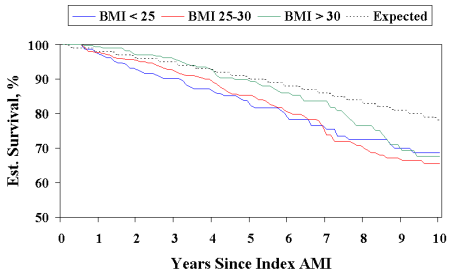
The effects of Carvedilol on myocardial morphology and functional outcome were studied in patients with chronic HM undergoing cardio-vascular bypass grafting (CABG). Nineteen patients (13 males, 62+/-9 years) eligible for CABG due to severe CAD were randomized into two groups: patients in group 1 (n=10) received Carvedilol (25 mg/day), patients in group 2 received placebo (n=9), starting from randomization 7-8 weeks prior to CABG until follow-up 4-6 months postoperatively, in addition to standard antianginous therapy and aspirin. Left ventricular ejection fraction (EF) and regional wall motion abnormalities (WMA, centerline method) were quantitated in cineventriculography at baseline and follow-up. Viability was assessed by Tc99m scintigraphy and F-18-FDG positron emission tomography. Intraoperatively, transmural needle biopsies were obtained for microscopic analysis and immunohistochemistry from hypokinetic but viable myocardial regions. EF in group 1 increased from 31±5% to 44±4% postoperatively (p<0.005), EF in group 2 increased from 30±6% to 40±6% (p<0.05 versus preoperatively and versus group 1). WMA in the center of myocardial dysfunction in group 1 increased from -2.1±0.4 to -0.6±0.5 (p<0.05), WMA in group 2 increased from -2.3±0.5 to -1.6±0.6 (p<0.05 versus pre and versus group 1). Microscopic analysis showed mild degenerative changes in group1 with mild fibrosis (28±7%) and no evidence for apoptosis. Biopsies in group 2 showed more apoptotic cell changes and progressive cardiomyocyte degeneration but similar mild-to modest fibrosis (33±6%). Early treatment with Carvedilol in patients with hibernating myocardium might delay progressive cardiomyocyte degeneration possibly due to anti-apoptotic and anti-oxidant effects, which might result in improved recovery of contractile function after revascularization.

1137-94 Age and the Lack of an Adverse Effect of Diabetes Explain the "Obesity Paradox" in Patients With Myocardial Infarction

Scott Wright, Joseph G. Murphy, Thomas G. Allison, Anil Nigam, Wayne L. Miller, Brent A. Williams, Ana G. Rosales, Guy S. Reeder, Allan S. Jaffe, Mayo Clinic, Rochester, MN

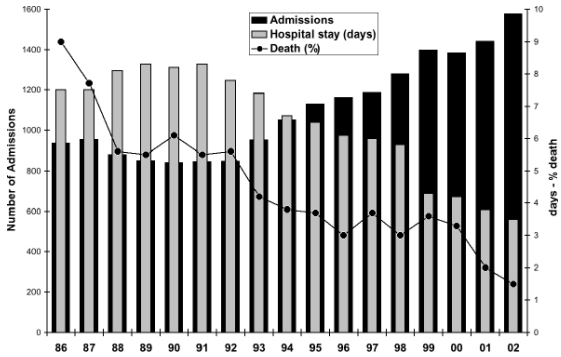
Background: The "obesity paradox" refers to improved survival among obese patients following acute myocardial infarction (AMI). The nature of this remains poorly defined.
Methods: We analyzed the outcome of 941 patients with AMI from 1988 until 2001. Obesity was defined as BMI ≥ 30, overweight as 25<BMI < 30 and normal weight as BMI < 25. Univariate and multivariate predictors of survival were analyzed.
Results: Obese patients were younger and less likely to be female at time of admission (p<0.01). The prevalence of diabetes was higher in obese patients (24%) compared to overweight (15%) or normal weight patients (13%), p <0.05. There were no differences in other clinical characteristics. Long-term mortality was significantly lower in the obese (RR 0.64) and overweight (RR 0.76) patients compared to normal weight patients (RR 1.0), p=0.04. Long-term survival among all three groups was less than age-predicted (see figure). Diabetes was not a univariate predictor of mortality risk in obese patients (RR NS) but was in non-obese patients (RR 1.77, 95% CI 1.26, 2.48), p < 0.01. After adjustment for age and diabetes, there were no longer significant differences: Obese (RR 0.74), overweight (RR 0.83) vs normal (RR 1.0), p=0.14. Conclusion: The obesity paradox following AMI appears to be largely a function of younger age at time of presentation and the lack of impact of concomitant diabetes. When adjusted for age, the long-term RR of death in obese and overweight patients is similar to normal weight individuals



1137-95 Demographics, Treatment, and Outcome of Acute Coronary Syndromes: 17 Years of Experience in a Tertiary Care Center

Jean-Pierre S. Awaida, Jocelyn Dupuis, Pierre Théroux, Michel Joyal, Pierre De Guise, Serge Doucet, Luc Bilodeau, Jean-François Tanguay, Richard Gallo, Jean Grégoire, Philippe Lavoie-Lallier, Laurent Macle, Anil Nigam, Montreal Heart Institute, Montreal, PQ, Canada

Background: There is limited epidemiological information about the evolution of demographics, treatment, and outcome of patients admitted to tertiary coronary care units (CCU) over the past 15 years.
Methods: We prospectively studied 18,719 patients admitted from April 1986 to March 2003 in a 22 bed CCU. The attending physicians filled in the discharge form, which was then entered in a computer database designed for the study.
Results: From 1986 till 2003, the number of admissions increased from 937 to 1577/year while hospital stay decreased from 7.5 to 3.5 days; mean age increased from 58.4 to 63.4 years and the proportion of males remained stable at about 70%. Use of coronary angiograms increased from 49.8% to 81.1% of all patients while fibrinolysis dropped from 12.2% to 0%. In-hospital mortality dropped from 9% to 1.5%. The percentage of Swan-Ganz decreased from 8.1% to 0.7% while intra-aortic balloon pump insertion remained stable. From 1995 till 2003, the proportion of stenting during PTCA increased dramatically from 0 to 86%. In the past 5 years, surgical revascularization remained stable around 20% of all admissions.
Conclusions: There has been a tremendous increase in efficiency with approximate doubling of the admissions turnover rate in a tertiary care CCU. Patients with acute coronary syndromes are stratified faster and treated more invasively. Therapeutic advances are reflected by an almost linear 0.5%/year decrease of in-hospital mortality.



1137-96 Clustering of Novel Risk Factors Correlates With the Metabolic Syndrome

Matthew A. Hook, John H. Chiu, Arman Askari, Niranjan Seshadri, Gregory L. Pearce, Dennis L. Sprecher, The Cleveland Clinic Foundation, Cleveland, OH

Background: Homocysteine, fibrinogen, lipoprotein (a) (Lp(a)), and C-reactive protein (CRP) have been shown to be independently associated with cardiovascular disease.However, little is known regarding the clustering of these novel risk markers and their correlation to the metabolic syndrome.
Methods: Data were collected from primary and secondary prevention patients entering a cardiology clinic (n=1306, mean age 55 +/- 9 years, 36% female (n = 469), 19% diabetics (n=243), mean waist circumference 98cm, 8% current tobacco users (n=110), mean systolic blood pressure 122 mmHg, median LDL 126 mg/dL, median HDL 43 mg/dL), including novel risk markers. We sought to determine whether the novel risk markers were clustered in distribution and/or correlated to the variables of metabolic syndrome, as defined by ATP III guidelines.
Results: These four novel biomarkers were clustered more than would be expected under the assumption of independence (p<0.001). The expression of metabolic syndrome increased from 11% when none of the four were elevated to 28% when 3 or 4 were elevated (p<0.001). **Conclusions:** Homocysteine, fibrinogen, Lp(a) and CRP cluster in an elevated state and are not independent of one another. The number of elevated novel biomarkers directly correlates to the presence of the metabolic syndrome

1137-97 Soluble CD40 Ligand in Predicting Coronary Artery Disease and Long-Term Outcomes in Stable Patients With Angiographically Defined Disease States

Jason M. Lappe', John F. Carlquist, Jeffrey L. Anderson, Matthew J. Kolek, Benjamin D. Horne, Bryant M. Whiting, Heath U. Jones, Robert R. Pearson, Johnny Walker, Joseph B. Muhlestein, LDS Hospital, Salt Lake City, UT, University of Utah, Salt Lake City, UT

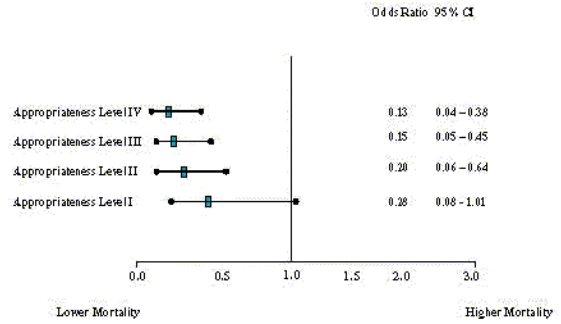
Background:
Elevated levels of soluble CD40 ligand (sCD40L) have been reported in patients with acute coronary syndrome and have been found to independently predict risk of future events in this population. However, to date, no study has correlated sCD40L levels and the long-term risks associated with coronary artery disease (CAD) in non-MI patients.
Methods:
Serum sCD40L levels using ELISA (R&D; Systems) were measured in 909 patients evaluated by angiography for the presence of CAD. Patients presenting with acute MI were excluded. A three-way matching scheme (by age [±5 years], gender, and time period of catheterization [±1 year]) was used to identify 303 patients with CAD (≥70% stenosis in ≥1 major vessel) who experienced a cardiac event (death, MI) within one year, 303 patients with CAD but with no events at one year, and 303 with no CAD.
Results:
The three groups were balanced, with patient age averaging 64 ± 11 years; 74% males. Median (SE) sCD40L levels were different for no-CAD patients (335 [60] pg/mL) compared to CAD (248 [65] pg/mL, p=0.01) and to CAD/event (233 [63] pg/mL, p<0.001) but not between CAD and CAD/event patients (p=0.24). After separating sCD40L levels into quartiles, performing logistic regression, adjusting for standard risk factors and C-reactive protein, and performing Bonferroni adjustment for multiple comparisons (p-critical = 0.017), there was a non-significant trend toward *decreased* risk of CAD vs no-CAD (Q4 vs. Q1: odds ratio [OR]= 0.71, 95% confidence interval [CI]=0.44-1.13, p=0.15) and CAD/event vs no-CAD (Q4 vs. Q1: OR=0.59, CI=0.37-0.96, p=0.03), but not for CAD/event vs. CAD (Q4 vs. Q1: OR=0.89, CI=0.56-1.41, p=0.61). Analyses showed no differences between men and women.
Conclusions:
In contrast to previously reported information in patients with acute coronary syndrome,

in these stable patients, elevated levels of sCD40L did not predict CAD and were not associated with a higher risk of clinical events (death, MI). In fact, a trend towards lower sCD40L levels in CAD compared to non-CAD patients was observed. This novel interaction of sCD40L with type of presentation raises interesting questions for CAD pathogenesis and prognosis and should be further evaluated.

1137-98 Impact of Combination Evidence-Based Medical Therapy on Mortality in Patients With Acute Coronary Syndromes

Debabrata Mukherjee, Kartik Giri, Jianming Fang, Stanley Chetcuti, Mauro Moscucci, Eva Kline-Rogers, Kim A. Eagle, University of Michigan, Ann Arbor, MI

Background: Antiplatelet drugs, beta-blockers, ACE inhibitors and lipid lowering agents have proven efficacy in reducing mortality in patients with acute coronary syndromes. However, the impact of the combination of these agents when used together on clinical outcomes has not been studied before.
Methods Patients presenting with acute coronary syndromes between 01/99 and 03/02 were identified. Based on discharge use of evidence-based therapies, we created a composite appropriateness score depending on the number of the drugs used divided by the number of the drugs indicated for each patient. The impact of the composite score on 6-month mortality was analyzed using a risk-adjusted logistic regression model.
Results: The odds ratio for death for all indicated medications used (appropriateness level IV) vs. none of the indicated medications used (appropriateness level 0) was [0.13, 95% CI 0.04-0.38, p=0.0002]; similarly for appropriateness level III vs. level 0 was [0.15, 95% CI 0.05-0.45, p=0.0008]; for appropriateness level II vs. level 0 was [0.20, 95% CI 0.06-0.64, p=0.006] and for appropriateness level I vs. level 0 was [0.28, 95% CI 0.08-1.01, p=0.051].
Conclusions: Use of combination evidence-based medical therapies was independently and strongly associated with lower 6-month mortality in patients with acute coronary syndromes. Such therapies, most of which are generic and inexpensive today, appear to offer a marked survival advantage when compared to patients where such therapies are omitted.



1137-99 Clopidogrel in Unstable Angina Patients Who Would Have Been Excluded From Randomized Pivotal Trials

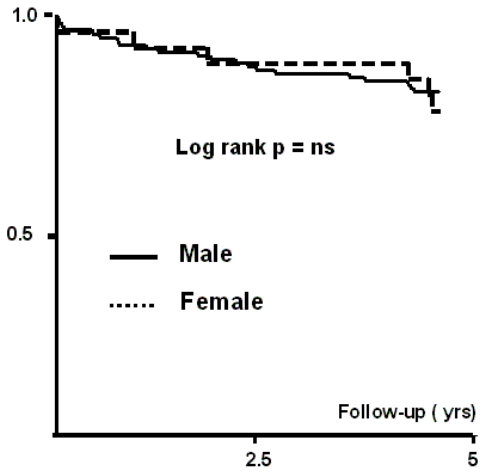
Laurent Payot, Jean Philippe Collet, Gilles Montalescot, Rémi Choussat, Jean philippe Metzger, Gérard Dobrinski, Daniel Thomas, Centre Hospitalier Universitaire Pitié-Salpétrière (AP-HP), Paris, France

Objectives:
We describe the characteristics and examine the efficacy and safety of Clopidogrel in unstable angina /non-ST-elevation myocardial infarction (UA/NSTEMI)patients who would have not been eligible for the Cure trial.We compared this group to the patients fitting the Cure criteria.
Background:
It is not known whether the benefit shown with clopidogrel in the selected population of pivotal trials can be extended to the real world.
Methods and Results:
All patients with UA/NSTEMI were anticoagulated with subcutaneous enoxaparin associated with a double antiplatelet regimen including a loading aspirin and 300mg clopidogrel as first line medical stabilization treatment. Among 517 consecutive patients, we identified 117 patients ("EP" for excluded patients)who would have not been eligible.This EP group was older,had a lower creatinine clearance, had more frequently a past-history of CABG or a diagnosis of non-Q MI on admission in comparison with patients without any of the exclusion criteria ("NEP"for non excluded patients). Moreover the EP had a lower ejection fraction (48% vs 55%, p<0,001), a higher TIMI risk score (3.27%vs 2.80%, p=0.0016), a longer hospitalisation duration (3.93 days ± 2.83 vs 3.11 days ± 1.64; p<0.0001) and a higher rate of diabetes (31.6% vs 21.7%, p<0.05). The use of GPIIb/IIIa inhibitors was similar in the two groups (41% vs 43%, p=NS). The EP group underwent less frequently PCI than those of the NEP group (56% vs 68%,p=0.01). There was a non significant trend for a higher rate of major bleeding at 30-day in the EP group (5.1% vs 2.7%,p=NS). The rate of major coronary events at 30 days (myocardial infarction and death) was higher in the EP group (14.5% vs 4.5%, p =0.0013). When considering severe renal failure (creatinine clearance<30 ml/min), there was still no significant difference in the rate of major bleeding (5.62 vs 2.24, p= 0.06), although the number of EP rose up to 160.
Conclusion:
Patients who do not fit the enrolment criteria of Cure trials have higher risk baseline characteristics for both bleedings and ischemic events. In these patients, the use of clopidogrel was associated with a moderate and non significant increase of bleedings compared to typical "CURE" patients.

1137-100 Five-Year Survival Data From the APRICOT Trials: Does Female Gender Really Portend Unfavorable Outcome?

Hendrik-Jan Dieker, Nick Clappers, Peter C. Kievit, Marc A. Brouwer, Paul J.P.C. van den Bergh, Wim R.M. Aengevaeren, Gerrit Veen, Freek W.A. Verheugt, University Medical Center St. Radboud, Nijmegen, The Netherlands

Background: Few studies have thoroughly addressed the unfavorable outcome of women after acute MI, especially in the long-term; discussion remains with respect to the impact of clinical and angiographic baseline differences. This is the scope of the current 5-year survival study.
Methods: Patients (n=452) had fibrinolysis (FL) for acute STEMI and an open infarct artery at 24-hour angiography. Three-month follow-up (FU) angiography and 5-year clinical FU (97%) were obtained.
Results: Of the 452 patients 75 (17%) were female. Women were older (59±11 vs. 56±9 yrs, p>0.01), more often known with hypertension (39% vs. 22%, p>0.01) and more often smokers than men (73% vs. 63%, p=0.08). Single vessel disease was more frequent among women: 69% vs. 54% (p=0.01). Baseline stenosis severity (QCA) was less severe: 54±14 vs. 58±13 (p=0.04). The 3-month reocclusion rate was similar in men and women (20% vs. 19%). 5-year survival did not differ (89% vs. 91%). Gender was not independently associated with survival.
Conclusions: Survival 5 years after successful FL did not differ between men and women, despite a less favorable clinical baseline profile. Women more often had single vessel disease and less severe culprit lesions, but similar reocclusion rates. These findings after successful FL challenge the often generalized association between gender and outcome and warrant further exploration as to whether this relationship is primarily driven by an association in the subset of patients after failed FL.



1137-101 Elevated Parathyroid Hormone Is an Important Predictor of Coronary Events in Patients With Chronic Hemodialysis

Takashi Kubo, Takuzo Hano, Masahiro Obana, Toshio Imanishi, Akira Baba, Kazushi Tsuda, Yoshiaki Tomobuchi, Mikio Arita, Ichiro Nishio, Wakayama Medical University, Wakayama, Japan

BACKGROUND: Secondary hyperparathyroidism is prevalent among patients with chronic hemodialysis and influences the calcium metabolism. Excess of parathyroid hormone (PTH) may play an important role in the development of coronary calcification and atherosclerosis. The aim of this study was to evaluate whether serum levels of PTH can predict risk for future coronary events.
METHODS: A consecutive series of 104 patients with chronic hemodialysis undergoing coronary angiography were enrolled in this study. We measured baseline serum intact PTH levels and long-term clinical outcomes were obtained. The incidence of coronary events (stable angina, unstable angina and acute myocardial infarction) due to new coronary lesions confirmed by angiography was compared with the serum intact PTH levels.
RESULTS: The prevalence of secondary hyperparathyroidism (intact PTH > or = 65 pg/ml, 311 +/- 284.1 pg/ml, mean +/- SD) was 60 of 104 patients (58%). During 3-year follow-up, the incidence of coronary events associated with new coronary lesions was significantly higher in patients with hyperparathyroidism than that in patients with normal PTH (27% vs. 5%, p<0.001). Univariate Cox regression analysis demonstrated that diabetes (HR=10.4, 95% CI=2.4 to 45.2, p=0.002), hyperparathyroidism (HR=7.8, 95% CI=1.8 to 34.3, p=0.006), obesity (HR=3.3, 95% CI=1.3 to 8.3, p=0.013) and hyperlipidemia (HR=2.6, 95% CI=1.1 to 6.6, p=0.042) were significant predictors of the developing coronary events, however, age, sex, duration of hemodialysis and other conventional risk factors were not. In a multivariate analysis, hyperparathyroidism remained an independent predictor of developing coronary events (HR=5.5, 95% CI=1.2 to 25.5, p=0.028).
CONCLUSION: In patients with chronic hemodialysis, the elevated PTH was an independent and strong predictor of coronary events after adjusting for conventional risk factors.