08:30 - 10:30 S5 - Epidemiology, Prevention & Rehabilitation Hall F

Chairs: **A. Caspi**
Y. Henkin

08:30 **Heart Rate Recovery Immediately after Exercise is a Predictor of Pre-clinical Coronary Atheroma in Asymptomatic Type 2 Diabetics**
I. Dobrecky-Mery, T. Gaspar, M. Azencot, N. Peled, N. Yaniv, L. Rozenblum, P. Vishnyak, S. Facher Eldeen, B.S. Lewis, D.A. Halon
Haifa

08:45 **Discontinuation of Vitamin E Results in a Dramatic Increase in the Incidence of Myocardial Infarction and a Rapid Deterioration of HDL Function in Individuals with Diabetes Mellitus and the Hp 2-2 Genotype**
S. Blum, U. Milman, C. Shapira, L. Andrew
Haifa

09:00 **Adherence with Guidelines for Secondary Prevention of Dyslipidemia in Primary Care – Where Is the Bottleneck?**
G. Vashitz, J. Meyer, Y. Parmet, R. Peleg, D. Goldfarb, H. Gilutz
Beer-Sheva

09:15 **Decreased Renal Function Associated with Incident Adverse Cardiovascular Outcomes in Patients with Acute Coronary Syndromes**
D. Pereg [1], M. Benderly [2], S. Behar [2], M. Mosseri [1]
[1] Kfar-Saba, [2] Tel Hashomer

09:30 **Long-Term Survival after First Acute Myocardial Infarction is Strongly Modulated by Smoking Status**
Y. Gerber, L. Rosen, Y. Benyamini, U. Goldbourt, Y. Drory
Tel Aviv

09:45 **Dissatisfaction with Married Life is Related Dose-Response to Increased CHD and Stroke Mortality and is Associated with Marked Reduction in Probability of Surviving Past age 80 years**
U. Goldbourt
Tel Aviv

10:00 **Relation between Red Blood Cell Distribution Width and Mortality in Patients With Acute Myocardial Infarction**
S. Dabbah, H. Hammerman, M. Kapeliovich, R. Beyar, W. Markiewicz, D. Aronson
Haifa

10:15 **Possible Effect Modification of History of MI on the Association Between Body Mass Index and Long Term Mortality**
M. Benderly [1,2], V. Boyko [1], U. Goldbourt [1,2]
[1] Tel Hashomer, [2] Tel Aviv

Heart Rate Recovery Immediately after Exercise is a Predictor of Pre-clinical Coronary Atheroma in Asymptomatic Type 2 Diabetics

Idit Dobrecky-Mery [1], Tamar Gaspar [2], Mali Azencot [1], Nathan Peled [2], Nisan Yaniv [1], Lena Rozenblum [1], Polyna Vishnyak [1], Saeed Facher Eldeen [3], Basil S Lewis [1], David A Halon [1]

[1] Cardiovascular Medicine, Preventive Cardiology, Carmel Medical Center, [2] Radiology, Cardiac Imaging, Carmel Medical Center, [3] Diabetic Clinic, Endocrinology, Clalit Community Health Services, Haifa, Israel

Background: Impaired heart rate recovery (HRR) after exercise is a function of vagal reactivation and an independent predictor of long-term mortality and in type 2 diabetics a marker of autonomic dysfunction. We examined the hypothesis that prevalence of pre-clinical coronary atheroma will be increased in diabetics with impaired HRR by analyzing data from a cohort of asymptomatic diabetics undergoing 64 channel contrast enhanced coronary CT angiography (CCTA) in the context of an ongoing prospective outcomes trial.

Methods: Symptom limited treadmill exercise was performed in 496 pts with DM and no history of CAD (age 63.2±5.4 yr, 55.8% women, duration of DM 9.9±7.6 yr, 25.5% insulin treated). HRR at 1 minute (HRR1) was calculated as peak HR - HR at 1 minute and chronotropic response as ratio of peak HR - resting HR to HR reserve [(220-age)-HR at rest].

Results: HRR1 predicted multi-vessel coronary atheroma on CCTA (Table). Findings were similar after adjustment for chronotropic response and were independent of Framingham but not of UK Prospective Diabetic Study (UKPDS) risk score (Table). Unadjusted findings were similar for prediction of significant luminal stenosis (>50%) (OR 0.8, 95%CI .67-.96, p=0.02) but were not independent of Framingham or UKPDS risk scores.

Heart rate recovery & multivessel plaque

	Odds ratio*	95% CI*	p
Univariate			
HRR1	0.8	.71-.92	.002
Adjusted for chronotropic response (CR)			
HRR1	.78	.68-.89	.001
CR	1.7	.72-3.6	.2
Adjusted for Framingham risk			
HRR1	.82	.72-.95	.01
Framingham	1.4	1.2-1.6	<0.0001
Adjusted for UKPDS risk			
HRR1	.86	.75-1.01	0.057
UKPDS	1.6	1.3-1.8	<0.0001

* Per 10 beats HRR1, 10% Framingham or 10% UKPDS 10 year risk

Conclusions: In asymptomatic type 2 diabetics 1. Autonomic dysfunction, as exemplified by impaired HRR post exercise, predicted presence of multi-vessel coronary atheroma on 64 slice CCTA independently of Framingham risk score. 2. UKPDS risk score was strongest predictor of multi-vessel coronary atheroma and of coronary luminal stenosis.

Discontinuation of Vitamin E Results in a Dramatic Increase in the Incidence of Myocardial Infarction and a Rapid Deterioration of HDL Function in Individuals with Diabetes Mellitus and the Hp 2-2 Genotype

Shany Blum [1], Uzi Milman [2], Chen Shapira [2], Levy Andrew [1]

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Background: Individuals with Hp 2-2 genotype and DM have a 2-5 fold increased incidence of CVD compared to individuals without Hp 2-2 genotype. We have shown in the ICARE study that vitamin E decreased this incidence by 50% comparing placebo in Hp 2-2 DM patients, and this may be due to severe HDL dysfunction in these individuals.

Methods: We prospectively determined the incidence of MI in ICARE participants after vitamin E was discontinued. We assessed HDL function after treatment with vitamin E or placebo in a crossover design in Hp 2-2 DM individuals.

Results: In individuals treated in ICARE with vitamin E the incidence of MI increased dramatically in the period after ICARE was terminated and vitamin E withdrawn (0.4% on vit. E vs. 1.8% off vit. E, p=0.03). In the 15 month interval after ICARE was terminated the incidence of MI was not significantly different in individuals who had received vitamin E vs. placebo (1.8% former vit. E group vs. 1.7% former placebo group, p=0.9). HDL function was significantly improved in Hp 2-2 individuals by vitamin E. However, 2 months after vitamin E was withdrawn HDL function had deteriorated to its level of dysfunction prior to the initiation of vitamin E.

Conclusions: Discontinuation of vitamin E is associated with an abrupt increase in the incidence of MI and a deterioration of HDL function in Hp 2-2 DM individuals. These studies support the pharmacogenomic application of the Hp genotype to determine whether an individual with DM should receive vitamin E.

Adherence with Guidelines for Secondary Prevention of Dyslipidemia in Primary Care – Where Is the Bottleneck?

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Background: There is a wide therapeutic gap between evidence-based guidelines for atherosclerosis prevention and practice which is primarily attributed to physicians' and patients' adherence.

Objective: To measure physicians' and patients' adherence with guidelines for secondary prevention of dyslipidemia.

Methods: Retrospective data analysis of 11,444 patient-specific prevention reminders that were sent to 95 physicians regarding 5,215 patients over 16 months. Physicians' and patients' adherence was estimated by matching the reminders to physicians' and patients' actions. Adherence was measured both "exactly" (follow reminder precisely) and "broadly" (take other actions).

Results: Physicians' adherence with pharmacotherapy recommendations was low relatively to patients' adherence with the physicians' recommendations (17.1% vs. 72.1%). Physicians adhered more to treatment initiation relative to up-titration (OR=1.56, $p<0.001$), whereas patients tended to adhere less to initiation relative to up-titration (OR=0.20, $p<0.001$). The "exact" adherence was greatest for lipids screenings (47.8%) compared to pharmacotherapy initiations (14.1%), up-titrations (12.1%), and metabolic consultations (5.9%). The "broad" adherence was greatest in up-titrations (91.6%), compared to the metabolic consultations (82.8%), lipids screenings (65.9%) and drug initiations (47.8%).

Conclusions: The "bottleneck" in pharmacotherapy was apparently physicians' adherence with the guidelines rather than patients' adherence with the treatments. The physicians were more compliant with treatment initiation, whereas the patients were more compliant with up-titrations. The physicians tended to follow the guideline "exactly" in simple clinical tasks, and follow it "broadly" in more complex tasks. Interventions to improve adherence should apparently be targeted at the physicians, in parallel to improving patients' adherence.

Decreased Renal Function Associated with Incident Adverse Cardiovascular Outcomes in Patients with Acute Coronary Syndromes

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Background: While renal dysfunction is associated with increased cardiovascular mortality following acute coronary syndromes (ACS) it is not clear whether this association exists with other major cardiovascular events and whether it is linear.

Methods: Included were 1744 patients with ACS enrolled in the 2008 ACS Israeli Survey (ACSIS). Estimated glomerular filtration rate (eGFR) was calculated using the modified diet in renal disease equation. Patients were divided into 5 groups according to the guidelines of the national kidney foundation (<45, intervals of 15 and>90 ml/minute/1.73m^2). Thirty-day composite of death, reinfarction and recurrent angina (DIA) was compared between groups.

Results: The average eGFR in all patients was 73.4±27.1 (3.4-169) ml/minute/1.73m^2. The prevalence of co-existing risk factors, prior cardiovascular disease and Killip class>1 was higher among patients with reduced eGFR. These patients however were less treated with ACE-inhibitors, angiotensin-receptor blockers, IIb-IIIa antagonists and coronary revascularization. After age-adjustment, there was a progressive increase in 30-day composite of DIA with declining eGFR (OR=3.59, 95% CI 2.18-5.99, for comparison between the highest and lowest eGFR groups). This association persisted after further adjustments for gender, diabetes mellitus, hypertension, smoking, dyslipidemia, prior cardiovascular disease, killip>1 and STEMI (OR=3.24, 95% CI 1.93-5.53). When eGFR was used as a continuous variable, the risk for 30-day composite of DIA increased by 2% for any 1 ml/min/1.73m^2 decrease in eGFR, (OR 1.02, 95% CI 1.008-1.03)

Conclusions: Renal dysfunction in ACS patients is associated with an increased risk for combined death, re-infarction and recurrent angina. This risk increases linearly with declining eGFR.

Long-Term Survival after First Acute Myocardial Infarction is Strongly Modulated by Smoking Status

Yariv Gerber [1], Laura Rosen [2], Yael Benyamini [3], Uri Goldbourt [1], Yaacov Drory [4]

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Background: Quitting smoking has been shown to improve prognosis after acute myocardial infarction (AMI). However, longitudinal data derived from community studies, with repeated assessment of smoking, are lacking. We compared survival post-AMI of non-smokers, pre-AMI quitters, post-AMI quitters, and persistent smokers.

Methods and Results: Consecutive patients aged ≤65 years discharged from all hospitals in central Israel after initial AMI between February 1992 and February 1993 were enrolled. Self-reported data on smoking were recorded at the index AMI and after 3-6 months, 1-2 years, and 5 years, with subsequent mortality follow-up lasting through December 2005 (median 8 years, 1,345 participants, 258 deaths). The age-standardized mortality rates (per 1,000 person-years) were 21.1 for non-smokers (n=358), 17.1 for pre-AMI quitters (n=277), 28.3 for post-AMI quitters (n=352), and 40.9 for persistent smokers (n=358). For pre-AMI quitters, the median (interquartile range) abstinence duration at the index AMI was 10 (5-18) years. In a proportional hazards model adjusted for age, sex, socioeconomic measures, cardiovascular risk factors, comorbidity, and disease severity indicators, the hazard ratios (HRs) for mortality were 0.48 (95% confidence interval (CI): 0.34-0.69) for non-smokers, 0.44 (95% CI: 0.30-0.65) for pre-AMI quitters, and 0.68 (95% CI: 0.49-0.94) for post-AMI quitters, compared with persistent smokers. Among ex-smokers, with further adjustment for age at quitting, the HR associated with pre- vs. post-AMI quitting was 0.51 (95% CI: 0.27-0.96). Among persistent smokers, after multivariable adjustment including pre-AMI smoking quantity, each reduction of 5 cigarettes smoked daily after the AMI was associated with a 12% decline in mortality (P=0.018).

Conclusions: Smoking cessation both before and after AMI improves survival. Quitting before initial AMI confers greater benefit. Among persistent smokers, reducing quantity appears to be protective.

Dissatisfaction with Married Life is Related Dose-Response to Increased CHD and Stroke Mortality and is Associated with Marked Reduction in Probability of Surviving Past age 80 years

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Rationale and design. Despite evidence accumulating over long years concerning possible roles of personal issues in affecting the health of vascular system, there is no unequivocal agreement on the exact parameters and magnitudes representing such association. We conducted an extensive study of demographic and personal, educational, anthropometric, biochemical and clinical variables among civil servants and municipal employees in 1963-68. Cause-specific mortality follow- up through 1986 permits analyzing of the latter as a function of those parameters. All-cause mortality is available through 2006, permitting ascertainment of survival past age 80- for every participant in the study.

Methods. Every subject responded in 1965 (N=9343) whether he considered his marriage successful, quite successful, not so successful or unsuccessful. 398 were unmarried. Mortality was ascertaining by matching with the national death registry using eth national ID and verifying names. Underlying cause of death was determined from ICD-8, ICD-9 and ICD-10 coding with a re-ascertainment and editing process at the central Bureau of Statistics.

Results. Mortality per 10,000 person years increased, with increasing dissatisfaction" from "quite successful" to unsuccessful marriage, for all-cause, CHD and stroke mortality (Table). Adjusting for age indicated Cox PH -estimated hazard ratios (HR) of 1.08 95% CI 0.95-1,24), 1.09 (0.86-1.38 and 1.16 (0.82-1.62) for the quite-, not quite- and unsuccessful marriage for death of CHD; 0.95 , 1.16 and 2.06 (1.31.-3.23) respectively for stroke mortality; and 1.02, 10.07 and 1.35 (1.13-1.61) for all-cause 23-year mortalities (p for trend<.01) for all endpoints. Further, 38% of those reporting unsuccessful marriage survived past age 80 as compared to 46-37% in the other three "success categories". In logistic regression the odds of surviving past age 80 years were 1.01, 0.97 and 0.69 (0.54-0-87) for the above three categories. In all of the above analyses, further adjustment for smoking, Socio-economic status, blood pressure, diabetes, socioeconomic status and serum cholesterol did not alter the results materially.

Conclusion. Through mechanism that require study unhappy marriage shows association with long-term mortality from vascular causes and hampers the aspiration of male working males to survive past age 80.

T a b l e : Mortality rates by reported success of marriage

Marriage successful?	CHD mortality	Stroke Mortality	All-cause Mortality
Very successful	51.9	17.5	164
Quite successful	52.2	15.1	155
Not so successful	53.5	18.7	165
Very successful	59.0	35.1	217

Relation between Red Blood Cell Distribution Width and Mortality in Patients With Acute Myocardial Infarction

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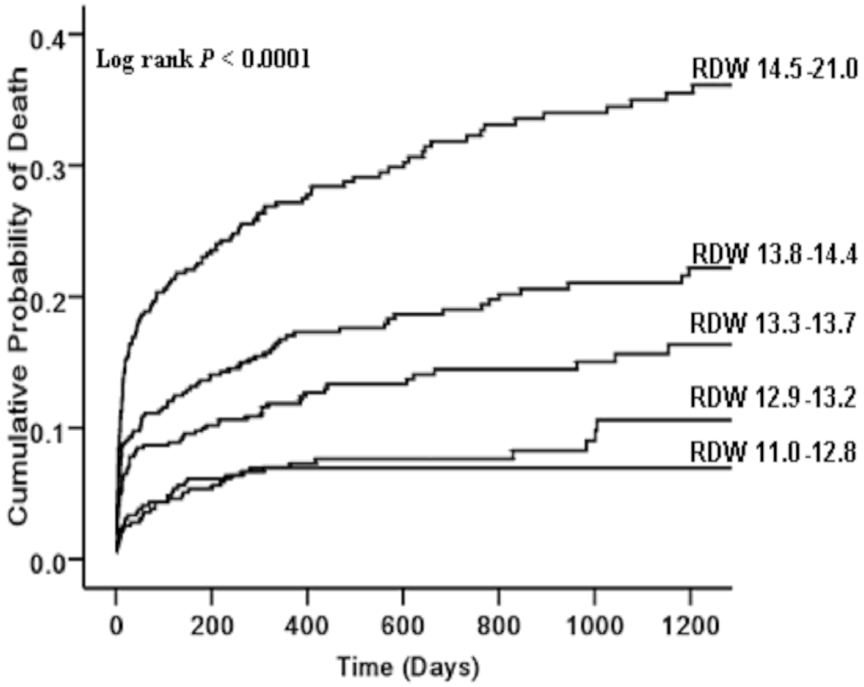
Background: Increased red blood cell distribution width (RDW), a measure of the variability in size of the circulating erythrocytes, has been shown to be associated with adverse outcomes in patients (pts) with heart failure and with coronary disease. However, there is no information regarding the prognostic significance of RDW in the acute phase of acute myocardial infarction (AMI).

Methods: We performed a post hoc analysis of data from a prospective study. Baseline RDW was measured in 2095 pts admitted with AMI and followed for a median of 19 months. We used Cox proportional hazards models to examine the association between quintiles of RDW and all-cause mortality, adjusting for the Global Registry of Acute Coronary Events (GRACE) risk score and baseline hemoglobin.

Results: During the follow period 362 pts died. There was a graded positive association between increased RDW and mortality across quintiles of RDW (Figure). In a Cox model, the adjusted HRs of pts with RDW in the 5th, 4th, 3rd, and 2nd RDW quintile compared with pts in the 1st quintile were 1.0 [95% CI, 0.6 to 1.7], 1.5 [95% CI, 1.0-2.3], 1.9 [95% CI, 1.2 to 2.9] and 2.7 [95% CI, 1.8 to 4.0], respectively (P for trend < 0.0001). The association between increased RDW and mortality remained highly significant in sensitivity analyses that excluded pts with anemia (Hb < 12 g/dl) and pts with abnormally low (<82 μm3) or high (>96 μm3) mean corpuscular volume.

Conclusions: There is a graded independent relation between increased RDW and the risk of death in pts with AMI.



Possible Effect Modification of History of MI on the Association Between Body Mass Index and Long Term Mortality

Michal Benderly [1,2], Valentina Boyko [1], Uri Goldbourt [1,2]

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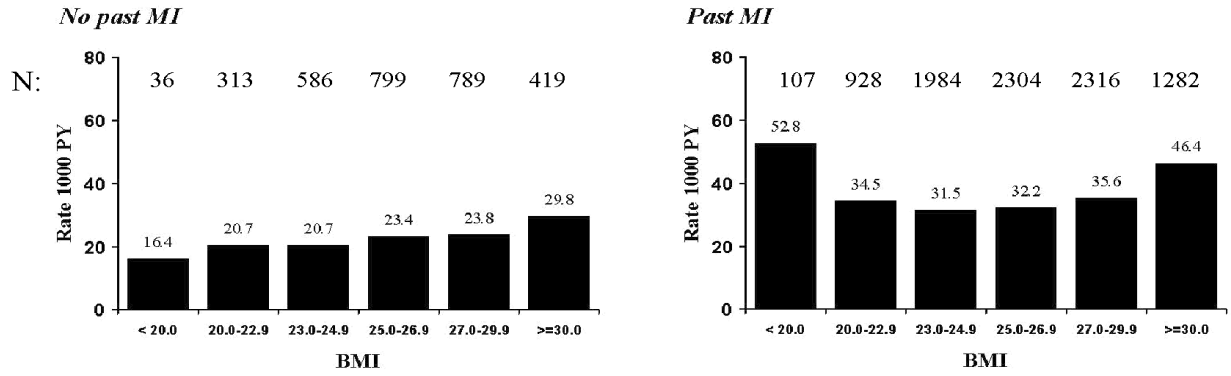
Reports among coronary heart disease (CHD) patients regarding mortality risk are inconsistent and range between a linear association, a U or J shaped one or even an inverse association ("obesity paradox"). We shought to study the long-term association between body mass index (BMI), and mortality and possible interaction with disease history among CHD patients.

Methods: Data on BMI and mortality were available for 12,466 male CHD patients (past MI or angina) screened for participation in the BIP study.

Results: The majority of patients (74%) had BMI between 23.0 and 29.9. Hypertension, diabetes, smoking, total cholesterol, triglycerides, HDL-C, were linearly related to BMI. Frequency of prior MI (overall 75%) did not significantly differ by BMI groups. The figure depicts age adjusted all-cause mortality rate/1000 person-year through follow-up median of 12 years.



In each BMI category, mortality risk was higher among MI survivors. History of MI seems to modify the association of BMI and mortality, which was U shaped among MI survivors, and linear among patients with only angina. The differences between patients with history of MI or without it persisted following adjustment for age, diabetes, peripheral vascular disease, smoking, COPD, cholesterol and systolic blood pressure.

Conclusion: Mortality risk associated with BMI differs among CHD patients according to history of MI. Further studies are needed to elucidate the nature of this observed interaction.