Both Lean Hypertensive and Frankly Obese CHD Patients are at Increased Risk for Long-term Mortality

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Background. The issue of excess weight in apparently healthy men and women as a risk factor for disease and mortality has gained increasing interest. Less is know about the significance of weight in coronary heart disease (CHD) patients. This association may differ according to hypertension status.

Patients and Methods. We used data from a screening of 15,700 CHD patients, screened for eligibility to participate in the secondary prevention trial Bezafibrate Infarction prevention (BIP). Follow-up lasted from 1990/2 to 1999, over a mean period of 8 yrs. Mortality was obtained by matching with the National Population registry and incident stroke leading to hospitalization was assessed in a special project. Groups of relative weight were defined as **1** [lean patients] for body mass index (BMI) below 20 Kg/squared meter, **2** for 20-22.99, **3** for 23-24.99, **4** for 25-26.99, **5** for 27-29.99 and **6** for >30 Kg/SqM meters [obese patients]. Multivariate analysis using a proportional hazards model yielded hazard ratio (HR) estimates controlling for age, sex, diabetes, hypertension and MI history.

Results. Among 9520 patients who were normotensive at entry, crude mortality rates during follow-up were 19, 19, 16, 17, 17, and 19% in BMI groups 1 to 6, respectively. Among 4630 hypertensive patients the corresponding rates were 30, 23, 20, 16, 19 and 24%, respectively. These findings, indicating that the "desirable weight" as well as the "mildly overweight" CHD patients (25-27 Kg/SqM) do better were substantiated by a multivariate analysis which produced the following adjusted HRs: 0.87, 0.70, 0.71, 0.76 and 0.93 for groups 2 to 6, with the leanest patients as the reference. Specifically for women, the "mild overweight" group enjoyed the longest survival.

Comments. Lean and obese CHD patients fared worse than "desirable" and so-called "mildly overweight" counterparts over 8 years after being assessed for eligibility in a trial of stable CHD, and the combination of leanness and hypertension appeared particularly undesirable, adding to the accumulating doubts concerning a universal recommendation to maintain weights yielding BMI below 25 Kg/SqM. Dietary and lifestyle advice should be weighed against these and similar findings**.** Further research needs to be pursued examining how these associations interact with patients' ages and previous smoking habits.

Elevated C-Reactive Protein Levels Predict Poorer Cognitive Function Among Coronary Heart Disease Patients

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Background- Chronic low-grade inflammation may be a risk factor for dementia in elderly persons. Our aim was to test the hypothesis that elevated concentrations of high sensitivity CRP (hsCRP) predict poorer cognitive function and in-particular executive function among patients with CHD.

Methods- A subgroup of CHD patients who previously participated in a trial of lipid modification (BIP trial) was assessed. CRP was measured by a high-sensitivity assay from thawed frozen (-70^{0}c) plasma samples collected at baseline. Cognitive scores were assessed more than 10 years later, using a validated set of computerized cognitive tests (Mindstreams Computerized Cognitive Battery; computing index scores summarizing performance in each cognitive domain and a global cognitive score). We compared means of cognitive scores normalized to age and education, between patients in the highest CRP tertile (CRP ≥3.6mg/L) and patients in the lower tertiles.

Results- Among 346 patients (mean age 72±6 yrs, 95% males, 19% diabetics) CRP levels at baseline were inversely correlated with both the global cognitive score (p=0.04) and with executive functions (p=0.02). The mean global and executive scores were lower among patients in the upper CRP tertile as compared to those in the lower two tertiles (91.6±11.3 vs. 95.4±11.3; p=0.004 and 93.3±11.5 vs. 97.9±12.4; p=0.001, respectively).

Conclusions- Increased CRP levels are associated with cognitive impairment and poorer executive functions among CHD patients. These results support the hypothesis that chronic low-grade inflammation may be involved in vascular cognitive impairment.

The Effect of Secondary Prevention on Recurrent MI; Results from the 2004 and 2006 ACSIS Survey

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Background:
The preventive effects of cardiovascular drugs after an acute myocardial infarction (AMI) are well established, but little is known concerning the effect of such secondary prevention on the characteristics of recurrent events. We therefore studied the characteristics of events and the patients who presented with recurrent MI (PMI - Previous MI group), in relation to their secondary prevention medications.

Methods:
Data was summed up from the 2004 and 2006 ACSIS. In the two surveys, there were 1207 PMI patients. This combined group was analyzed according to multiple variables.

Results:
65% of PMI patients were treated prior to admission with 3-4 secondary preventive drugs (platelet inhibitors, beta blockers, angiotensin enzyme inhibitors or statins), 28% with 1-2 drugs and 7% were not treated with any drug. Seven day mortality was 5% for patients with 3-4 drugs, 2% for 1-2 drugs and 0% for the 0 drugs group (P=NS). Thirty day mortality was 6%, 5% and 0%, respectively (P=NS). However, an analysis according to the TIMI score showed that in the high TIMI group, when adjusted for age, diabetes and ST elevations, there was a statistically non-significant opposite trend for lower mortality rates in the 3-4 drugs patients (OR= 0.88, confidence limits 0.49 to 1.61), whereas adjusting for sex, diabetes and ST elevations in the low TIMI group showed no difference in risk of death in patients treated with more or less drugs.

Conclusions:
PMI patients are under-treated with secondary preventive drugs prior to admission. Overall, there is a trend for higher mortality rates in those who are treated with more drugs. However, when adjusted for confounding factors, there is no change in mortality in the low TIMI score patients, and a non significant trend for a reduced death rate for the high TIMI score patients, when treated with more drugs. Thus, the higher risk found in PMI patients treated with more drugs is due to more co-morbidities and risk factors, and not the medical treatment itself.

Low Grade Inflammation in Asymptomatic Healthy Adults During Bouts of Respiratory Tract Infections in the Community: Potential Triggers for Cardiovascular Events

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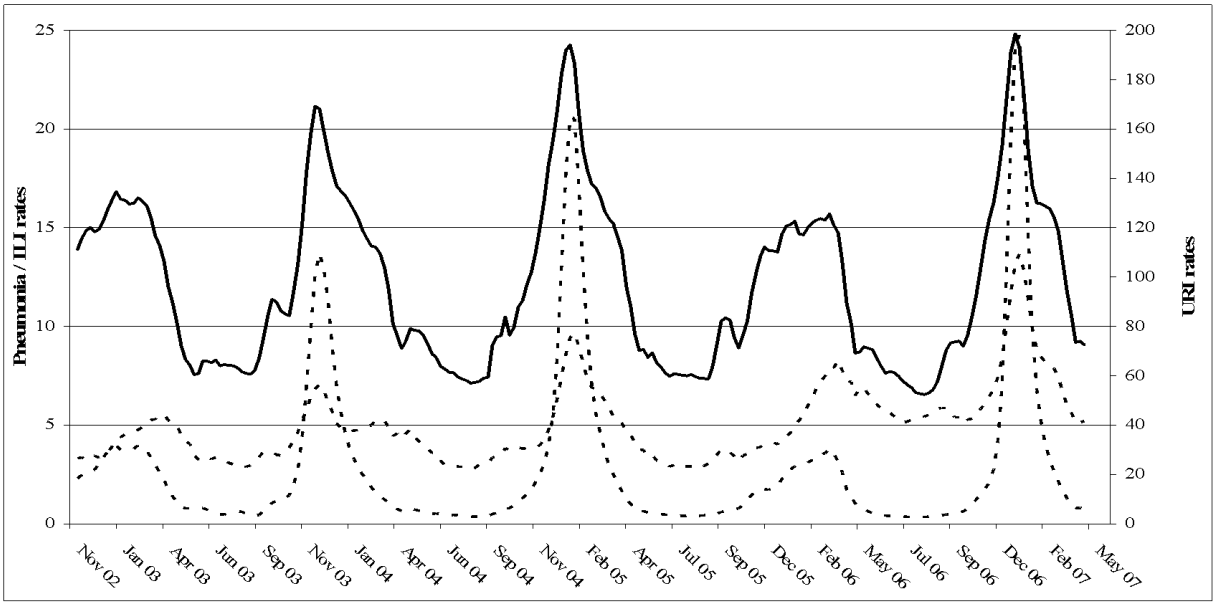
Background: Cardiovascular morbidity and mortality demonstrate a well documented seasonal pattern. We explored the possibility that low grade inflammation is evident in asymptomatic adults during bouts of acute respiratory tract infection/inflammation in the community.

Methods: We examined the concentration of high-sensitivity C-reactive protein (hs-CRP) as well as quantitative fibrinogen in completely asymptomatic adults during a routine screening health program and correlated the results with weekly epidemiological data related to the appearance of acute respiratory tract infection/inflammation in the community (figure 1).

Results: Included were 5315 male and 2795 female at the mean (SD) of 45 (11) years. We demonstrated a statistically significant seasonal variation in the concentrations of hs-CRP and fibrinogen using the cosinor analysis. Following adjustment for a relatively large number of possible confounders, the weekly burden of acute respiratory infection/inflammation had a significant influence on the inflammation-sensitive biomarkers in the asymptomatic cohort. The magnitude of this influence could reach as much as 10% (2%-17%) in hs-CRP concentrations in women and 8.16 (5.44-10.88) mg/dl in fibrinogen concentrations in men.

Conclusion: Changes in the concentrations of two inflammation-sensitive biomarkers can be noted in completely asymptomatic adults at the time of increased burden of acute respiratory tract infection/inflammation in the community. The possibility exists that these inflammatory changes represent occult and asymptomatic infections that could by themselves trigger acute atherothrombotic events.

Respiratory illness rate curves in the community during the time period of the study.



Relation of Exercise Capacity to Sub-Clinical Coronary Artery Disease in Asymptomatic Patients With Type II Diabetes

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Background: Patients with type 2 diabetes mellitus (DM) may have limited exercise capacity (ExC) despite no clinical history of coronary artery disease (CAD). The importance of sub-clinical CAD in determining ExC is unclear. We examined relation of ExC to sub-clinical CAD, defined by 64 slice coronary computed tomographic angiography (CTA), in diabetic subjects with no history of CAD.
Methods: 423 pts (63±5.3 yrs, 56% women) enrolled in an ongoing prospective study of cardiovascular outcomes in asymptomatic subjects with DM, underwent 1) maximal, symptom limited graded treadmill exercise testing to define ExC (in metabolic equivalents [Mets]) and ECG defined, exercise induced, myocardial ischemia and 2) CTA to define presence of significant (>50%) coronary luminal stenosis, non-obstructive coronary atheroma and coronary calcium score.
Results: Determinants of peak exercise capacity differed in men and women. In men coronary plaque was related to duration of exercise but not in women (Table).Duration of DM correlated with duration of exercise in women (r=0.27, p=0.001) but not in men (r=0.09, ns).

Exercise Capacity

	METS(MEN)	P-VALUE	METS (WOMEN)	p-value
Calcium score <median	11.2±2.3		7.8±2.1	
Calcium score >median	9.6±2.6	<0.001	7.3±2.2	ns
Plaque any +	10.1±2.6		7.6±2.1	
Plaque any -	12.2±1.9	<0.001	7.5±2.4	ns
Multi-vessel plaque+	9.8±2.5		7.2±2.1	
Multi-vessel plaque-	11.6±2.3	<0.001	7.8±2.3	0.07
Stenosis+	9.8±2.5		7.1±2.4	
Stenosis-	10.8±2.6	0.06	7.6±2.1	ns
Multi-vessel Stenosis +	9.4 ±2.0		6.7±2.4	
Multi-vessel Stenosis -	10.5±2.6	ns	7.6±2.2	ns

Conclusions: In **men** peak exercise capacity decreased in presence of non-obstructive or obstructive coronary artery disease on CTA but was was unrelated to longer history of diabetes mellitus. In **women** peak exercise capacity was not significantly related to presence of sub-clinical coronary artery disease but correlated inversely with duration of DM.

Combined Assessment of C-Reactive Protein and Uric Acid Levels for Risk Stratification in Coronary Heart Disease Patients

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Background: C-reactive protein (CRP) is an established risk factor for cardiac events in coronary heart disease (CHD) patients. Recently, elevated serum uric acid (SUA) was also suggested to be associated with adverse outcome in this population. We hypothesized that combined assessment of CRP an SUA would provide incremental prognostic information to single marker measurement.

Methods: The risk of major cardiac events (comprising fatal or nonfatal myocardial infarction or sudden cardiac death) during mean follow-up period of 6.2 years was related to increasing tertiles of CRP and SUA levels, in a population of 2966 CHD patients enrolled in the Bezafibrate Infarction Prevention (BIP) trial.

Results: The rate of major cardiac events was directly related to increasing tertiles (1 to 3) of both CRP (11.4%, 14.2%, and 17.3%, respectively; p for trend < 0.001) and SUA (12.6%, 12.9%, and 17.6%, respectively; p for trend = 0.002). However, when combined assessment of the 2 markers was employed, CRP levels were shown to be associated with adverse outcome only in patients with low SUA (Figure 1A), whereas among patients with elevated SUA cardiac event rate was increased at all levels of CRP (Figure 1B). Consistently, in multivariate analysis elevated CRP was independently associated with outcome in patients with low SUA (HR=1.55; p=0.007), but was not a risk factor among patients with elevated SUA (HR=1.04; p=83).

Conclusions: Combined assessment of CRP and SUA improves risk stratification in CHD patients. Patients with elevated SUA exhibit a high risk of cardiac events regardless of CRP levels.

Figure 1: Rate of Cardiac Events by CRP Tertiles