABG or medical therapy in the occlusive pattern (Fig.1)



Six month outcomes according to ISR type were available in 67 pts.

The incidence of recurrent PCI increased in the diffuse restenosis type compare to the focal group, as well as MACE of 14.6% versus 42% p=0.05. There was no increment in mortality or myocardial infarction.

**Conclusions** - Although focal restenosis pattern is described in the majority of the pts, treatment modalities varied and remain to be defined. The pattern of DES is a predictor of the need for reintervention. The overall intermediate-term prognosis is favorable.

## **In-Stent Restenosis : Different Time Course of Clinical Presentation between Drug Eluting Stents and Bare Metal Stents**

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**Background:** In-stent restenosis (IRS) of drug eluting stents (DES) is relatively infrequent . The timing and clinical presentation of IRS following implantation of DES is not well characterized.

**Aim:** To evaluate the clinical presentation of IRS after DES implantation .

**Methods.** Retrospective study of 78 pts (age: 65±10 y.) out of 1418 pts who had PCI between 4/04 and 10/06 and required a second procedure for IRS. Patient data was prospectively recorded in a computerized database. Demographic, clinical, angiographic and angioplastic characteristics were studied. We compared the clinical presentation and its timing after the initial procedure between patients initially given BMS (N=69 ) and those given DES patients (N=9).

**Results:** Patients initially treated with DES or BMS who later developed ISR had similar baseline clinical, angiographic and angioplasty characteristics during the initial procedure.

The time to the second procedure was 226 ± 172 days for the whole group. The clinical presentation of ISR was similar in BMS and DES : STEMI: 3% vs 22% , NSTEMI: 22% vs 26% ; unstable angina 49% vs. 33% and stable angina in 10% vs. 22%,. A trend for differences in the timing of the presentation of ISR was observed. ISR presented clinically during the initial six months in 58% of BMS pts vs 11% in DES, between 6 to 12 months in 26% of BMS and 33% in DES and after twelve month ISR presented in 56% of patients treated with DES in comparison with 16% in patients receiving BMS (p=0.08).

**Conclusion:** The clinical presentation of instent restenosis is similar in DES and BMS. However, there is a significant delay in the timing of clinical presentation of ISR in patients treated with DES. Whether this observation is an additional expression of the delayed healling of the arterial wall observed in drug eluting stents should be further investigated .

## Long Term Results of Drug Eluting Stenting of Bifurcation lesions: A Systematic Approach Towards Stenting

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**Background:** The optimal stenting strategy in coronary artery bifurcation lesions is unknown. Recent studies suggest that, independent of stenting strategy; excellent clinical and angiographic results were obtained with percutaneous treatment of de novo coronary artery bifurcation lesions with drug-eluting stents [DES]. A systematic coronary stenting approach for bifurcation lesion using DES is needed. A strategy of using two DES may be preferred if the side branch is of adequate size and heavily diseased, while in other cases a 'simpler' approach of stenting the main vessel only, with optional (provisional) stenting of the side branch may be appropriate.

**Objective:** The strategy of systematic coronary stenting in bifurcation lesions was evaluated in a large single-center observational study during a two-year inclusion period.

**Methods & Results:** The study included 170 patients with a mean age of 63±12 years, 78% male, 52% with acute coronary syndromes. The LAD/diagonal bifurcation was involved in 63.5% of cases. Anti GP 2b/3a drugs were used in 72% of cases. In 78% of cases sirolimus-eluting stents [Cypher] were used. Initial two stents strategy was used in 63 pts [37%], while in 107 pts the strategy was stenting of the main branch with provisional stenting of the side branch, of whom 7 crossed to side branch stenting also due to procedural indications [dissection or unsatisfactory angiographic results].

|                  | Six months [n=170] | One year [n=170] | Two years [n=85] |
|------------------|--------------------|------------------|------------------|
| Death            | 1.2%               | 1.8%             | 3.5%             |
| MI               | 4.7%               | 4.7%             | 8.2%             |
| Stent thrombosis | 1.8%               | 1.8%             | 3.5%             |
| TVR              | 5.3%               | 7.1%             | 14%              |
| CABG             | 4.1%               | 4.7%             | 8.2%             |
| MACE             | 10%                | 13%              | 27%              |

**Conclusions:** Our results would indicate that a systematic approach towards PCI in bifurcation lesions with careful attention to procedural technique and using DES is associated with favorable long-term clinical results.

## Procedural and Clinical Results of Percutaneous Patent Arterial Duct Closure in Adults

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**Background:** Patent arterial ducts (PDA) of clinical importance are rare in adults. They may require percutaneous device closure.

**Aim:** To examine the procedural and clinical outcomes of patients with PDA closure at the adult congenital heart unit in-order to characterize this relatively uncommon patients' group.

**Results:** We studied 28 pts. (20 female) who had PDA closure over a 13 years period; mean age at catheterization was 41±16 yrs (range 18-72) and mean age at diagnosis was 30±21 yrs. NYHA FC was I in 9 pts., II in 12, III in 6 and IV in one. In 19 pts. there was a continuous murmur. Echocardiography showed LV diastolic diameter 55±6 mm and left atrial area 24±5 cm<sup>2</sup>. LV systolic function was good in 21, lower limit in 2, mild dysfunction in 2 and mild-moderate dysfunction in 3 pts. Diastolic function was normal in 16, delayed relaxation in one, restrictive in 5 and unknown in 6 pts. Two patients each had mild-moderate and moderate mitral regurgitation. Duct diameter by echo was 4.5±1.3 mm and by angiography 3.7±1 mm. Hemodynamics: Qp/Qs=1.6±0.4, mean pulmonary artery pressure 22±9 mmHg, mean right atrial pressure 6±2 mmHg, LVEDP 17±6 mmHg, cardiac index 3.2±0.8 l/min m<sup>2</sup> and pulmonary vascular resistance 1.8±1.2 Woods x msq. **Devices used:** 3 were closed with 17 mm Rashkind umbrella, 8 with Gianturco coils and 17 with Amplatzer PDA occluders (sizes 6/4 n=4, 8/6 n=9, 10/8 n=2, 12/10 n=1, 14/12 n=1). **Procedural success and complications:** None of the Rashkind and Amplatzer devices had a residual leak. One Amplatzer device was pulled through a very short duct, and another one was implanted on a later session. One patient had two coils with a very mild residual leak. One patient had hemolysis due to post coil residual leak and had a second coil implanted. One coil embolized to the pulmonary artery and was successfully retrieved. There were no late complications. On follow up echocardiograms, the LV diastolic diameter decreased to 50±13 mm (p=0.01), left atrial area to 21±5 cm. In 3 patients, echocardiogram on the day post procedure showed decrease in diastolic diameter, increase in wall thickness and a new abnormal relaxation pattern, presumably due to the abrupt reduction of preload. **Clinical outcomes:** Of the 19 patients who were in NYHA FC II or worse before PDA closure, 11 improved by one FC, 6 did not improve and in 2, FC post procedure is not known. One patient died 3 years post procedure from worsening mitral regurgitation and severe LV dysfunction despite initial improvement. **Conclusions:** Percutaneous PDA closure is feasible in all ages, with a very high success rate and very low rate of minor and transient complications, mostly related to coils. In recent years, Amplatzer devices have been used successfully, without complications or residual leaks, even in relatively large ducts. Post procedure there is a significant decrease of LV size and in many also an improved functional capacity.

## Referring Patients for Coronary Angiography Solely by the Internist: The CAFAIN-D Project.

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**Background** Increased demands of internal departments (ID), persistent growth in catheterization activities and short medical staff enforced us to develop on line interactive computerized flow chart for referring pts for coronary angiography (CA) without involving cardiac consultant.

**Aim:** Testing a model of referred pts from ID to CA using on-line interactive computerized data supplied by the ID directly into the catheterization laboratory (CL).

**Methods:** After each round in every ID, authorized physician asked to fill clinical, ECG, GXT, and laboratory data related to every potential candidate for CA. The clinical data are: pts age, angina type, previous CA and iodine allergy. ECG changes, GXT results, troponin, hemoglobin, platelet count and urea levels are also described. Using this type of model we examined: mean waiting time for CA, the rate of normal angiogram (NCA) and PCI during one month in two different periods: 10/2006 using cardiac consultant versus 10/2007 using internist.

**Results:**

| October                | 2006<br>Cardiac Consultant | 2007<br>Internist | p-value |
|------------------------|----------------------------|-------------------|---------|
| Total N of CA          | 92                         | 130               |         |
| Number of CA from ID   | 42 (46%)                   | 69 (53%)          | 0.12    |
| Waiting for CA. (days) | 3.1±0.2                    | 2.8±0.2           | ns      |
| Total N. of NCA        | 19 (20%)                   | 24 (18%)          | ns      |
| NCA' from ID           | 4/42 (9%)                  | 10/69 (14%)       | 0.22    |
| PCI from ID            | 12/42 (30%)                | 32/69(46%)        | 0.032   |

In 10/2007 only 1 patient was rejected from CA due to atypical angina, anemia and renal failure and CA was delayed for 7 days due to end stage renal failure in other one. By this model we shorted waiting time for CA and noticed increased rate of PCI's from ID's.

**Conclusions:** Referring pts for CA by the internist using computerized flow chart data is easy, feasible and comparable to the task undertaken by cardiac consultant.

## A model for Measuring Guidelines Implementation

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**Background:** There is a "treatment gap" between the clinical guideline recommendations and actual performance. As a result, many patients do not reach target goals. Dyslipidemia monitoring provides a good example for evaluating this phenomenon. A common definition of compliance with dyslipidemia monitoring is having one lipid profile test per year (AMA, 2005). Such an approach does not comply with guideline recommendations that relate to changes of treatment and LDL-C levels over time.

**Aim:** To Develop an appropriate system to measure guidelines implementation.

**Methods:** We built a flexible model to define compliance with dyslipidemia monitoring, depending on LDL levels, change of treatment and guideline recommended for monitoring interval.

**Participants:** Cardiovascular patients aged 40-80 who had been hospitalized for CABG, PTCA, Coronary catheterization, or any ACS or ACS beginning on 1/2000 until 1/2004 (n= 3435).

**Results:** According to the traditional definition of compliance, one lipid profile a year compliance rate was 85.9%. However, using our flexible model, only 65.8% of patients actually complied with lipid monitoring guidelines (p<0.0001).

**Conclusions:** A flexible model for measuring compliance is far more sensitive than present orthodox systems and it enables detecting a larger portion of the population at risk that do not comply with guidelines of risk monitoring. The flexible model is generic and can be adjusted for monitoring other risk factors, since the parameters of target goal, medication and recommended monitoring intervals can be changed readily.

## Smoking History : A Predictor of Right Coronary Artery Narrowing

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**Background:** Smoking history is a major predictor for premature coronary atherosclerosis. Its association with narrowing of the right coronary artery (RCA), although guessed, was not studied systematically. We conducted a retrospective analysis of our data base and hospital records in order to clarify this issue.

**Methods:** Among patients aged <65 years subjected to coronary angiography during 2006, demographic and pertaining clinical data of those identified as harboring single vessel coronary artery (CAD) disease were analyzed.

**Results:** A) Among smokers, myocardial infarction and diabetes were observed in 42(22%) and 39 patients (20%), respectively. Four patients were afflicted with both conditions. Obesity was observed in 32(17%) patients.

B) An overall difference in the distribution of disease location was observed between smokers and non-smokers ( $p < 0.0001$ ). This significant difference permitted the pairwise comparison of specific locations by smoking status, as shown below:

|             | RCA             | LCX            | LAD              | LMCA           | Total      |
|-------------|-----------------|----------------|------------------|----------------|------------|
| Non-Smokers | 46 (14%)        | 59(18%)        | 214(66%)         | 7(2%)          | 326        |
| Smokers     | 82 (42%)        | 39(20%)        | 65(34%)          | 7(4%)          | 193        |
| <b>All</b>  | <b>128(25%)</b> | <b>98(19%)</b> | <b>279 (54%)</b> | <b>14(24%)</b> | <b>519</b> |

| <u>Comparisons</u>   | <u>p value</u> |
|----------------------|----------------|
| 1) RCA vs LCX        | 0.02           |
| 2) RCA vs LAD        | <0.0001        |
| 3) RCA vs LMCA       | 0.13 (NS)      |
| 4) RCA vs others     | <0.0001        |
| 5) RCA vs each other | <0.0001        |

**Conclusion:** Among single vessel CAD patients, **smoking history** predicted a **threefold** incidence of **RCA** narrowing.

## Comparative Analysis of Quantitative Fibrinogen, hsCRP and the Number of Diseased Vessels in Patients with Coronary Artery Disease

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### Introduction

HsCRP and fibrinogen are relevant biomarkers in atherothrombotic cardiovascular diseases. We have conducted a prospective study to reveal the correlation between these biomarkers and the number of diseased vessels in patients with stable and unstable coronary artery diseases.

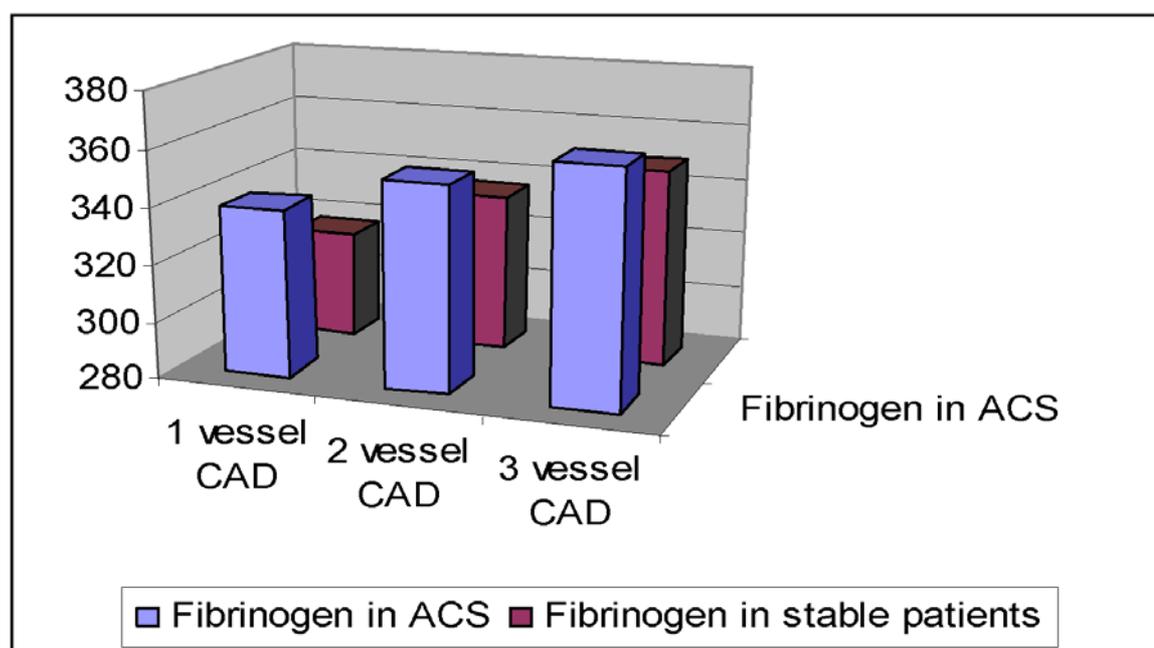
### Methods

Patients with stable and acute coronary syndromes who underwent coronary angiography at the Tel Aviv Sourasky Medical Center were prospectively collected. A blood sample was taken for fibrinogen and hsCRP levels.

All patients gave their informed consent in accordance to the local ethics committee.

### Results

We have collected 199 stable and 545 acute coronary syndrome patients undergoing angiography. The patients were divided according to their coronary artery disease status (1,2, or 3 vessels). The correlation between fibrinogen and the number of diseased vessels was significant in acute coronary syndrome ( $r=0.1$ ,  $p=0.01$ ) and borderline in stable patients ( $r=0.14$ ,  $p=0.053$ ). CRP was not correlated to the severity of CAD in both clinical scenarios. Figure 1 displays the fibrinogen values of the different groups.



### Conclusion

Quantitative fibrinogen could be a useful biomarker to reveal the presence and extent of CAD.

## **Liver Enzymes and Inflammation - Sensitive Biomarkers. Relevance for Apparently Healthy Individuals and Those with Atherothrombotic Risk**

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**Objective:** Recent studies have pointed to the association of cholestatic liver enzymes with the presence of low grade inflammation and thus to atherothrombosis. We have presently explored the possibility that the above mentioned associations be an early event, before clinically overt atherothrombosis.

**Methods:** Included were 3,422 men and 1,622 apparently healthy women who attended a routine health screening program and in whom there was no evidence for diabetes mellitus, history of an atherothrombotic event or intake of hepatotoxic medications.

**Results:** A significant age and body mass index (BMI) was noted between most of the different liver enzymes including alkaline phosphates (ALP), gamma glutamyl transferase, alanine aminotransferase and aspartate aminotransferase and the four inflammation-sensitive biomarkers that have proven relevance for atherothrombosis and include the white blood cell count (WBCC), high sensitivity C-reactive protein (hs-CRP) quantitative fibrinogen and the Westergren's erythrocyte sedimentation rate (ESR). The best correlations were noted between ALP and the respective above mentioned inflammation-sensitive biomarkers being  $r=0.166$   $p<0.001$ ,  $r=0.198$   $r<0.001$ ,  $r=0.224$   $p<0.001$  and  $r=0.088$   $p<0.0001$  in men and  $r=0.06$   $p=0.018$ ,  $r=0.247$   $p<0.001$ ,  $r=0.255$   $p<0.001$  and  $r=0.156$   $p<0.001$  in women. The correlations for GGT were similar although somewhat lower.

**Conclusions:** An association between several enzymes that are used in daily practice as markers of liver damage and low grade inflammation exists in this population. The finding of these associations in the range that is currently considered "normal" is new and paves the way for the potential detection of liver disorders and eventual atherothrombosis at a relatively early stage.

## **Exploring the Usefulness of Inflammation-sensitive Biomarkers to Reveal Potential Gender Differences in Relation to Low Grade Inflammation in Individuals with the Metabolic Syndrome**

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**Objective:** Gender differences exist in the expression of different inflammation-sensitive biomarkers in relation to the metabolic syndrome (MetS). We have presently explored these differences in relation to commonly used inflammation-sensitive biomarkers including the high sensitivity C-reactive protein (hs-CRP), quantitative fibrinogen, erythrocyte sedimentation rate (ESR), white blood cell count (WBCC) and the absolute number of polymorphonuclear leukocytes.

**Methods:** A cross sectional analysis of a group of apparently healthy men (n=5,560) and women (n=3,049) in whom the results of the above mentioned inflammation-sensitive biomarkers were analyzed in relation to the different components of MetS.

**Results:** The concentration of hs-CRP increased pari-pasu with the number of components of the MetS, the differences between the genders being significant regarding any number of components of the MetS. Regarding fibrinogen, the influence of gender turned significant for waist only, similarly to the results of the ESR. None of these interactions was found to be significant for both the WBCC and the absolute number of polymorphonuclears.

**Conclusions:** Quantitative fibrinogen, the ESR, WBCC as well as the absolute number of polymorphonuclear leukocytes are not sensitive enough to reveal the potential gender differences in relation to the various components of the MetS and the expression of the low grade inflammation. High sensitivity CRP does have the capability to reveal these differences.

## **Low Grade Inflammation in Individuals with the Hypertriglyceridemic Waist Phenotype. Another Feature of this Atherogenic Dysmetabolism**

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**Objective:** We explored the possibility that the recently described "hypertriglyceridemic waist" (HTGW) phenotype, a risk for future coronary artery disease (CAD), is associated with the presence of low grade inflammation.

**Methods:** This is a cross sectional study in a cohort of apparently healthy non-diabetic employed individuals in whom the presence of low grade inflammation was determined by using the high sensitivity C-reactive protein (hs-CRP) assay. We have presently analyzed the results obtained in 7,186 apparently healthy individuals, at a mean+SD age of 44+11 years.

**Results:** We identified 406 individuals (90.6% men) with the HTGW phenotype according to the cut-off points of waist girth of  $\geq 90$  cm for men and  $\geq 85$  cm for women and triglycerides levels of  $\geq 177$  mg/dl. In addition, we identified 473 individuals (64.3% men) with the metabolic syndrome (MetS) according to the updated ATP III criteria. The mean+SD of hs-CRP was 1.3+2.9 mg/l for the 5,879 individuals who had neither the HTGW phenotype nor the MetS, 2.0+2.5 mg/l for those who had the HTGW phenotype and no MetS, 2.7+2.6 for 473 individuals with the MetS and no HTGW phenotype while those who had both atherogenic disorders presented a hs-CRP concentration of 2.8+2.3 mg/l.

**Conclusions:** In this cohort of apparently healthy non-diabetic employed individuals, the HTGW phenotype had a similar prevalence as the MetS and was associated with the presence of low grade inflammation and the HTGW phenotype is relatively prevalent and could be a simple and inexpensive way to single out individuals at risk for future CAD.

## Is there a Relationship between Lipid Profile and the Presence of Coronary Plaques as Assessed by Multislice Computerized Tomography

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Multislice Computed Tomography(MSCT) is an excellent noninvasive visualization tool for detection of coronary plaques(CP).There are little data available about whether there is a direct relationship between blood lipid levels and presence of coronary plaques and their morphology .In the present study we evaluated the relationship between total cholesterol and LDL levels and the presence of CP in general and soft plaques(SP) in special. Using a 64 slice MSCT Philips we included 170 consecutive asymptomatic or oligo symptomatic patients undergoing routine MSCT All patients had lipid profile prior to the CT and the image processing and plaque evaluation was done by an independent specialist unaware of the lipid profile. From the 170 patients studied 107 had CP and 77 had SP

The following results were obtained for total cholesterol values:

| P values | Normal coronaries  | Plaques present |                            |
|----------|--------------------|-----------------|----------------------------|
|          | <b>63</b>          | <b>107</b>      | N                          |
| P<0.001  | 20.6%) <b>13</b> ( | <b>61</b> (57%) | Total cholesterol >200mg/L |
| P<0.001  | <b>50</b> (79.4%)  | <b>46</b> (43%) | Total cholesterol <200mg/L |

When LDL cholesterol was evaluated similar findings were obtained:

|         | Normal coronaries | Plaques present   |                          |
|---------|-------------------|-------------------|--------------------------|
|         | <b>63</b>         | <b>107</b>        | N                        |
| P<0.011 | <b>35</b> (56.%)  | (74.8%) <b>80</b> | LDL cholesterol> 100mg/L |
| P<0.011 | (56%) <b>28</b>   | <b>27</b> (25%)   | LDL< cholesterol 100mg/L |

When patients with SP alone were evaluated similar results were found:

|         | Rest of the pts   | Soft plaques      |                          |
|---------|-------------------|-------------------|--------------------------|
|         | <b>93</b>         | <b>77</b>         | N                        |
| P<0.001 | <b>50</b> (53.8%) | <b>65</b> (84.4%) | LDL cholesterol>100mg/L  |
| P<0.001 | <b>43</b> (46.2%) | <b>12</b> (15.6%) | LDL cholesterol100< mg/L |

Thus it appears from our data that there is a strong relationship between the hyperlipidemia and presence of CP and especially SP in an asymptomatic population.

## **Brachial Artery Endothelial Function Predicts Platelet Function in Healthy Subjects and in Patients with Coronary Artery Disease**

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**Background:** Platelets play a key role in acute vascular thrombosis, while platelet activation occurs in conditions associated with impairment of endothelium-dependent flow-mediated vasodilation (FMD). Nitric oxide (NO), a key product of the endothelium, is antithrombotic via potent antiaggregating and antiadhesive properties. Endothelial dysfunction is a systemic disorder and a key variable in the pathogenesis and complications of atherosclerosis.

**Methods:** To explore the association between platelet function and endothelial function, we prospectively assessed FMD in 122 consecutive subjects, 41 (34%) with coronary artery disease (CAD) and 81 (59%) healthy controls. Following overnight fasting and discontinuation of all medications for  $\geq 12$  hours, percent improvement in endothelium-dependent brachial artery FMD (%FMD) and endothelium-independent, nitroglycerin-mediated vasodilation (%NTG) were assessed using high resolution (15 MHz) linear array ultrasound. Platelet function tests were assessed immediately at the end of endothelial function testing.

**Results:** Both groups were comparable regarding CAD risk factors, BMI, lipid panel, homocysteine, platelet number, heart rate, and diastolic blood pressure, while systolic blood pressure was significantly higher in controls compared to CAD patients ( $136\pm 18$  vs  $126\pm 19$  mmHg,  $p=0.02$ , respectively). The use of aspirin, plavix and beta blocker agents was significantly more common in CAD patients compared to controls (81% vs 11%,  $p<0.01$ ; 58% vs 0%,  $p<0.01$ ; and 58% vs 7%,  $p<0.05$ , respectively). %FMD, but not %NTG, was significantly lower in CAD patients compared to controls ( $15\pm 7\%$  vs  $11\pm 6\%$ ,  $p<0.01$  and  $17\pm 8\%$  vs  $16\pm 8\%$ ,  $p=0.27$ , respectively). %FMD was significantly associated with ADP-induced platelet aggregation by conventional aggregometry ( $r=-0.38$ ,  $p<0.001$ ), platelet adhesion ( $r=-0.42$ ,  $p<0.01$ ) and aggregation under flow condition ( $r=-0.56$ ,  $p<0.01$ ), even after controlling for age, aspirin and plavix use. ADP- and arachidonic acid-induced platelet aggregation were significantly lower in CAD patients compared to controls ( $43\pm 25$  vs  $84\pm 14\%$ ,  $p<0.01$  and  $45\pm 32$  vs  $84\pm 24$ ,  $p<0.01$ , respectively), most probably due to the common use of anti-platelet therapy.

**Conclusion:** Endothelial function assessed by brachial artery %FMD is inversely associated with platelet function in healthy subjects and CAD patients, suggesting that endothelial function may play a major role in determining platelet reactivity.

## **Correlates Of QT Interval in an Ethnically Diverse Population**

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**Background:** Long QT syndrome (LQTS) is a disorder of myocardial repolarization characterized by a prolonged QT interval on the electrocardiogram (ECG). This syndrome is associated with an increased risk of a characteristic life-threatening cardiac arrhythmia, known as Torsade de Pointes. LQTS may be either genetic or acquired.

**Aim:** To describe the correlates associated with corrected QT interval (QTc) in a multi-ethnic population, diverse by cardiovascular disease risk.

**Subjects and Methods:** Participants were derived from a random sample of the general population of Hadera District in Israel, stratified by ethnicity (Arabs and Jews), gender and age (range: 25-64). Information on demographic and lifestyle characteristics was obtained by personal interviews, and blood pressure and anthropometric measurements, fasting blood samples and resting ECG records were subsequently obtained. ECG records were coded using the Minnesota coding system. QTc was calculated by dividing the QT interval by the square root of the RR interval (in seconds). **Results:** ECG recodes were obtained in 587 participants; Mean age (SD):48.5 (11.1) years, 51% males. On multivariate linear regression analysis, variables positively associated with QTc were: female gender (p<0.001), Arab ethnicity (p<0.001), systolic blood pressure (p<0.001), body mass index (BMI) (p=0.002), and triglycerides levels (p=0.044). Other characteristics (e.g. NSAIDs drug therapy and CRP levels) found to be significantly associated with QTc on univariate analyses were no longer significantly associated with QTc after adjusting for the effects of gender, ethnicity and BMI.

**Conclusion:** Our findings show that in the general population, the QTc interval is associated with female gender, Arab ethnicity, and some characteristics of the metabolic syndrome (i.e. increase BMI, hypertension and hypertriglyceridemia). The clinical significance of these findings should be further studied in longitudinal studies.

## **Compliance with Clopidogrel Treatment after Implantation of Drug Eluting Stents in the Bedouin Population of the Negev**

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Gabriel Rosenstein, Harel Gilutz, Doron Zahger, Reuben Ilia

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**Background:** Long term dual antiplatelet therapy is essential after implantation of drug eluting stents (DES). Compliance with antiplatelet therapy has been associated with social, economic and cultural factors. This association has not been previously examined in the Israeli population.

**Aim:** To investigate the characteristics and compliance with antiplatelet treatment after DES implantation in the Bedouin population of the Negev.

**Methods:** A retrospective comparison of 54 Bedouin (age: 59±13) and 615 Jewish patients (age: 63±12, p=0.018) residents of Negev who underwent DES implantation between 4/04 and 10/06. Data were prospectively collected in computerized databases. Clinical, angiographic and angioplasty characteristics, medical treatment as well long term clinical outcome were studied. The duration of treatment with aspirin and clopidogrel after DES as a marker of compliance was analyzed.

**Results:** Bedouins treated with DES less often had dyslipidemia ( 67% vs. 81%, p<0.05) and more often had diabetes mellitus ( 55% vs 34%, p<0.01) and moderate to severe left ventricular dysfunction ( 58% vs. 36%, p=0.03) . No differences were seen in other risk factors, angiographic findings and angioplasty characteristics. During a median follow up period of 618 days a higher frequency of myocardial infarction (13% vs. 5%, p=0.02) was seen in the Bedouins. No significant differences were seen in all cause mortality ( 13% vs. 7%), stroke (2% vs. 3%), revascularization (21% vs.16%) or the combined end point of death, MI, stroke and revascularization (33% vs. 25%,). During the first year of follow up Bedouin took clopidogrel for 148 days±105 as compared to 256±122 days in Jews (p=0.01). Clopidogrel was used without interruption during 108±105 days in Bedouins and during 225±108 in Jews (p<0.01). Aspirin was used without interruption for 420± 315 days in Bedouins and for 549± 302 days in Jews (p<0.01).

**Conclusions:** Bedouins treated with DES have a shorter period of treatment with clopidogrel in comparison with Jews. The reasons of this finding and its relationship with the higher frequency of myocardial infarction observed in the Bedouin population require further investigation

## **Novel Instrumented Retractor to Monitor Tissue Disruptive Forces During Median Sternotomy**

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**Objectives:** Acute and chronic pain after median sternotomy is common and often underestimated. The mechanical retractors used for the median sternotomy exert significant forces on the skeletal cage. Our hypothesis is that instrumented retractors can be developed to enable real-time monitoring and control of retraction forces. This may provide equivalent exposure with significantly reduced forces and tissue damage, and thus less post-operative pain.

**Methods:** A novel instrumented retractor was designed and fabricated to enable real-time force monitoring during surgical retraction. Sixteen mature sheep underwent median sternotomy. Eight median sternotomies were retracted at a standard “clinical pace” of  $7.25 \pm 0.97$  minutes to 7.5 cm without real-time monitoring of retraction forces. The other eight median sternotomies were retracted to the same exposure using real-time visual force feedback and, consequently, a more deliberate pace of  $12.05 \pm 1.73$  minutes ( $p < 0.001$ ). Retraction forces, blood pressure, and heart rate were monitored throughout the procedure.

**Results:** Full retraction resulted in an average force of  $102.99 \pm 40.68$  N at the standard clinical pace as compared to  $64.68$  N with force feedback (a 37.2% reduction,  $p = 0.023$ ). Standard retraction produced peak forces of  $368.79 \pm 133.61$  N, whereas force feedback yielded peak forces of  $254.84 \pm 75.77$  N (a 30.9% reduction,  $p = 0.084$ ). Heart rate was significantly higher during standard clinical retraction ( $p = 0.024$ ).

**Conclusions:** Using the novel instrumented retractor resulted in lower average and peak retraction forces during median sternotomy. Moreover, these reduced retraction forces correlated with a reduction in animal stress as documented by lower heart rate.

## Long Term Experience of Wrapping the Ascending Aorta with Dacron Mesh as Definitive Treatment for Aneurysmal Dilatation

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**Background:** The management of the mildly to moderately dilated ascending aorta in cardiac surgery remains controversial. Therapeutic options have included radical aortic resection with synthetic graft substitution, external aortic reinforcement or wrap with or without partial aortic wall excision, and a watch and wait approach.

**Methods:** Over the last 20 years, 102 patients with aneurysmal dilatation of the ascending aorta underwent wrapping of the ascending aorta with a fine Dacron mesh from the ventricular-aortic junction to the origin of the innominate artery. For the last ten years, the wrap was anchored to the aortic annulus with pledgeted sutures. Aortic diameters up to 6 cm, without focal areas of thinning, were wrapped. Aortic diameters > 6 cm, or with focal thinning, underwent tailored aortic wall resection and wrapping. Primary endpoints of the study included mortality, aortic diameter growth, dissection and/or rupture.

**Results:** The mean age of the group was  $54.7 \pm 19.54$  yr (range, 12 to 90). A single patient underwent aortic wrapping without cardiopulmonary bypass. Sixty-six patients (65%) required additional aortic valve surgery. Five patients (5%) had reinforcement of dilated sinuses with glutaraldehyde-treated pericardial patches combined with wrapping. Twenty-seven patients (26%) had combined coronary and valve surgery, and two patients had coronary revascularization alone. There was neither early nor hospital mortality. Among the 81 patients (79%) we were able to contact, there were 7 (7%) late deaths at 0.5, 1, 3 and 9 years after operation, unrelated to aortic pathology. Various levels of follow up were obtained in the 88 patients (86.2%). In 78 patients, echocardiograms, CT angiograms or MR angiograms were obtained. Two of these patients had developed aneurysmal dilatation of the sinuses below the wrap and required reoperation. No patient in whom the mesh wrap was anchored to the aortic annulus required reoperation. All eighty-one patients that were contacted by us, and followed by referring physicians, were asymptomatic and free of problems related to the aorta. The mean preoperative diameter of the ascending aorta was  $49.2 \pm 7.8$  mm (mean  $\pm$  SD) (range: 35 to 87). The mean post-wrap intraoperative diameter was  $32.8 \pm 3.5$  mm (range: 20 to 45). The mean follow-up postoperative aortic diameter was  $35.3 \pm 5.7$  mm. The average change in the aortic diameter during the follow up period was  $2.77 \pm 2$  mm (mean  $\pm$  SD), a mean of 8%. The mean follow-up period was 5.7 years, median: 4.77 years; range: 9 days – 21 years. There were no infections or other early complications related to the wrap.

**Conclusions:** Dacron mesh support of the moderately dilated aneurysmal ascending aorta, alone or in conjunction with coronary revascularization, aortic root surgery and/or valvular operations, is safe and durable. Dacron mesh is transparent and stretchable, permitting tight girdling of the aorta. These properties prevent hematoma formation, facilitate proximal vein graft anastomoses, and provide visualization and access to aortic suture lines. Finally, this technique retards further aortic dilation, altering the natural history of aortic aneurysms.

## **Can LIMA-RIMA 'T-Graft' Supply the Right Coronary System?**

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### **Study objectives:**

In the current literature, there is uncertainty whether RIMA 'T-GRAFT' can safely supply multiple coronary bypasses, and whether it can provide the RCA system. In the present study, we evaluate the outcome of patients who underwent CABG surgery using LIMA-RIMA 'T-graft' of more than 4 bypasses and the distal anastomosis of the RIMA was to the RCA system.

### **Methods:**

Between 6.2005 and 11.2006, 30 consecutive patients underwent the above mentioned surgery. Average age was 56.2, female gender was 13.3 % ,the incidence of diabetes- 26.7%, moderate + left ventricular dysfunction -13.3%, left main disease - 26.7%, unstable angina- 53.3%, average number of bypasses was 4.63, average EUROSCORE -3.41%.

### **Results:**

There was no mortality in our series; all patients were weaned from mechanical ventilation in less than 24 hours. Postoperative course was uneventful and patients were discharged in less than 7 days. One patient had a superficial wound infection that did not necessitate surgical intervention.

In mid term follow up (1.5 year) – there was no mortality, no admissions due to ischemic heart disease, and no complaints of angina pectoris. All patients had an up to date echocardiography study. LV function was unchanged in 20 patients and improved in ten patients.

### **Conclusion:**

LIMA RIMA 'T'-graft can safely be used for multiple bypasses. With proper technique, The RIMA can supply the RCA territory with good mid term results. By that, we can avoid harvesting other conduits and use the best conduit for all the heart.

## Prognostic Value of Predictors for Prolonged Mechanical Ventilation after Cardiac Surgery

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**Background:** Prolonged mechanical ventilation after cardiac surgery is associated with higher mortality and morbidity. Identification of preoperative variables, which may lead to prolonged mechanical ventilation, may help develop better strategies for postoperative ICU management. The aim of our study was to identify risk factors for prolonged postoperative mechanical ventilation.

**Methods:** Four hundred and eight consecutive patients who underwent coronary artery bypass grafting (CABG) with or without aortic valve replacement (AVR) composed the study population. Patients were classified as those ventilated less than 48 hours – group I (396 patients) and those ventilated more than 48 hours – group II -prolonged ventilation (12 patients). Multivariable analysis was used for risk factors identification.

**Results:** Postoperative mortality for patients in group I was 1.8% compared with 42% for group II ( $p < 0.001$ ). Preoperative predictors for prolonged mechanical ventilation included older age (OR=1.1,  $p=0.03$ ), emergency surgery (OR=4,  $p=0.02$ ), and lower ejection fraction (OR=1.1,  $p < 0.001$ ). The addition of intraoperative variables to the model adds combined CABG and AVR as a predictor for prolonged ventilation (OR=6,  $p=0.04$ ).

**Conclusions:** The ability to identify patients at increased risk for prolonged mechanical ventilation may allow the development of pre-emptive strategies to optimize patient's condition and ICU management.

## Preoperative Hemoglobin Level as a Predictor for Outcome after Cardiac Surgery

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**Background:** Anemia is a known risk factor in many fields of medicine. The purpose of this study was to assess how pre-operative hemoglobin levels affect the outcome after cardiac surgery.

**Methods:** The data set includes 408 consecutive patients who underwent coronary artery bypass surgery in our institution. We studied the patients according to their preoperative hemoglobin (Hb) levels, Group A (Hb $\leq$ 11 mg/dl, 41 patients), Group B (Hb $>$ 11 mg/dl, 367 patients). Endpoints studied were perioperative mortality, prolonged ICU stay ( $>$ 72 hours), and prolonged hospital stay ( $>$ 10 days).

**Results:** There were more females in group A (18% vs. 8%,  $p=0.007$ ), and more hypertension (12 vs. 6,  $p=0.04$ ). Patients in group A were older ( $69\pm 11$  vs.  $66\pm 10$ ,  $p=0.04$ ), and had reduced preoperative creatinine clearance ( $59\pm 34$ ,  $85\pm 25$ ,  $p<0.01$ ).

Perioperative mortality was higher in group A, 12% compared with 3% in group B ( $p=0.02$ ). More patients in group A had Prolonged ICU stay, 16% compared with 6% in group B (0.05). More patients in group A had Prolonged hospital stay, 23% compared with 5% in group B ( $<0.001$ ). After adjustment for other confounding factors, multivariable logistic regression analysis identified Hb $<$ 11 mg/dl as an independent predictor for perioperative mortality (OR=5.6,  $p=0.001$ ).

**Conclusions:** Hb $<$ 11 mg/dl is an independent predictor for perioperative mortality and prolonged length of stay after cardiac surgery. Hemoglobin Correction should be considered prior surgery.

## **Successful Treatment of Disseminated Cutaneous Trichosporon Asahii Infection with Voriconazole in a Heart Transplant Recipient: The Importance of Multidisciplinary Approach.**

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**Purpose:** Infections with uncommon fungal pathogens are more frequently reported in immunocompromised hosts, particularly among hematological patients and transplant recipients. We report what we believe to be the first case of successful management of disseminated cutaneous *Trichosporon asahii* infection with orally administered voriconazole in a heart transplant recipient.

**Methods and Materials:** A 59-year-old man with end-stage non ischemic cardiomyopathy was ventilated and supported with high doses of inotropes and an intra-aortic balloon pump for 3 days before he underwent a successful orthotopic heart transplantation at April 12<sup>th</sup> 2007. His pre-transplant assessment revealed reversible elevated pulmonary vascular resistance and pre-renal azotemia. His immediate post operative recovery was complicated with worsening signs of right ventricular failure despite NO, sildenafil and diuretic therapy. His kidney function deteriorated requiring emergent hemodialysis. A biopsy proven acute rejection was treated with high dose steroids. While in the cardiac intensive unit, a black skin lesion was seen in his right leg diagnosed by the dermatologist as small necrosis of the skin due to the long standing severe edema. As the skin lesion enlarged, culture from a punch biopsy of the lesion showed growth of *Trichosporon Asahii*. Oral voriconazole 200 mg twice a day was started.

**Results:** Despite continuous treatment with the recommended voriconazole dose, local progression of the skin lesion was not halted. Below knee amputation was considered but eventually not done due to rapid dissemination of the fungal infection to both inner thighs and left hand. The mycophenolate mofetil was suspended and as the Immuknow levels were low trough levels of tacrolimus were maintained low. The voriconazole dosage was doubled after blood samples sent abroad found low levels of the drug. During the next days the dissemination of the lesions stopped. Due to improvement in his renal function, the hemodialysis was suspended, the right ventricle gradually recovered and the edema resolved. Surgical debridement was done and homograft skin was transplanted. Two weeks later, autologous skin grafts were taken from the outer right thigh and all the wounds were covered. This last skin grafting was very successful and by August 7<sup>th</sup> the patient was sent home. The voriconazole dose was reduced to 600 mg a day but MMF was not re-introduced yet (20<sup>th</sup> Sept. 2007).

**Conclusions:** The first case of successful management of disseminated cutaneous *Trichosporon asahii* infection with orally administered voriconazole in a heart transplant recipient is described. The multi disciplinary approach was essential for achieving this favorable outcome.

## **Surgery for Hypertrophic Obstructive Cardiomyopathy**

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**BACKGROUND:** Surgical treatment of patients with obstructive cardiomyopathy (HOCM) includes relief of left ventricular outflow tract (LVOT) obstruction and correction of mitral regurgitation and is indicated when disabling symptoms refractory to maximal medical management are present. Transaortic septal myectomy (Morrow procedure) is regarded as a standard surgical approach for this condition. Recent advances in understanding the anatomy and physiology of LVOT obstruction resulted in several changes in surgical strategies. Standard myectomy can be performed in combination with one of several techniques of mitral valve repair for correction of structural abnormalities of the mitral apparatus in patients with HOCM.

We review our experience of surgical management of patients these using several techniques for different mitral pathologies.

**METHODS:** Four patients with HOCM were operated between September and October 2006. Mean age was 63.5 years. All patients had typical marked systolic anterior motion (SAM) resulting in severe LVOT obstruction and severe mitral regurgitation. Transesophageal echocardiography was used in all patients preoperatively and postoperatively to guide and assess adequacy of resection, LVOT gradient and mitral valve function. Concomitant coronary artery bypass grafting was performed in two patients.

In two cases septal myectomy was done through standard transaortic approach. The others two patients had additional pathologic changes of the mitral valve, (ruptured chords to the posterior leaflet, anterior leaflet enlargement) requiring surgical intervention on the mitral valve. In one the patients, we used transatrial transmitral approach to the LVOT with temporary detachment of the anterior mitral leaflet that proved to be very helpful for extended myectomy. Mitral valve repair included resection of posterior leaflet due to ruptured chords, anterior leaflet extension and annuloplasty. In the other case we applied the edge-to-edge Alfieri stitch technique, which eliminated the SAM, LVOT gradient, as well as the MR.

**RESULTS:** All four patients survived surgery. No ventricular septal perforation occurred, and none of the patient needed permanent cardiac pacing. Serial postoperative echocardiography demonstrated that the LVOT gradient, mitral regurgitation and SAM of the mitral valve were significantly reduced if not eliminated.

**CONCLUSIONS:** Surgical relieve of LVOT obstruction produce significant hemodynamic improvement in patients with severe symptomatic HOCM. Choice of the surgical method depends on the anatomic and physiologic derangement of the LVOT and the underlying pathology of mitral regurgitation. Transatrial-transmitral approach to the LVOT proved to be very helpful for extended myectomy.

### **Stents and CABG: Financial Impact.**

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*Background:* Coronary artery revascularization with either angioplasty/stent implantation (PCI) or bypass surgery (CABG) is common, and clinical results have been comparable. However, the burden on health care systems has not been widely studied.

*Methods:* Our departmental database was queried for all patients undergoing pure CABG between 2000-2006 (group 1). Subsequently, all patients undergoing first time coronary intervention (PCI or CABG) at Shaare Zedek Medical Center between 2002-2004 were enrolled (group 2). Hospital records as well as outpatient records were reviewed to document utilization of health care facilities and cost.

*Results:* In group 1 there were 1121 patients. Of these, 315 had prior PCI and 22 had prior CABG. The mean interval between PCI-CABG was 2.4 years, in 116 (37%) within 1 year of the initial procedure. The mean interval between CABG-CABG was 13 years, in 2 (9%) within 1 year. Group 2 included 432 patients: 180 received a bare metal stent (BMS), 71 a drug-eluting stent (DES), and 181 underwent CABG. Data from a pilot group of 25 patients was available 1 year after intervention: 9 BMS, 9 DES and 7 CABG. Six (33%) patients in the PCI group required a repeat procedure, compared to none in the CABG group. Initial cost of hospitalization per patient was \$11643 for CABG compared with \$6329 for PCI. By 1 year the cost per patient was unchanged for CABG and increased to \$9344 for PCI, due to re-intervention. Utilization and costs of ambulatory services were similar in both groups.

*Conclusions:* While initial cost of CABG is higher than that of PCI, patients undergoing PCI require more repeat interventions and at shorter intervals. At longer follow-up we may expect to see more need for re-intervention in both groups. With limited resources available, the choice of procedure should take into account not only clinical benefit, but also long term financial considerations.

## Implementing a Novel Integrated Heart Failure Disease Management Program in Israel

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**Background:** Heart failure (HF) is associated with frequent hospital admissions, impaired quality of life (QoL), high mortality and high healthcare costs.

**Objectives:** To design and implement a disease management (DM) program aiming to reduce mortality and hospital re-admissions, and improve patients' QoL while containing costs of healthcare.

**Eligibility:** Patients (NYHA class III-IV), hospitalized for HF.

**Program Design:** The program is implemented nationwide, within the framework of Maccabi Healthcare Services. It includes two main components:

- ◆ Regional HF centers
- ◆ A national call-center

Eligible patients are evaluated at the HF centers by cardiologists and HF nurse specialists. A drug therapy plan is delineated by cardiologists and self-care education is delivered by nurses. Patients are provided with telemetric equipment for home-monitoring of weight, heart-rate and blood-pressure. Between subsequent visits to the HF centers, DM is given by nurse specialists at the HF centers and the call-center, guided by the treatment plan, tele-monitoring information, and designated protocols. DM activities include lifestyle counseling, titration of drug therapy, monitoring of adherence and side-effects, and problem-solving in the case of acute events.

**Program evaluation:** Evaluation is carried out using a randomized controlled trial design. Patients allocated to the usual-care (control) arm are followed exclusively by their primary practitioners and cardiologists. After recruitment, patients in both study arms (DM and usual-care) are re-evaluated every 6 months for process and outcome measures.

**Outcome Measures:** Hospital re-admissions, QoL, all-cause mortality, and costs of care.

**Current Program Status:** A national call-center and four regional HF centers are currently operating and patients are being recruited.

## Marked Transient Reduction of HDL and Other Lipoproteins in Acute Peri-Myocarditis

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### Background

Acute peri-myocarditis is a major inflammatory disease that may lead to impaired cardiac function. Although the disease is well recognized, the clinical picture may be confused with myocardial infarction (MI). While, alterations in plasma lipoproteins concentration are known to take place in trauma, severe sepsis and even acute MI, the lipoprotein levels in acute peri-myocarditis have not been studied. The purpose of this study was to investigate the lipoprotein levels in patients with Acute peri-myocarditis .

### Methods

Thirty consecutive patients 29 (96.6%) males age 31±10, with first episode of acute peri-myocarditis were enrolled in the study. Acute peri-myocarditis diagnosis was confirmed by the following: clinical history, ST ↑ or PR ↓ on EKG, elevated inflammation markers and echocardiographic findings. Patients' detailed medical history, EKG, Echocardiography and blood tests including lipid profile were obtained within 24 hours from admission. Follow up examination repeating the same parameters were obtained upon recovery.

### Results

Low levels of lipoproteins were found upon admission. Markedly decreased level of HDL was observed, 82% of the patients had HDL < 40, 39% had extremely low level of HDL < 25 mg/dl. After recovery HDL level increased in 96% of patients (average change 114.7%). Significant changes in the levels of LDL and TG were also observed.

| mg/dl             | Admission    | Follow-up    | Average change | P value |
|-------------------|--------------|--------------|----------------|---------|
| Total Cholesterol | 130.35±21.05 | 157.04±41.43 | 23.46%         | ≤0.001  |
| HDL               | 27.16±13.58  | 44.06±11.88  | 114.72%        | ≤0.001  |
| LDL               | 77.2±20.9    | 93.19±27.29  | 21.18%         | 0.004   |
| TG                | 119.1±78.37  | 147.32±79.97 | 59.33%         | 0.024   |

### Conclusions

Low lipid profile was found during acute peri-myocarditis.

Marked reduction of HDL levels during acute peri-myocarditis is a new marker for the disease, and may assist in differentiating acute peri-myocarditis from acute coronary syndrome.

## **Importance of Interventricular Septal Motion for the Remodeling of the Right and Left Ventricles in Patients with Coronary Artery Disease – an Echocardiographic Study**

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**Background:** The interventricular septum (IVS) is an important part of both the right and left ventricles (RV and LV) but there is little information about its influence on biventricular remodeling.

**Methods:** Included in our analysis 179 stable ambulatory patients with history of coronary artery disease (myocardial infarction and or CABG). Patients with LBBB and significant valvular dysfunction were excluded. Echocardiograms were analyzed to obtain long and short axis dimensions of LV and RV (sphericity index (SI) was calculated as their ratio). Patients were stratified into 4 groups according to quantitative analysis of IVS motion (groups 1-4; normal, mild, moderate and severe impairment). Comparison among groups was performed using ANOVA.

**Results:** LV ejection fraction decreased from 49% (group 1) to 26% (group 4). LV long axis was (mm) 78, 82, 84 and 91 for groups 1-4 respectively,  $p < 0.0001$ . Similarly short axis was 47, 50, 55 and 63 respectively,  $p < 0.0001$ . The SI was 1.66, 1.66, 1.54 and 1.46 respectively,  $p < 0.0001$ . Values for RV were: long axis – 74, 78, 79 and 84 respectively,  $p < 0.0001$ ; short axis – 39, 41, 41 and 46 respectively,  $p < 0.0001$ ; SI – 1.92, 1.95, 2.01 and 1.85, respectively,  $p = NS$ . Mild degree of IVS motion abnormality was already associated with LV remodeling while RV remodeling occurred only at a later stage (the RV SI decreased only in group 4). RV dysfunction and remodeling correlated with LV dysfunction (and remodeling), with IVS motion abnormality, but not with pulmonary artery pressure.

**Conclusions:** LV and RV remodeling were strongly related to the degree of IVS motion abnormality. RV dimensions increase even with mild degree of IVS motion abnormality while the RV SI decreases only at a later stage. RV function and remodeling is related to IVS motion (ventricular interaction) and not to pressure overload.

## **Therapeutic Hypothermia for Comatose Patients: VF Versus Other Initial Rhythm – does it Matter?**

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**Background:** Unconscious adults after out-of-hospital cardiac arrest (OHCA) should be treated with mild induced hypothermia (MIH) when the initial rhythm was ventricular fibrillation (VF) (ILCOR 2003). No data and no recommendations exist regarding other rhythms. We conducted a current practice survey in order to assess efficacy of MIH in patients after OHCA due to non-VF rhythm.

**Methods:** Eighty six consecutive OHCA patients (68 VF, 18 non-VF) were cooled by MTRE Criti Cool™ external cooling system. Patients were analyzed according to their initial rhythm and according to their neurological outcome on discharge, defined by their cerebral performance category (CPC).

**Results:** Out of sixty-eight patients with VF 42 patients (62%) had favorable outcome (CPC 1-2) and 32% died. Among the non-VF group 4 patients (22%) had favorable outcome ( $p < 0.001$  versus VF) and 67% died ( $p = 0.008$  versus VF). Differences in baseline characteristics between the favorable and unfavorable non-VF groups were in age and severe co morbidities. Outcome was worse when time from collapse to return of spontaneous circulation (ROSC) was more than 25 minutes or (a trend to worse outcome) when the patient was presented to the emergency room with convulsions or hemodynamic instability.

**Conclusions:** In our experience, MIH is less efficient in non-VF compared to VF patients. Factors that seem to influence their outcome are: age, co morbidities, time duration from collapse to ROSC, convulsions and hemodynamic instability at presentation.

## The Value of Troponin-I Curve after Primary PCI for ST Elevation Myocardial Infarction

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**Background:** After thrombolysis in ST elevation myocardial infarction (STEMI), cardiac troponin-I (CTnI) curve demonstrated two peaks. The ratio between the early to late peak has been shown to carry important prognostic value. The magnitude and course of troponin after reperfusion with primary percutaneous intervention (PPCI) have never been investigated.

**Methods:** The study comprised 73 consecutive STEMI patients in whom PPCI was performed within 12 hours of pain onset. CTnI and creatinine kinase (CK) were prospectively determined every 4 hours during the first 24 hours and every 24 hours during the next 3 days. Data regarding clinical course, echocardiography and angiography were prospectively collected.

**Results:** 73 patients were followed (79% male, mean age 60±13 years). In contrast to thrombolysis, after PPCI there was only one peak after 4-8 hours from admission in most of the patients (73%). Late troponin peak (> 8h) was associated with a late arrival of >6h from pain onset, unsuccessful re-vascularization, distal embolization or re-ischemia. When patients were stratified into two groups using the median peak CTnI value as a cut off point (53.7 µg/L), patients with higher troponin levels had a higher rate of decrement left ventricular function (ejection fraction ≤45%), (67% versus 43%, p=0.005).

**Conclusions:** The characteristics of CTnI curve in acute STEMI patients undergoing PPCI differs from that of thrombolysis with a single peak after 4-8 hours, demonstrating a sharp 50% decline within 24 hours of admission. Higher peak levels correlate with worse ventricular function.

## **C-Reactive Protein as a Predictor of Active Coronary Disease and Worse Prognosis in Chest Pain Unit**

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**Objectives:** In recent years chest pain units (CPU), have been proven to be an efficient modality for evaluating low-medium risk patients with chest pain. Although C-reactive protein (CRP) was proven to be an inflammation marker and an emerging cardiovascular and atherosclerosis risk factor, its prognostic value in CPU evaluation has yet to be determined.

**Methods:** The study comprised 621 consecutive patients admitted to the Tel Hashomer CPU. High sensitivity (hs)-CRP was determined in all patients within 8-12hrs of admission. As per CPU protocol all patients were monitored with an ST-analyzer monitor for ST changes and malignant arrhythmias. Patients were tested for troponin levels on admission and after 8-12hrs. Those ruled out for acute myocardial infarction (AMI) underwent non-invasive testing (stress SPECT thallium scan, stress echo, cardiac CT) for detection of significant coronary artery disease (CAD).

**Results:** 120 out of 621 patients (19%) had hs-CRP $\geq$ 6 (high CRP); 501(81%) had CRP<6 (low CRP). There were no significant differences in baseline characteristics. 21% of high CRP patients were hospitalized compared with 11% of low CRP patients (p=0.006, OR 2.05, 95% CI 1.22-3.45). Although both high and low groups had similarly low incidents of AMI (2.5% vs. 2.2%, p=0.7), high CRP patients had a higher incidence of significant CAD by non-invasive testing (14% vs 7%, p=0.013) and eventually were more likely to undergo percutaneous coronary intervention for significant CAD.

**Conclusion:** CRP carries an important predictive value and may contribute to the fast tract chest pain evaluation of low-medium risk patients.

## STEMI Culprit Lesion Angiographic Characteristics Affect Clinical Outcome

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### Background:

Culprit lesion characteristics may influence the technical approach and clinical outcome in patients undergoing primary PCI due to AMI.

### Methods:

We evaluated the angiographic characteristics and MACE in 344 consecutive patients undergoing primary PCI between January 2005 and July 2007 in Hadassah University Hospital. Based on angiographic criteria patients were divided to into 2 groups: complicated (group A) and simple simple (group B) culprit lesions.

### Results:

Average pain to needle time was 126 minutes. Culprit lesion was localized in the proximal and middle segments of the artery in 256 patients (74%). TIMI O - I flow on admission was detected in 328 patients and TIMI II-III flow in 16 patients. Single, double and triple vessel disease occurred in 40%, 35% and 25% of patients, respectively. Anterior wall MI comprised 46% of the cases. Six patients did not undergo PCI of which two underwent urgent CABG. Cardiogenic shock on admission occurred in 5% of the patients, 4% had malignant arrhythmia and 1% had mechanical complications due to AMI. Group A included 192 patients with large arteries (n=6), bifurcation lesions (n=44), large intracoronary thrombus (n=78), ostial lesions (n=9), acute on chronic occlusion (n=11), uncertain localizations (n=7), simultaneous occlusion of two arteries (n=5), acute instent thrombosis (n= 11), acute graft thrombosis (n=10) and need for multivessel PCI (n= 11). Group B included 152 patients with simple coronary occlusions. The differences in outcome are described in the following table:

|         | N   | Angiographic success | Final TIMI flow II - III | Massive distal embolization | In hospital mortality |
|---------|-----|----------------------|--------------------------|-----------------------------|-----------------------|
| Group A | 192 | 80%                  | 80%                      | 16%                         | 2                     |
| Group B | 152 | 98%                  | 95%                      | 7%                          | 0                     |
| P       |     | 0.001                | 0.001                    | 0.012                       | 0.2                   |

### Conclusion:

In our single center experience, complicated lesions are the majority of lesions negotiated during primary PCI. These lesions are associated with lower angiographic success and worse clinical outcome.

## **Characteristics of Recurrent versus First AMI; Results from the ACSIS 2006 Survey**

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**Background:** Little is known regarding the nature of a recurrent myocardial infarction. We sought to compare the characteristics of an event, in patients presenting with a recurrent MI (PMI – Previous MI group) to those with a first MI (FMI group).

**Methods:** Data was collected from the 2006 ACSIS (Acute Coronary Syndrome Israeli Survey) - a biannual survey on acute myocardial infarction performed in 26 intensive cardiac care units in Israel during a two-month period. 2074 patients suffered from MI, 30% of who were PMI patients

**Results:** *Presented here are only results with  $P < 0.05$ .*

**Presentation:** When compared to the FMI group, PMI patients had more risk factors and comorbidities. During the event less PMI patients presented with atypical angina (55 vs. 61%), more with heart failure (7 vs. 3%). Electrocardiographically, less PMI patients had ST elevation (26 vs. 51%); more patients had ST depression (27 vs. 18%), as well as lack of ECG changes (27 vs. 15%). **Treatment:** PMI patients were less likely to receive reperfusion therapy (medically or percutaneously); 12 vs. 25% of patients were treated with primary percutaneous coronary intervention (PCI); 47% compared to 69% had PCI during hospitalization, and 4% compared to 8% were treated with thrombolysis. **Outcomes:** PMI had more complications than FMI patients; heart failure (17 vs. 10%), pulmonary edema (13 vs. 7%), cardiogenic shock (6 vs. 4%), mitral regurgitation (5 vs. 2%) and acute renal failure (7 vs. 4%). Mortality was higher among patients with PMI; 4 vs. 2% at 7 days and 6 vs. 4% at 30 days.

**Conclusions:** 1. PMI patients were less likely to present with STEMI, possibly due to increased secondary preventive treatment for their disease, vessel collateral formation, and earlier self-referral. 2. Patients with PMI suffered more major complications during hospitalization than FMI patients, and experienced higher mortality rates.

## **Right Ventricular Dysfunction in Isolated Anterior ST Elevation Myocardial Infarction**

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**Background:** Isolated occlusion of LAD does not usually affect right ventricular (RV) function. We describe for the first time a series of patients in who isolated anterior ST elevation MI (STEMI) was associated with right ventricular dysfunction.

**Methods:** We retrospectively identified all patients admitted to our medical center between 9/1996 and 1/2007 who had an anterior STEMI, had single vessel disease involving either the LAD, diagonal or ramus arteries who were found to have unexplained RV dysfunction by echocardiography within 24 hours of admission. Patients with any other cardiac pathology or pulmonary hypertension were excluded. Five patients fulfilled these criteria out of 438 patients who had a similar coronary anatomy but no RV dysfunction (1.14%). Demographic, clinical, echocardiographic and angiographic characteristics were studied. Echocardiographic and angiographic data were reviewed by a “blinded” investigator.

**Results:** A blinded investigator confirmed the diagnosis of RV hypokinesis in all subjects. All patients with RV dysfunction were men and their mean age was 52 (range: 40 to 60) years. All of them had no prior cardiac history. All patients had moderate – severe LV dysfunction. Echocardiographic follow-up was available for one patient 5 months after admission; RV dysfunction was completely resolved and LV dysfunction significantly improved. The coronary angiograms of all subjects were reviewed; absence of disease in the RCA was confirmed but we could not identify a coronary basis for RV dysfunction.

**Conclusion:** Isolated anterior STEMI not involving the RCA may rarely lead to significant RV dysfunction in relatively young subjects.. The mechanism for this previously undescribed observation is unclear. Complete resolution of RV dysfunction is probably common.

## **Therapeutic Hypothermia in Survivors of out of Hospital Cardiac Arrest is also Beneficial after Cardiac Asystole.**

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Out of hospital cardiac arrest is a condition with high mortality and devastating morbidity. Patients who are found in ventricular fibrillation generally have a more favorable outcome than patients found in asystole, which at some places are considered hopeless. This has led many physicians to a less aggressive approach in patients found in asystole. Results from recent clinical trials suggest a beneficial effect of induced mild hypothermia on the neurological outcome and mortality in patients with out of hospital cardiac arrest, and this therapeutic modality is now part of the guidelines. During the last five years we induced mild hypothermia in 102 survivors of out of hospital cardiac arrest. During their stay in the ICCU, 38% regained consciousness and 20% died. 52 patients were initially found in ventricular fibrillation, 35 patients in asystole and the other patients in a variety of other conditions, mainly asphyxia and electromechanical dissociation. Consciousness was regained by 50% of the ventricular fibrillation patients, 31% of the asystole patients and two of the 9 COPD patients. We conclude that cardiac asystole is not a hopeless condition, and induced mild hypothermia may be beneficial in some of these patients.

## **Spontaneous Reperfusion in ST-Elevation Myocardial Infarction is Associated with more Distal Coronary Lesions**

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**Background:** Spontaneous reperfusion (SR) of the infarct-related artery may occur in patients with ST-segment elevation myocardial infarction (STEMI). Limited data are available on angiographic characteristics of these patients. The objective of this study was to examine if there are differences in the distance of the culprit lesion from the coronary ostium in patients with STEMI with and without SR.

**Methods:** Patients who presented with acute STEMI within 12 hours after pain onset and who underwent coronary angiography were entered into the study. Measurement of the distance from the coronary ostium to the culprit lesion was performed. SR was defined as significant relief of chest pain with an at least 50% resolution of ST segment elevation on follow-up electrocardiograph

**Results:** A total of 469 patients with STEMI were included in the study of whom 77 met criteria for SR and 392 who did not. A highly significant difference was seen in ostial to culprit lesion distance with the culprit lesion in the SR group being more distal than those in the non-SR group ( $45 \pm 22$  mm vs  $39 \pm 20$  mm, p-value < 0.009).

**Conclusions:** In conclusion, our findings demonstrate that the location of the culprit lesion in STEMI patients who undergo SR is more distal in the involved artery than in STEMI patients without SR. Our findings suggest that the relatively lower thrombus burden and greater amount of vasoreactivity in these lesions may increase the chances of SR.

## **Preadmission on the Ambulance Tirofiban Infusion for STEMI Patients on the Way to Primary Percutaneous Intervention.**

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Aim: Determining the feasibility and safety of pre admission diagnosis of STEMI by a mobile intensive care unit (MICU) team using telemedicine, and early administration of the GP IIb/IIIa inhibitor (Tirofiban) on the way to immediate PCI

Method and results: During the time February 2006 up to November 2007 27 patients with suspected STEMI were evaluated in the ambulance, using HeartView™ and ECG trans-telephonic Recorder/Transmitter to the cardiac care unit. The diagnosis was confirmed by the cardiologic on call in 24 of them and a loading dose of Tirofiban was infused. The study group included 22 males (91.2%), mean age  $59.9 \text{ y} \pm 13.5$ , HTN in 47%, DM 20%, smokers 47%, anterior wall infarct in 45.8% and cardiogenic shock in 2 patients (8.3%).

The drug was given  $27 \pm 6$  minutes pre arrival to the hospital, and  $33 \pm 19$  minutes pre initiation of the angiography. an ST segment resolution pre angiography was noted in 20.4% and initial TIMI grade flow of 2 or 3 was demonstrated in 40% of the patients.

All patients had successful PCI to the culprit artery. The hospitalization course was uneventful for all patients, and no excess bleeding complications were noted. All patients were discharge home after  $4.4 \pm 1.6$  days.

For analysis, a comparison was done between the study group to consecutive 145 other STEMI patients treated with primary PCI during the same time period in our center. No statistically significant difference was found for clinical, laboratory and outcome parameters.

Conclusion: based on this small pilot study, pre hospital diagnosis of STEMI using telemedicine equipment, and initiating GP IIb/IIIa antagonist seems to be feasible and safe, yet a larger study is needed for evaluation of beneficial effect.

## Pseudonormal Electrocardiogram During Evolving Myocardial Infarction and Severity of the Infarct Related Artery (IRA) Stenosis

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Pseudonormalization of negative T waves is a well known indicator of myocardial ischemia. Pseudo-normalization of T waves during evolving ST elevation myocardial infarction (STEMI) and its correlation with the IRA has not been described. We studied the coronary angiographies of 34 pts. with STEMI which were divided into 2 groups according to their ECG evolution. Group A consisted of 18 pts whom during the course of STEMI evolved to a normal ECG pattern within 24 hours of admission. Group B consisted of 16 pts with T wave inversion within 24 hours. All pts of group A had T wave inversion at a later time or after PCI of the IRA. The table presents a summary of the relevant data.

|           |     | Group A            | Group B        | P value |
|-----------|-----|--------------------|----------------|---------|
| Patients  |     | 18                 | 16             |         |
| Male      |     | 13                 | 13             |         |
| Mean age  |     | 57,6               | 58,7           | NS      |
| IRA       |     | 14LAD,<br>3Cx,1RCA | 12LAD,3Cx,1RCA |         |
| %stenosis | LAD | 91.8(SD=10.6)      | 85.3 (SD=11.7) | P<0.07  |
|           | Cx  | 86.7% SD=5.8       | 68.3 SD=16.1   | P<0.07  |
|           | RCA | 91% SD=8.2         | 70.5 SD=21.7   | NS      |

Results: There were no demographic differences between both groups. The severity of coronary stenosis was significantly higher in group A for the LAD, Cx and RCA, however for the RCA the severe stenosis was not statistically significant since there was only one pt. in each group. Thus, we conclude that this regressive pseudo normal pattern is a transitional ischemic stage probably due to incomplete revascularization of the IRA. These findings may explain cases of myocardial infarction with apparently normal ECG at presentation.

## **ST Deviation Pattern in Acute Myocardial Infarction is not Related to Lesion Location**

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**Background:** Myocardial infarction may be classified as ST-elevation MI (STEMI) or non-ST elevation MI (NSTEMI). In STEMI the culprit artery is usually occluded, whereas in NSTEMI it is usually patent. The location of the ruptured plaque may influence the MI type. Herein we examine whether the distance from the coronary ostium to the culprit lesion is different in STEMI as compared to NSTEMI.

**Methods:** We reviewed our database and selected patients who presented with an acute MI and underwent coronary angiography within 7 days of admission. The analysis included 754 patients of whom 514 had STEMI and 240 had NSTEMI. QCA was performed and the distance from the ostium of the coronary artery to the site of thrombosis was measured.

**Results:** For both STEMI and NSTEMI patients the first 50mm (LAD and LCX) or the first 60mm (RCA) of the coronary artery contained 75% of the culprit lesions. There were no significant differences in median distances from the vessel ostium to the site of thrombosis between STEMI and NSTEMI patients

**Conclusions:** the distance from coronary ostium to culprit lesion is similar in STEMI and NSTEMI patients. Culprit lesion location does not appear to influence the development of STEMI as opposed to NSTEMI.

## **Seasonal Variation in Myocardial Infarction is Limited to Patients with ST-Elevations on Admission**

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**Background:** Previous studies have demonstrated a seasonal variation in the incidence of acute myocardial infarction (AMI) with an increase in cases during the winter months. These studies have not assessed whether ST-elevation MI and non-ST-elevation MI exhibit similar changes. The object of this study was to compare the seasonal variation of STEMI as compared to NSTEMI.

**Methods:** All patients who presented with AMI and underwent coronary angiography within 7 days of admission were identified via the institutional database. STEMI diagnosis required admission ECG demonstrating ST elevation in at least two contiguous leads. All acute MI's not meeting criteria for STEMI were defined as NSTEMI. Patients were divided into monthly and seasonal groups based on the date of admission with MI.

**Results:** A total of 784 patients were included; 549 patients with STEMI on the basis of the admission ECG and 235 with NSTEMI. When STEMI patients were analyzed by season there were 170 patients (31%) in the winter months, a statistically significant difference of excess MI. ( $p < 0.005$ ). When NSTEMI patients were analyzed there were 62 patients (26%) in the winter with no statistically significant difference in the seasonal variation.

**Conclusions:** Our findings suggest that the previously noted seasonal variation in the incidence of AMI is limited to patients presenting with STEMI. This suggests there are important physiological differences between STEMI and NSTEMI, the nature of which remain to be elucidated.

## A Pilot Study on Physical Conditions Related to Right Ventricular Infarction and Cardiogenic Shock in Acute Myocardial Infarction (AMI)-PCI Data

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In 1170 primary PCI for AMI (2000-2006) 123 (10.5%) were described as right ventricular infarction (RVI) and 102 (8.72%) accompanied by cardiogenic shock (CSh) -factors negatively affecting AMI prognosis. The **aim** of this study was to check if these two conditions are related by some specific environmental physical activity markers.

**Methods:** daily physical activity parameters geomagnetic (GMA)-I-IV levels and cosmic ray activity –by neutron activity on the Earth's surface (imp/min) were obtained for each day in the study period (n=2557), days of AMI with culprit artery at LAD, RCA, CRX - and at days with AMI –right ventricular and with cardiogenic shock.

**Results:** patient characteristics-it was significantly more men in the RVI group (p=0,0005) as in the CSh and, inverse, for women (p=0,06). Patients in the CSh group were older than in RVI (p<0,0002). Woman >80y. old were more often in the CSh group. (p=0,05). On days of both RVI and CSh it was higher CRA (neutron) activity as at the whole study period (p=0,0003 for RVI; p=0,018 for CSh) and higher as in LAD, RCA AMI for RVI, (p=0.006 -LAD, 0,027-for RCA; p=0.014 for CRX) and CSh-AMI (p=0,009 for LAD; p=0,029 for RCA; 0.089 for CRX). RVI took place more often than CSh at two highest levels of GMA. (p=0,06).

**Conclusion:** AMI is accompanied by RVI and CSh on days with higher CRA compared with other groups of AMI; RVI is more often seen with concomitant high levels of GMA than AMI with CSh. CSh patients were older than RVI and woman in CSh prevailed.

It can be presumed that higher neutron (CRA) activity is predisposing to expanded myocardial damage in AMI.

## **Cardiac Telemedicine from the Prospective of the Patient and the Physician: an Update**

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Telemedicine, a direct offshoot of cutting-edge technology, is assuming an important place in modern healthcare. 'SHL' telemedicine provides professional care to subscribers who contact its monitor center by telephone, describe their symptoms to the professional staff, and transmit their real-time ECGs (lately by cardiobeeperes with cellular telephone transmission). These data, combined with those stored in a central computer for instant access, determine individually appropriate therapeutic measures, including the dispatch of mobile intensive care units.

The telecardiological system monitors blood pressure, pulmonary peak flow, and selected cardiac parameters. The new 'Telemarker' device for transtelephonically measuring cardiac markers in whole blood was found safe and efficacious for independent use at the patient's home.

There are currently >60,000 'SHL' subscribers (age range 15-102 years). Since its establishment (1987), the service has handled >9,100,000 calls and ECG transmissions: solely telephonic medical assistance was required by >85% of the callers. SHL's CHF program led to 66% fewer hospitalizations.

Telemedicine services improved diagnosis and benefitted survivors of AMIs by decreasing mortality at one year from discharge following infarction. In addition numerous cases of unexplained episodes of weakness and pre-syncopacal episodes were also diagnosed as arising from rhythm and conduction disturbances.

Transtelephonic instruction to laymen who provided basic life support measures until professionals arrived at the scene resulted in a 10% survival rate of otherwise terminal patients.

Accurate diagnosis in the pre-hospital setting of patients with cardiac symptoms enhances identification of those with acute coronary syndromes, conserves resources by appropriate triage, and improves patients' motivation to seek medical assistance.

## The Value of Computed Tomography Coronary Angiography before Invasive Coronary Angiography in Patients after Coronary Artery Bypass Grafts

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**Background:** Coronary imaging using multidetector computed tomography (MDCT) might be an initial non-invasive modality for the diagnosis of coronary artery disease. In patients after coronary artery bypass grafts (CABG) the value of MDCT before invasive coronary angiography (ICA) had not been tested.

**Objective:** To examine the value of MDCT in patients after CABG who are planned for ICA with optional percutaneous coronary intervention (PCI).

**Methods:** We enrolled patients post CABG, high risk for ICA, who were admitted to our department for ICA due to acute coronary syndrome or electively for angina and objective ischemia on stress testing. All patients before ICA had undergone 64-slice MDCT for the detection of culprit vessel stenosis. Patients who had MDCT finding of significant stenosis (diameter stenosis >50%) had undergone ICA with optional PCI.

**Result:** Seven patients, 5 male and 2 female, mean age  $77 \pm 5$  years were enrolled till now. According to MDCT finding, 4 patients underwent successful PCI of target saphenous venous graft (SVG) (PCI group); 3 of them had selective imaging of target vessel only. Three patients in whom MDCT showed significant target vessel stenosis were, according to ICA, not suitable for PCI (non-significant stenosis in 2 and chronic total occlusion in 1 patient), (intention to treat group). One patient in this group had selective imaging of target vessel only. Mean fluorescence time in patients with selective imaging of target vessel was  $7 \pm 4$  minutes (min) compared with  $9.5 \pm 12$  min in those with non-selective imaging. The mean amount of contrast media that given during ICA was  $90 \pm 76$  ml compared with  $110 \pm 45$  in selective and non-selective imaging respectively. All patients early after PCI and during the follow-up were clinically stable and uneventful.

**Conclusion:** In our study patients, MDCT before ICA is feasible and safe. MDCT guided PCI was associated with high procedural success rate, less fluorescence time and less amount of contrast media. In 3 of 7 patients the MDCT were not accurate with ICA findings. For statistical power, our study is still in progress.

## **Mild Therapeutic Hypothermia Improves Outcome after Out-of-Hospital Cardiac Arrest**

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Treatment of coma following resuscitation with mild hypothermia has been incorporated into the guidelines following publications showing improvement in survival and neurological status after resuscitation for ventricular fibrillation (VF). We present the results of this treatment in our coronary care unit from 02/2003- 10/2007.

Results: Thirty patients (80% male) between ages of 23-82yrs were treated with mild hypothermia (34°C) following resuscitation. 23 had VF, 1 had VT and 6 had asystole as initial rhythm. Twenty two patients (73%) survived to discharge from hospital, 16 (53%) were discharged in good condition or moderate neurological deficit, and 6 (20%) had severe anoxic brain damage or vegetative state.

Predictors for good outcome included age <65yrs, length of resuscitation, and number of DC shocks. Asystole was not a predictor of poor outcome as 5 of the 6 patients admitted with asystole were discharged home with good neurological function.

Conclusions: This series of patients treated with mild hypothermia confirms the results of the randomized trials and suggests that treatment with hypothermia improved the outcome of survivors of sudden cardiac death and its indication may be broadened to include patients admitted not only with VF but also after asystolic cardiac arrest.

## **Patients' Personality and Spouses' Ways of Giving Support: Which Contributes More to the Recovery after First ACS?**

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**Background:** In married couples the support provided by the spouse can be an important element in the healing process of the patient. Few studies have looked at the spouses' styles for giving support in the clinical context of recovery from an acute coronary syndrome (ACS). Coyne and Smith (1991, 1994) categorized three possible support styles of the spouse: active engagement, protective buffering and overprotection. They predicted that only the active engagement would be beneficial for the patients, however this was not empirically verified. Based on the person-environment fit model (Martire, Druley, Stephens & Wojno, 2002), our assumption was that support from the spouse will be beneficial for the patient recovery only as a function of the patient own personality characteristics.

**Objective:** The current study's main goal was to explore, in a prospective format, the nature of the interaction, between the spouses' ways of giving support and the patients' attachment personality style, to recovery outcomes of patients six months after their first ACS.

**Method:** The target population consisted of Jewish men, with the diagnosis of first ACS, admitted to the cardiac care unit at Meir medical center, Kfar Saba, Israel, between March 2005 and July 2006 (N=216). The study sample consisted of all patients and spouses who agreed to participate in the study and who completed the study questionnaires at Time 1-during hospitalization (N= 77), and at Time 2- six months after hospitalization (N=69). At time 1, the spouses completed the *Ways of Giving Support Questionnaire* (WOGS; Bunnk, et al, 2006), and the patients completed the *Experiences in Close Relationships* scale (ECR; Brennan, Clark & Shaver, 1998). Outcomes measured were: depression and anxiety reduction, BMI reduction, blood lipids improvement, Hs-CRP reduction, smoking cessation, rehabilitation program attendance and resuming work

**Results:** No main effect was found for attachment style in the prediction of the dependent variables. Two main effects were found for ways of giving support: active engagement predicted decrease in patients' BMI and over-protectiveness predicted non attendance in rehabilitation programs. Ten significant interactions were found between the patients' attachment styles (anxiety or avoidance) and the three ways of giving support of the spouses (active engagement, protective buffering and overprotection). These interactions correlated mostly with the patients' behaviors (i.e. smoking cessation, rehabilitation attendance and resuming work).

**Conclusions:** The interpersonal dynamics determining appropriate behavior following a medical crisis are complex and are an important element for further study. It is recommended that cardiac rehabilitation programs take in to consideration the contribution of the spouses' supportive style to the behavior and recovery of the male patient.

## **Factors Affecting non Attendance in Cardiovascular Rehabilitation Programs.**

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**Background:** Attendance in phase-II cardiac rehabilitation program (CPR) is poor, and dropout rates of patients who start participation is unacceptable.

**Aim:** To identify factors influencing patients' decisions to attend cardiac rehabilitation programs.

**Methods:** Semi-structured interviews were conducted with 33 patients attending CPR, compared with 25 dropout patients that contacted the CPR.

**Results:** The age was of attending patients were 59.3±8 years, 73% were males.

Most of attending patients, 82% (n=29) could identify a reason for the cardiac event vs. only 36% (n=9) among non attending (p= 0.0002). Social environment in the rehabilitation center was identified as supporting further attendance among 68% of attending patients. Employment and distance from rehabilitation center was a reason for not participating in 90% of non attending patients. Surprisingly, health improvement was a minor factor influencing attendance decision in both groups. Information and encouragement delivered by the GP's were minimal and non influential in both groups. Factors not affecting attendance were: gender, employment, physical activity, spouse support and income.

**Comments:** Strategies should be developed for encouraging greater attendance by training GP's to identify and encourage eligible patients for CRP. Rehabilitation at out of work hours may enhance attendance. Distance is still a major obstacle of attendance, suggesting the importance of home-based rehabilitation.

## **Use of Attenuation Correction to Improve Accuracy of SPECT Myocardial Perfusion Imaging. Initial Experience at Hadassah Hospital**

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**Objective:** To assess prospectively the impact of attenuation correction (AC) on SPECT myocardial perfusion imaging (MPI) diagnostic accuracy.

**Patients:** Thirty two patients were referred to MPI: 11 patients for chest pain without known ischemic heart disease and 21 because of persistent chest pain after myocardial infarction and/or revascularization,

**Methods:** In addition to routine MPI, an x-ray tomography (GEMS –Hawkeye CT) was performed. Slice thickness was 1 cm. The CT Hounsfield units were transformed, for each pixel, into the corresponding attenuation coefficient for the used radioisotope (Tl-201 or Tc-99m). Ordered subsets expectation maximization (OSEM) algorithm was used for SPECT computer reconstruction to generate images with and without AC. The AC and non AC images were interpreted separately by 2 nuclear medicine physicians. A 6 to 12 months follow up period included close clinical follow up and, if necessary, coronary angiography. A consensus panel composed of cardiologists and NM physicians correlated the SPECT AC and non AC interpretations with the clinical and angiographic data.

**Results:** 1) Eight patients with normal AC MPI experienced no cardiac event during the follow up period. Seven of them showed 9 perfusion abnormalities on the non- AC data: in the infero-septal wall (5/7), apex (2/7) and anterior wall (2/7, male pts). 2) Eleven patients had inferior wall abnormality on the non-AC images and underwent angiography. Seven of them with abnormality seen also on the AC images had significant coronary disease in the RCA/Circumflex arteries. The other four with normal AC images had normal angiography of those arteries. 3) Two women with anterior wall perfusion abnormality on both AC and non AC images had a normal LAD coronary artery angiography. 4) In 10 patients with multiple perfusion abnormalities in territories other than the inferior wall, the correlation of angiography was better with the AC than with the non-AC images.

**Conclusions:** AC MPI may not perfectly correct for anterior wall defects, in particular for breast artifacts. However AC greatly improves the diagnostic accuracy of MPI SPECT and should be considered as becoming standard practice.

## A Novel Noninvasive Digital Arterial Pulse Wave Analysis During Deep Breathing as an Indicator of Significant Coronary Artery Disease – A Two Center Study.

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**Background:** Previous studies have indicated that fluctuations in pulse wave amplitude (PWA) might be a predictor of coronary artery disease (CAD). Therefore analysis of the respiratory modulation spectral response (RMR) of the PWA during deep breathing at a frequency of 0.1 Hz can be performed by the novel Cardiometer® device, utilizing a photo plethysmograph sensor, attached to the patient's finger and proprietary software. We evaluated this noninvasive simple test as an indicator of significant CAD

**Methods:** The RMR results of 195 consecutive pts; (mean age  $63.1 \pm 11.6$  years, 73% male) referred for coronary angiography in two academic medical centers (97 pts in Rabin MC and 98 pts in Barzilai MC), were compared with their coronary angiography results. Patients with luminal stenosis of  $\geq 70\%$ , or left main stenosis  $\geq 50\%$  were classified as having significant CAD. The Cardiometer RMR test was performed in the recovery room of the catheterization laboratory prior to the procedure, excluding CABG and STEMI. RMR was analyzed after baseline 20 seconds spontaneous breathing, followed by 70 seconds of guided deep breathing at 0.1 Hz. The test was repeated post procedure in 152 pts following PCI or diagnostic catheterization.

**Results:** The RMR (normal ranges 78% [best] to 0% [worst]) was significantly lower in pts with significant CAD (n=118) vs. pts with non-significant CAD (n=77) ( $14.57 \pm 23.15$  vs.  $38.75 \pm 19.68$ ,  $P < 0.001$ ). The improvement in post procedure RMR was significantly higher in pts who had undergone successful PCI (n=107) as compared to pts (n=88) who had only diagnostic catheterization only ( $27.51 \pm 23.45$  vs.  $20.00 \pm 25.91$ ,  $P < 0.05$ ). RMR was lower in pts (29/195) with recent MI ( $14.35$  vs.  $25.83$ ,  $P < 0.05$ ). By using a receiver operating characteristic analysis, we identified an RMR  $< 29\%$  (sensitivity 81.4%, specificity 76.6%; positive and negative predictive values: 84.2%, 72.8%, respectively) to be the optimal cut-off value for predicting significant CAD. The clinical characteristics and the RMR results were similar in the two centers.

**Conclusions:** The novel digital PWA analysis test during deep breathing using the Cardiometer device is a simple, non-invasive bedside or office based test to detect significant CAD and to monitor patients with CAD post PCI.

## **Association between HbA1c and Erectile Dysfunction in Non-Diabetic Men with and without Ischemic Heart Disease**

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**Introduction:** HbA1c is biomarker of endothelial dysfunction in non-diabetics. Endothelial dysfunction is implicated the pathophysiology of erectile dysfunction (ED) as well as ischemic heart disease (IHD). Although HbA1c levels are associated with ED in diabetic men, the association between HbA1c levels, ED and IHD has never been studied in non-diabetic men.

**Methods:** A total of 119 men underwent coronary angiography and filled the Sexual Health Inventory for Males questionnaire (SHIM). Excluded were men with diabetes mellitus and men with chronic inflammatory process. SHIM scores 21 or less represented ED.

**Results:** Included were 70 men, mean ages 59.4±13.3 years. Mean SHIM scores were 16.8±8.1 and mean HbA1c levels were 5.6±0.6% for the whole cohort. HbA1c levels were associated with SHIM scores ( $r=-0.34$ ;  $p=0.004$ ) for the whole cohort. HbA1c levels were not higher among men with IHD ( $n=52$ ) compared with men without IHD ( $n=18$ ), and among men with ED ( $n=47$ ) compared with men without ED ( $n=23$ ).

**Conclusions:** HbA1c levels are associated with ED among non-diabetic men with and without IHD. This finding sheds a new light on the clinical use of HbA1c in non-diabetics, and in men with IHD in particular.

## **Clinical Pharmacology in the Coronary Cathlab: Incidence of Drug Related Problems in Patients Undergoing Coronary Angiography**

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### **Background:**

Drug related problems (DRP's) are underreported and consequently are an underestimated cause of morbidity and mortality. Recent epidemiologic evidence estimates that DRPs are the fourth to the sixth leading cause of death in USA. Important risk factors for adverse drug events or reactions included polypharmacy, female sex, drugs with a narrow therapeutic range, renal failure and advanced age. Over 50% of DRP is estimated as preventable. Interventional cardiology deals with relatively sick patients that are under polypharmacy therapy. The objectives of this study were to evaluate the frequency and the predictors for medication errors and adverse drug events in this high-risk population.

### **Methods:**

Consecutive patients undergoing coronary angiography were interviewed and their records surveyed by a clinical pharmacologist for DRP (defined as adverse drug events, drug interactions, medication errors, dosage problems, frequency problems, drug- illness interaction, drug- age interaction, lack of drug in therapy and partial therapy problems). Detected DRP were further evaluated by a clinical cardiologist familiar with the patient.

### **Results:**

165 patients were studied, 108 DRPs were detected in 64 patients (40%). DRPs were detected in older patients ( $65\pm 10$  vs.  $59\pm 1$ ,  $p<0.01$ ) that were treated with more drugs ( $7.46\pm 2.7$  vs.  $6.6\pm 2.5$ ). Patients with DRPs had a higher incidence of co-morbidities including diabetes mellitus and previous organ transplantation and were significantly under-treated with beta blockers, statins and aspirin.

### **Conclusions:**

Drug related problems are very frequent in patients undergoing coronary interventions and may significantly affect morbidity in this already sick population. Meticulous screening for DRP may reduce their incidence and improve patient care and well being.

## Detection of Significant Coronary Artery Diseases Employing a Novel, Non-Invasive Finger Pulse Wave Analysis During Deep Breathing Exercise: a Validation Study

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**Introduction:** Previous studies have indicated that fluctuations in pulse wave amplitude can predict coronary artery disease (CAD). Recently we demonstrated that respiratory modulation response (RMR), a spectral analyzing of pulse wave amplitude change derived from finger photoplethysmograph sensor during deep breathing at a frequency of 0.1 Hz. can detect the presence of significant CAD. The purpose of the study was to evaluate whether pre specified RMR value defined in a previous study can be used as a test to detect significant CAD.

**Methods:** The RMR test was prospectively performed in 102 consecutive patients referred for coronary angiography prior to the procedure, excluding only STEMI and prior CABG patients. Their RMR was analyzed by proprietary software, after baseline 20 seconds of spontaneous breathing, followed by 70 seconds of guided deep breathing at 0.1 Hz. The physician performing the angiography was blinded to RMR results. Based on the previous study, the pre-specified cut-off on RMR for indicating significant CAD was 30%. Receiver operating curve (ROC) methodology was used to assess RMR accuracy vs. % stenosis; 50% or 70% for each separately. **Results:** Valid RMR signal was achieved in 98 (96%) patients, 68.4% male, mean age  $64.6 \pm 11.3$ . Angiographically, 77.6% of patients demonstrated coronary artery stenosis  $>50\%$  and 66.3% stenosis  $>70\%$  in one or more major epicardial vessels. ROC analysis yielded area under the curve (AUC) of 0.80 (95% CI: 0.71 – 0.89) and 0.82 (0.73 – 0.91) respectively for Stenosis  $>50\%$  and  $>70\%$  ( $p < 0.001$  for both). The table demonstrates RMR 30% accuracy in detecting significant CAD. **Conclusion:** RMR is an accurate, non-invasive, simple and safe test for detecting significant CAD.

### Accuracy of RMR Classification by Stenosis %

| Accuracy Parameter              | Coronary Stenosis | Angiography |
|---------------------------------|-------------------|-------------|
|                                 | $> 50\%$          | $> 70\%$    |
| Sensitivity                     | 72.4%             | 80.0%       |
| Specificity                     | 86.4%             | 81.8%       |
| Positive Predictive Value (PPV) | 94.8%             | 89.7%       |
| Negative Predictive Value (NPV) | 47.5%             | 67.5%       |

## **Hypoxia Controls the Hemostasis of Naturally Occurring Regulatory T Cells via Hypoxia Inducible Factor-1**

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**Background** - Hypoxia is a negative regulator of T cells stimulation, cytokine production and proliferation, inducing a shift towards T<sub>H</sub>2-cell responses and inhibition of T<sub>H</sub>1-cell responses. Recently, different studies have reported the involvement of hypoxia inducible factor-1 (HIF-1) in the regulation of T cell proliferation and activation. Naturally occurring CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup> regulatory T cells (Tregs) are a subpopulation of suppressive lymphocytes which maintain immune homeostasis and self tolerance. Herein, we aim to investigate the effect of hypoxia and HIF-1 $\alpha$  activation on the occurrence and function of Tregs.

**Methods and Results** - Incubation of Jurkat T cells under hypoxia (1%O<sub>2</sub>) resulted in a marked increase in both HIF-1 $\alpha$  activity and Foxp3 expression as determined by ELISA and flow cytometry, respectively. This effect was abolished by retroviral transduction of siRNA directed against HIF-1 $\alpha$ . Additionally, transduction of stabilized HIF-1 $\alpha$  in Jurkat cells dose dependently increased Foxp3 expression levels. Exposure of human peripheral blood-derived mononuclear cells and mouse splenocytes to hypoxic conditions resulted in a significant increase in Foxp3<sup>+</sup> population among CD4<sup>+</sup>CD25<sup>+</sup> cells. This was accompanied by an elevated capacity of hypoxia-treated CD4<sup>+</sup>CD25<sup>+</sup> isolated cells to suppress the proliferation of CD4<sup>+</sup>CD25<sup>-</sup> responders. Eventually, HIF-1 $\alpha$  over-expression in mouse splenocytes by hydrodynamic naked DNA injection resulted in elevated mRNA levels of Foxp3 and total CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup> cells number, compared to control.

**Conclusions** – Hypoxia regulates the hemostasis of naturally occurring regulatory T cells via expression of HIF machinery.

## **The Haptoglobin 2 Genotype is Associated with Increased Redox Active Hemoglobin Derived Iron in the Atherosclerotic Plaque**

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**Background.** The Haptoglobin (Hp) gene is polymorphic with two classes of alleles (1 and 2). The Hp 2-2 genotype is a major determinant of CV risk in DM individuals. We hypothesized that Hp genotype dependent differences in protecting against hemoglobin induced oxidative injury and in promoting clearance of hemoglobin would be manifested as increased oxidation from hemoglobin derived iron in the atherosclerotic plaque.

**Methods and Results.** Immunohistochemical analysis of plaques from C57Bl/6J Apo E<sup>-/-</sup> Hp 1-1 or C57Bl/6J Apo E<sup>-/-</sup> Hp 2-2 mice demonstrated a marked increase in plaque hemoglobin in Hp 2-2 mice. In order to determine if plaque hemoglobin could be derived from extravasation of hemoglobin we injected <sup>125</sup>I labeled Hp-Hb complexes into Apo E<sup>-/-</sup> mice and found markedly greater extravasation of the Hp 2-Hb complex into the plaque. Oxidation in the plaque was monitored by assessing in situ oxidation induced fluorescent activation of Dihydrorhodamine (DHR). DHR fluorescence was increased in Hp 2 plaques and was found to correlate and colocalize with iron and hemoglobin. The oxidation of DHR in the plaque was inhibited by iron chelation.

**Conclusions.** The increased oxidation present in Hp 2 plaques appears to be due to hemoglobin iron. Agents which prevent iron induced oxidation may have considerable value in decreasing oxidation and inflammation in Hp 2 plaques thereby reducing the risk of plaque rupture and atherothrombosis in Hp 2 DM individuals.

## **Effect of Pacing Lead Position on Ischemic Left-Ventricle Functioning: Should We Change the Strategy of Lead Placement in Cardiac Resynchronization Therapy?**

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**Background:** Although the benefit of Cardiac Resynchronization Therapy is widely recognized many patients with ischemic cardiomyopathy fail to show improvement. We hypothesize that beneficial local myocardial functions will be obtained by pacing the weak ischemic regions, since pacing decreases energy consumption at the pacing site. The study tests the local and global short term effects of the opposing strategies: pacing at the lateral 'last activated' site or at the ischemic site. **Methods:** Myocardial infarction (MI) was created in the anteroseptal region by ligation of a large branch of the LAD, in open chest anesthetized sheep (n=5). A flowmeter was placed on the ascending aorta. Sonocrystals were implanted in the LV endocard and in the ischemic region. Local and global LV functions were assessed before and after the coronary ligation in three pacing modes: normal sinus, septal pacing at the ischemic site or lateral pacing. **Results:** At both baseline and ischemia, pacing on either site didn't significantly affect the global EW. However, huge decrease in the anteroseptal work was observed during local pacing (p<.005) while the lateral pacing slightly increases the work of the ischemic region. Moreover, pacing in the ischemic region diminished the post-systolic shortening work (active work during diastole) and thus improves the diastolic function (n=3, p<.05). **Conclusions:** Redistribution of the workload, reducing the work of weaker areas and loading the healthier regions, is feasible through pacing the ischemic regions. Improving the balance between mechanical demands and energy supply and improving cardiac diastolic function may promote myocardial reverse remodeling.

## **Toll-like Receptor 4 (TLR4) and Macrophage Migration Inhibitory Factor (MIF) Expression in the Myocardium Following Ischemic Injury or LPS Injection**

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MIF and TLR4 play an important role in the regulation of innate immune responses. Inflammation participates in the pathology of ischemic heart disease and in myocardial contractile depression during septic shock. The inflammation in cardiovascular disease is associated with the activation of immune cells and cardiac myocytes, which secrete interleukin 1 beta (IL-1  $\beta$ ) and tumor necrosis factor alpha (TNF $\alpha$ ).

**Aim:** To investigate the time course of myocardial dysfunction and cytokine expression in models of LPS induced sepsis and myocardial ischemia (MI) induced by LAD ligation, and to determine the changes in the myocardial gene and protein expression of TLR4 and MIF.

Mice were challenged to sepsis with LPS or subjected to MI. Myocardial levels of IL-1 $\beta$  and TNF $\alpha$  increased significantly after MI or LPS injection reaching the maximum at 4 hours. The IL-1  $\beta$  and TNF  $\alpha$  levels remained high in the MI group, whereas in LPS injected group, levels returned to baseline within 72 hours. The decrease in hemodynamic function following LPS injection was transient, maximizing at 4 hours (78 $\pm$ 11 mmHg, 65 % of baseline values). In MI hemodynamic function decreased to 67 $\pm$ 8.5mmHg, 58 % of baseline values, after 24 hours (p<0.05), remaining so for 72 hours. Although myocardial TLR4 and MIF gene expression increased after LPS and MI challenge, the TLR4 protein expression remained unchanged while MIF increased after an initial decrease.

**Conclusion:** In addition to their role in the immune response, TLR4 and MIF depress cardiac function in both ischemia and LPS injury.

## Rapamycin Protects Heart Cultures against Hypoxia via Ryanodine Receptors

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**Introduction:** Ryanodine receptors (RyR2), the major intracellular Ca<sup>2+</sup> release channel in the cardiac muscle, play an essential role in excitation-contraction coupling by regulating the release of Ca<sup>2+</sup> from the sarcoplasmic reticulum (SR) for binding to the contractile apparatus. RyR2 channel function is a subject to exquisite levels of modulation via diverse mechanisms, including interaction with accessory proteins such as FKBP12.6. Rapamycin (sirolimus) is an antibiotic that inhibits protein synthesis through mammalian target of rapamycin (mTOR) signaling and is used as an immunosuppressant. The proposed mechanism for the anti proliferative effect of rapamycin is based on its ability to bind to its intracellular receptor, the FK506 binding protein (FKBP12.6). Rapamycin confers preconditioning-like effect against myocardial infarction through opening of mitochondrial K<sub>ATP</sub> channels. Our goal was to study the interactions between rapamycin and RyR2 in hypoxic heart cultures in order to elucidate the protective mechanism induced by rapamycin. Heart cultures were exposed to 90 min hypoxia and reoxygenation. Rapamycin (10 μM) and ryanodine (2 μM) attenuated by 40-50% LDH or CK leakage from cardiomyocytes that were subjected to hypoxia and reoxygenation. Ryanodine (100 μM, a concentration that closes the channels) chelerythrine (2 μM -PKC inhibitor) abolished the protective effect of rapamycin, indicating that opening of ryanodine channels are involved in the protective mechanism of rapamycin against hypoxia. Desmin immunostaining and MTT measurements confirmed the result of cardioprotection. In order to study the mechanism of cardioprotective effect of rapamycin, [Ca<sup>2+</sup>]<sub>i</sub> was recorded in cells that were loaded with indo-1. Fluorescent ratio of 410/490 nm was measured. Rapamycin caused [Ca<sup>2+</sup>]<sub>i</sub> elevation by about 20%, which was accompanied with inhibition of spontaneous contractility. This elevation of [Ca<sup>2+</sup>]<sub>i</sub> and inhibition of contraction lasted as long as rapamycin remained in the culture dish. Caffeine caused the release of Ca<sup>2+</sup> from the SR. However, if caffeine was given following rapamycin then it did not cause [Ca<sup>2+</sup>]<sub>i</sub> release, probably because of SR depletion of Ca<sup>2+</sup> by rapamycin. Pretreatment with ryanodine (100 μM), prevented rapamycin-induced [Ca<sup>2+</sup>]<sub>i</sub> release. Conclusion: Rapamycin protects heart cultures against hypoxia via opening of ryanodine receptors, elevating of cytosolic [Ca<sup>2+</sup>]<sub>i</sub> and activating PKC.

## **Bone Marrow from Exercise Trained Diabetic Rats Induces Angiogenesis in the Mice Ischemic Hind Limb**

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The prevalence of cardiovascular diseases increases with age and moreover in diabetic patients and it is associated with reduced angiogenesis potency. **Purpose:** To investigate the capability of exercise in diabetic aged rats to induce angiogenesis in mice hind limb ischemia following bone marrow (BM) transplantation. **Methods:** One year old diabetic (Streptozotocine) and non diabetic SD male rats (n=22) were assigned to 2 weeks of exercise using voluntary activity wheel (Ex&Diab) or remained sedentary (Sed; Sed&Diab). There after, whole BM was aspirated and transplanted to the center of the hind limb ischemia ( $0.3 \times 10^6$  cells in 2 injections) of nude female mice 3 days after inducing the ischemia. Mice kept 2 weeks until sacrificed. Limb perfusion was measured with Laser Doppler on day 0, 7, and 14. Upon sacrifice, the muscle tissue was removed and stained with BS-1 lectin. **Results:** Aged exercise rats accumulated on average  $164 \pm 100$  meters/day while aged Ex&Diab rats accumulated  $60 \pm 17$  meters/day,  $p=0.03$ . Limb function showed an  $80\% \pm 14\%$  recovery in the Ex&Diab BM transplanted mice compared with a  $88\% \pm 9.7\%$  recovery in the Sed&Diab mice ( $p=NS$ ). Capillary number was significantly higher in the Ex&Diab BM transplanted mice compared with their sedentary counterpart ( $p=0.0373$ ) and it was correlated with improved tissue perfusion ( $51.1\% \pm 8.6\%$  vs.  $37.4\% \pm 5.7\%$ , for Ex&Diab vs. Sed&Diab respectively,  $p=0.031$ ). **Conclusions:** Exercise training stimulates BM of aged, diabetic rats which demonstrated angiogenic capacity after transplanted to hindlimb ischemia in mice. Our preliminary findings emphasize the role of exercise on bone marrow regeneration in advanced age and with diabetes.

## **The Molecular Mechanisms Responsible for the Divergent Regulation of Cytokine Secretion by Macrophages after Binding Hb-Hp1 and Hb-Hp 2 to CD163**

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We have recently demonstrated that the haptoglobin 2-2 genotype is associated with an increased risk for diabetic cardiovascular disease. In addition to serving as an antioxidant it has been proposed that Haptoglobin, as mediated through the CD163 receptor, may also have an immunomodulatory function.

In this work, we sought to determine if the protein products of the two haptoglobin alleles differed in their ability to modulate the cytokine profile produced by macrophages in response to the haptoglobin-hemoglobin complex. Human PBMCs were cultured in the presence of complexes formed by the protein products with hemoglobin. We found that the haptoglobin 1-hemoglobin complex stimulated the secretion of significantly more Il-6 and Il-10 than the haptoglobin 2 -hemoglobin complex, and that the release of these cytokines is dependent on the binding of the haptoglobin-hemoglobin complex to the CD163 receptor.

Studies using specific kinase inhibitors have revealed that both CK2 and PKC are involved in the CD163 signaling mechanism that leads to increase in cytokine production. We found that there is no significant difference in the ratio of the amount of CD163/casein kinase 2 $\alpha$  or  $\beta$  associated with CD163 between cells that were or were not stimulated with Hp-Hb complex. However we found that binding of Hp1-1:Hb result in a significant increase in CK2 activity associated CD163 compare to Hp2-2:Hb. We conclude that Hp1-1:Hb increased cytokine production compare to Hp2-2:Hb due to increase in the activity of of CK2. We also showed that phosphorylation of CK2 is critical for its increase in specific activity.

## **Circulating Apoptotic Progenitor Cells in Congestive Heart Failure**

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**Background:** Circulating CD34<sup>+</sup> endothelial progenitor cells (EPCs) are increased in conditions associated with ischemia and can potentially support angiogenesis and vasculogenesis. EPC levels were found to correlate positively with NYHA level and all-cause mortality in congestive heart failure (CHF). Recently, we identified a novel population of apoptotic progenitor cells which was elevated in patients with acute coronary syndrome (ACS).

**Aims:** we sought to determine whether apoptotic progenitor cells are elevated in patients with heart failure, similarly to ACS patients. In so doing, we considered early, reversible apoptotic CD34 cells and late, irreversible apoptotic progenitors, whose plasma membrane is no longer intact and thus represent necrotic cells.

**Methods:** Peripheral blood mononuclear cells were isolated by Ficoll density-gradient from 58 patients with various degrees of heart failure and 26 healthy controls. Apoptosis in progenitor CD34<sup>+</sup> cells was assessed using the Annexin V-PE/PI detection kit, and FACS analysis was performed with triple staining for CD34, annexin-V and propidium iodide. The percentage of early and late apoptotic progenitor cells was determined in the subject groups and was correlated with clinical characteristics.

**Results:** There was no significant difference in total CD34<sup>+</sup> cells or early apoptotic progenitors between healthy subjects and CHF patients ( $p=0.326$ ) or between severe vs mild/moderate CHF groups ( $p=0.544$ ). We found an elevated number of late apoptotic progenitors in the severe CHF group compared with the mild/moderate CHF group ( $p=0.03$ ). There was also an inverse correlation between late apoptotic progenitors and ejection fraction ( $r = -0.252$ ,  $p=0.028$ ) as well as a positive association with NYHA class ( $r = 0.223$ ,  $p=0.046$ ).

**Conclusions:** In the interplay between cytokines enhancing progenitor cell mobilization and those precipitating their apoptosis, our results could support the hypothesis that increasing severity of heart failure shifts the balance towards enhanced progenitor cell apoptosis. The lower the ejection fraction, the poorer the forward flow, which may increase tissue ischemia and endothelial damage. Therefore, apoptotic progenitor cells ought to be evaluated in future studies as a potential predictive biomarker in CHF.

## **Altered Hemostasis of Naturally Occurring Regulatory T Cells in Patients with Congestive Heart Failure.**

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*Background:* Patients with congestive heart failure (CHF) have been shown to exhibit dysregulation of the immune system. Naturally occurring CD4+CD25+Foxp3+ regulatory T cells (Tregs) are a subpopulation of lymphocytes which are thought to play a significant role in regulation of the immune system. Their number and function is compromised in certain disorders involving the immune system such as SLE and MS and in acute coronary syndrome. We hypothesized that the number of Tregs in patients with CHF will differ from that of healthy subjects.

*Methods:* Peripheral blood mononuclear cells were isolated using Ficoll density gradient and triple-stained with antibodies to CD4, CD25 and Foxp3. The number of Tregs was evaluated by a Fluorescence activated cell sorter (FACS).

*Results:* 55 patients with CHF, including 46 with coronary artery disease, and 28 healthy subjects were examined. The number of CD4+CD25+Foxp3+ cells was significantly higher in the CHF group in comparison with the control group ( $3.07\% \pm 1.04$  &  $1.71\% \pm 0.56$  respectively, age matched P value= 0.002). Subgroup analysis showed that Treg numbers in patients with CAD and CHF were significantly higher in comparison with non-ischemic CHF patients ( $3.26\% \pm 0.97$  &  $2.12\% \pm 0.84$  respectively, age matched P value= 0.019).

*Conclusions:* In patients with CHF the number of CD4+CD25+Foxp3+ Tregs is increased. This may further our understanding of the involvement of the immune system in CHF.