Comorbidities Convey Important Prognostic Information for Post MI Risk Stratification

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

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

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

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

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

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

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

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

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

Conclusion: Among community patients with MI, low SES is related to higher risk profile and poorer treatment. Low income is associated with a large increase in mortality risk when accompanied by low education, suggesting a double jeopardy phenomenon.
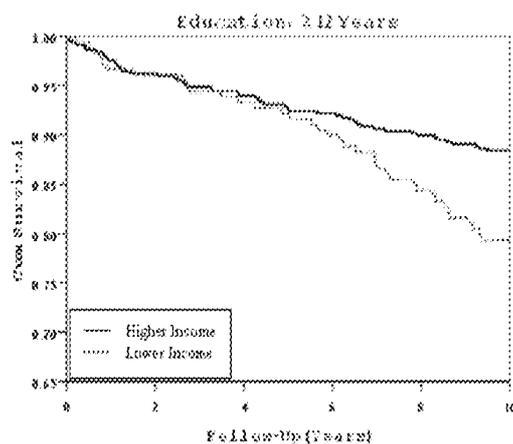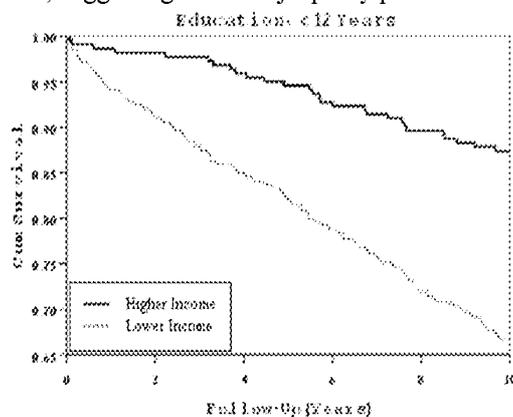
Influence of the Socio-Economic Level on the Characteristics and Outcomes of Patients Treated with Percutaneous Coronary Interventions

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

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

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

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

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

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

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

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

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

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

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

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

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Background: Supervised exercise training is an important modality in preventing recurrent cardiac events. Today many patients come to cardiac rehabilitation after successful angioplasty, with good functional capacity, and with low risk on exercise testing. These individuals can initiate exercise outside of a rehabilitation center but the need exists for follow up and monitoring. RPE 13 has been advocated as a useful and validated surrogate for monitoring individuals during exercise yet the number of studies in cardiac patients is limited. Documenting improvement over time using RPE 13 facilitates patients' self evaluation.

Methods: All patients were assessed on entry and at follow up to our cardiac rehabilitation center using a branching, symptom limited stress test. Borg ratings were recorded and blood pressure, heart rate responses, and mets at both RPE 13 and RPE 19 were entered into our database. Rates of improvement were calculated using both max mets (RPE 19) and mets at RPE 13. Data was assessed on 2785 patients for whom valid data was available.

Results:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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Background: There is little experience in pregnant patientis with previously diagnosed dilated cardiomyopathy (DCM). These patients are usually advised firmly against further pregnancies.

Study aim: To exam the ussfulness of serial echocardiographic follow-up and plasma N-Terminal Pro-B-type natruiretic peptide (NT-ProBNP)evels in the management of pregnant women with preexisting DCM.

Methods: We prospectevlly enrolled pregnant women with known DCM or diagnosed in the first trimester of pregnancy. Demographic, clinical caractheristics, serial echocardiographic studies and plasma ProBNP levels at base line, 30 weeks pregnancy, one and 90 day post-partum were prospectively collected.

Results: Between June 2004 to March 2007 we enrolled 7 women fulfilling the study criteria. The mean age was 33.5 ± 3.3 years, (24 to 41), 6 caucasian, four (57%) primagravidas, two of them became pregnant after assited reproduction technique and multiple past abortions. There was a high prevalence of hypothyroidism (57%) and only one cases of diabetes mellitus, chronic hypertension, and rheumatic arthritis.

The delivery and post-partum were complicated in three patients (42%): acute heart failure resolved conservatively in two, and one with major pulmonary embolism.

The left ventricular ejection fraction (LVEF) was stable throughout the pregnancy (baseline 35% ±2.8,

30 weeks 33% ±2.9) and post-partum (1 day 35% ±2.8, 90 days 34% ±3.1). Similar stable behavior was observed regarding left ventricular dimensions, LVESD - 43.3 ±2.7 and LVEDD - 57.3±3.3 at baseline compared with 44.1±3.1 and 58.7±3.1 respectively. Two patients had demostrated good myocardial contraction reserve in pre-gestational dobutamine stress echocardiography.

The NT-ProBNP levels rised significantly in the early post-partum in all 3 patients with complications. In one additional patient the NT-ProBNP showed similar behaivor but without clinical event. In the remaining 3 patients the NT-ProBNP levels were in the upper limit range and increased only slightly one day post-partum and decreased 90 days later.

Conclusion: Serial Pro NT-BNP levels, as opposed to echocardiography, may be a better clinical tool in monitoring and management of pregnant women with preexisting DCM. An early rise in NT-ProBNP level appears to predict the occurrence of adverse events.

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

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

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

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

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

Table (%):

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

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

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