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
All	**128(25%)**	**98(19%)**	**279 (54%)**	**14(24%)**	**519**

Comparisons	p value
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 Quantitive 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.
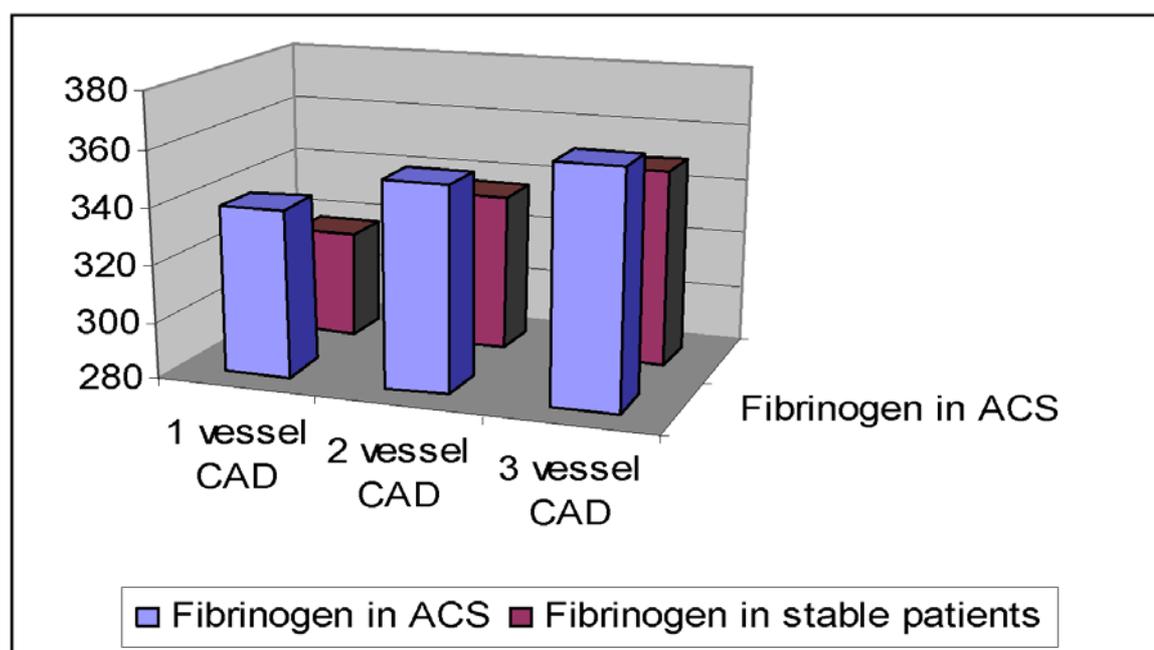
Conclusion

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 $r=0.06$ $p=0.018$, $r=0.247$ $p<001$, $r=0.255$ $p<0.001$ 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, te 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 ≥90 cm for men and ≥85 cm for women and triglycerides levels of ≥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	
	63	107	N
P<0.001	20.6%)13 (	61 (57%)	Total cholesterol >200mg/L
P<0.001	50 (79.4%)	46 (43%)	Total cholesterol <200mg/L

When LDL cholesterol was evaluated similar findings were obtained:

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

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

	Rest of the pts	Soft plaques	
	93	77	N
P<0.001	50(53.8%)	65(84.4%)	LDL cholesterol>100mg/L
P<0.001	43(46.2%)	12(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±18 vs 126±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±7% vs 11±6%, p<0.01 and 17±8% vs 16±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±25 vs 84±14%,p<0.01 and 45±32 vs 84±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 hypertrigliceridemia). 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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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$\pm$105 as compared to 256 ± 122 days in Jews ($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