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hood and adult socio-economic position (Model 1) and for total cholesterol, HDL, triglycerides, apolipoprotein A1, apolipoprotein B, Lp (a), systolic and diastolic blood pressure,  $VO_2max$  and smoking (Model 3).

	Unadjusted	Model 1	Model 2
Normal (BMI=18.5-25.0) N=476	3.73	3.62	3.32
Overweight (BMI=25.1-30.0) N=255	3.89	4.12	3.97
Òbese (BMI=30.1-35.0) N=75	6.04*	5.85*	5.24*
Very obese (BMI>35.0) N=22	10.41‡	8.72†	7.03*

differs from those in the normal range \* p<0.05, † p<0.01, ‡ p<0.001

Conclusion: CRP is independently related to obesity in healthy young adults. Chronic inflammation may contribute to the increased risk of atherosclerotic disease associated with obesity.

#### 1033-139 Estrogen Receptor Alpha Gene Polymorphism Is Associated With Coronary Artery Disease Severity

<u>Arthur Pollak</u>, Ariel Rokach, Anat Blumenfeld, Laura J. Rosen, Luba Reznik, Rivka Dresner Pollak, Hadassah University Hospital, Jerusalem, Israel, Hebrew University School of Medicine, Jerusalem, Israel

Background: Estrogens have beneficial effects on the cardiovascular system partially mediated by estrogen receptor alpha (ER a). Alternations in ERa expression may affect the atheroprotective role of estrogens. We hypothesized that genetic variation in the regulatory region of the ER  $\alpha$  gene is associated with the angiographic severity of CAD. Methods: We studied 496 consecutive patients (72% men, 28% women) who had coronary angiography. Severity of CAD was assessed by: 1) the number of major coronary vessels with at least one >50% narrowing (NMCV); 2) the number of vessels with any narrowing (NCV); 3) the total number of narrowings (NN). The length of the dinucleotide repeat thymine & adenine (TA repeats) upstream of exon 1 of the ER $\alpha$  gene, was determined by PCR. The median number of TA repeats was used to categorize the population into 3 groups: long alleles genotype (both alleles ≥18 repeats), short alleles genotype (both alleles <18 repeats), and mixed genotype (short & long allele). Since the contribution of genetic factors is expected to be more prominent in younger subjects, patients were divided into younger and older groups, age≤55 (n=128) vs. age>55 (n=368). The relationship between TA length and the severity of CAD was assessed by analysis of covariance, stratified by age group. Sex and major CAD risk factors (diabetes, hypertension, hyperlipidemia, smoking, obesity, family history) were included as confounding factors

**Results:** Young patients with long alleles genotype had a significantly greater number of narrowed coronary arteries compared to those with short alleles genotype (NCV 3.7 $\pm$ 2.4 vs. 2.5 $\pm$ 1.8, respectively, p<0.02). Similarly, young patients with long alleles had a higher total number of coronary narrowings compared to those with short alleles (NN 4.5 $\pm$ 2.7 vs. 3.1 $\pm$ 2.2, respectively, p<0.02). A trend towards a higher NMCV in young patients with long alleles was also observed (IMCV 2.0 $\pm$ 1.1 vs. 1.6 $\pm$ 0.9, long vs. short, p=NS). These differences were not observed in older patients.

**Conclusion:** The length of the TA dinucleotide repeat in the regulatory region of the ER $\alpha$  gene is associated with the angiographic severity of CAD in young subjects, independent of the major coronary risk factors.

#### POSTER SESSION

## 1034 Aortic Diseases: Prevention, Risk, and Repair

Sunday, March 30, 2003, Noon-2:00 p.m. McCormick Place, Hall A Presentation Hour: 1:00 p.m.-2:00 p.m.

#### 1034-140 Surgical Intervention Is Superior to Medical Therapy in the Management of Type A Aortic Intramural Hematoma

Kevin J. Mikielski, Andrew Thomas McRae, III, Marc S. Penn, Monvadi B. Srichai, Richard D. White, Richard A. Grimm, The Cleveland Clinic Foundation, Cleveland, OH

Background: Aortic intramural hematoma (AIH) is a variant of aortic dissection. The management of Type A AIH remains controversial. This study was performed to determine the optimal treatment strategy for Type A AIH.

Methods: Transesophageal echocardiography (TEE), computed tomography (CT), and magnetic resonance imaging (MRI) databases were queried for "intramural hematoma" and "AIH." Charts and imaging studies were reviewed to identify cases of Type A AIH. Patients with Marfan's disease, traumatic AIH, and penetrating aortic ulcer were excluded. Mortality was determined via Social Security Death Index.

Results: Thirty cases of Type A AIH were identified between April 1991 and July 2001. Diagnosis was made by TEE alone (n=13), CT or MRI alone (n=1), and a combination of TEE and CT or MRI (n=16). Mean age was 68 +/- 12 years and 53% of patients were female. Hypertension was present in 90% of cases and 80% presented with chest and/or back pain. Pericardial effusion and aortic regurgitation were present in 57% and 73% of cases, respectively. Surgical intervention (ascending aorta graft placement) was utilized in 22/30 (73%) cases. The in-hospital mortality rate was significantly lower with surgical

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intervention (0/22, 0% Versus 3/8, 38%, p=0.002). Patients treated with surgical intervention had a significantly lower mortality rate according to Kaplan-Meier survival curves (p=0.022).

Conclusion: We conclude that surgical intervention is superior to medical therapy in the management of Type A AIH.





#### Coronary Artery Involvement in Patients With Acute Type A Aortic Dissection: Clinical Characteristics and In-Hospital Outcomes

Eduardo Bossone Rajendra H. Mehta, Santi Trimarchi, Jeanna V. Cooper, Dean E. Smith, Arturo Evangelista, Truls Myrmel, Jae Oh, Christoph A. Neinaber, Kim A. Eagle, Eric M. Isselbacher, On behalf of the International Registry of Acute Aortic Dissection (IRAD) Investigators, University of Michigan, Ann Arbor, MI, Massachusetts General Hospital, Boston, MA

**Background** The clinical characteristics and outcomes of patients with type A acute aortic dissection (AAD) with coronary artery involvement (CAI) have not been well studied. **Methods** Accordingly, we evaluated 475 AAD patients enrolled in IRAD (1/97-12/01). CAI was defined as extension of AAD into the coronary ostia or compromise blood flow to any coronary artery caused by the dissection. **Results**: CAI occurred in 64 (13.5%) of AAD patients and affected all ages and both sexes equally. Hypertension (83% vs 68%, p=0.01) and diabetes (9.7% vs 3.3%, p=0.03) were more common in CAI patients, whereas other comorbid conditions were similar in the 2-groups. Presenting symptoms (chest pain, syncope, heart failure, hypotension, or neurological deficit) and chest Xray findings were esimilar in the 2 groups. Although, CAI patient were more likely to show new Q wave or ST elevation on ECG (16.7% vs 4.3%, p=0.001), these findings were present in only 1 of 6 CAI patients. Aortic arch involvement and presence of periaortic hematoma, aortic regurgitation and pericardial effusion were more common in CAI patients. In-hospital management and outcomes of the 2 groups were similar. Only myocardial ischemia or infarction occurred more frequently in CAI patients (table).

In-hospital Complications	Overal I	With coronary involvement	Without coronary involvement	p- valu e
All Neurological deficits (%)	137 (30.4)	19 (31.1)	118 (30.3)	0.9
Coma/Altered Consciousness (%)	33 (8.3)	4 (7.3)	29 (8.5)	1.0
Myocardial ischemia/ infarction (%)	73 (16.6)	26 (44.8)	47 (12.3)	<.00 1
Mesenteric ischemia/ infarction (%)	24 (5.4)	3 (5.1)	21 (5.5)	1.0
Hypotension (%)	151 (33.9)	20 (33.9)	131 (33.9)	1.0
Mortality (%)	139	17 (26.6)	122 (29.7)	0.6

**Conclusions:** CAI occurs infrequently in AAD patients and contrary to popular belief is not associated with greater mortality compared to AAD patients without CAI. It is the presence of extensive type A dissection, more than just CAI, that predicts outcomes.

#### 1034-142 Renal Failure on Presentation Predicts Morbidity and Mortality in Aortic Dissection

Joshua A. Beckman Rajendra H. Mehta, Eduardo Bossone, Jeanna V. Cooper, Dean E. Smith, Udo Sechtem, Linda Pape, Patrick T. O'Gara, Brigham & Women's Hospital, Boston, MA

Background: Vascular complications in aortic dissection are common and augur adverse outcomes. In the setting of an acute aortic dissection (AAD), the importance of renal failure (RF) as an adverse prognostic indicator remains incompletely defined. We sought to determine the clinical correlates and complications of AAD associated with (RF). Methods: The records of 1078 patients in IRAD were evaluated. RF was defined as a serum creatinine greater than 2.0 mg/dL on presentation or an increase of greater than 0.7 mg/dl from baseline. Chi squared analysis was performed on specific endpoints. Results: RF was noted in 85 patients from IRAD (7.8%). Subjects with and without RF were similar in age (62 vs. 63 y) and sex (34.1 vs 31.3% female). The clinical presenta-

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tion differed between the two groups. Patients with RF were less likely to present with chest pain (65.5% vs. 76.5%, p=.02) and syncope (6 vs. 13.8%, p = .04), but were more likely to have hypotension (35.4 vs. 19.9%, p = .0011) and an altered mental status (18.3 vs. 9.5%, p = .01). Patients with RF were also more likely to suffer vascular complications of AAD including mesenteric ischemia (20.2 vs. 2.2%, p <.0001) and limb ischemia (20.0 vs. 7.9%, p = .0003). Finally, RF on presentation adversely affected survival (mortality 39.3 vs. 21.4%, p = .0002).

Conclusions: The presence of RF identifies a subgroup of patients at particularly high risk for vascular complications and death. This simple marker should prompt evaluation for visceral and limb ischemia to ensure the use of appropriate medical and surgical strategies to reduce morbidity and mortality from AAD.

#### 1034-143 Endovascular Stent-Graft Repair of Descending Thoracic Aortic Penetrating Atherosclerotic Ulcers: Mid-Term Results

<u>Philippe Demers.</u> D. Craig Miller, R. Scott Mitchell, Stephen T. Kee, Lynn Chagonjian, Michael D. Dake, Stanford University School of Medicine, Stanford, CA

Background: The objective of this study was to determine the effectiveness of endovascular stent-graft (S-G) treatment of patients with descending thoracic aortic penetrating atherosclerotic ulcers (PAU) and identify risk factors for treatment failure. Methods Between March 1993 and January 2001, endovascular repair of descending thoracic aortic PAU with first- (custom-fabricated) and second generation (commercial) stent-grafts was performed in 26 patients (mean age 70 years, range 55-85), six (23%) of whom had rupture. Fourteen patients (54%) were judged not to be reasonable surgical candidates for a conventional open operative procedure because of various comorbidities. Follow-up was 100% complete (average 51 months, max 114 mo, 12 patients remaining at risk at 5 years). Outcome variables considered in the multivariable analysis included all deaths and treatment failure (composite end-point comprising endoleak, stent-graft mechanical fault, late aortic event, reintervention, and/or aortic-related or sudden, unexplained late death). Results: Three patients (12%) died within 30 days, and 2 had an early type I endoleak. No surgical conversions were necessary. Procedural success rate was 92% at the time of discharge. Actuarial survival estimates at 1, 3 and 5 year were 85±8%, 76±8% and 70±10%, respectively. Actuarial freedom from treatment failure at the same times was 81±8%, 71±9% and 65±10%. Multivariable analysis identified previous stroke and female gender as independent risk factors for death. For treatment failure, these predictors were maximal aortic diameter and female gender. Conclusions: These mid-term results indicate that endovascular S-G repair is effective in selected high surgical risk, elderly patients with PAU located in the descending thoracic aorta, as such localized pathology is an ideal target for a S-G. Strict serial radiological imaging follow-up is mandatory to detect late complications.

#### 1034-144 Perioperative Myocardial Ischemic Complications Following Abdominal Aortic Aneurysm Repair Lead to Substantially Increased In-Hospital Costs

<u>Kristian B. Filion</u>, Louise Pilote, Seema Haider, Mark J. Eisenberg, Jewish General Hospital/McGill University, Montreal, PQ, Canada

Background: Perioperative myocardial ischemic complications (PMICs) have serious clinical implications for patients undergoing abdominal aortic aneurysm repair (AAA). Our objective was to determine the magnitude of the cost increase with an episode of PMIC following AAA repair.

**Methods:** We compared the cost of treating 1,057 consecutive patients undergoing AAA repair between 1997 and 2001 at 6 U.S. and 4 Canadian hospitals (n=505 and n=551, respectively). PMIC was defined as the occurrence of perioperative compestive heart failure (CHF), myocardial infarction (MI), or death. Patients were subdivided into 2 categories according to the occurrence of perioperative complications: 1) no complications (81.3%), and 2) PMICs (18.7%). Participating hospitals used the same cost accounting system to provide patient-level clinical and cost data. Canadian costs were converted to U.S. dollars using purchasing power partiles.

**Results:** Patients experiencing an episode of PMIC were more likely to be women and the elderly (27.9% vs 16.0%, p<0.0001; age<75: 16.2% vs age>=75: 22.5%, p=0.01). Patients experiencing PMICs were also more likely to be admitted for non-elective surgery (25.5% vs 11.8%, p<0.0001). Rates of diabetes mellitus were higher among those experiencing PMICs (29.1% vs. 17.8%, p=0.02), while rates of prior MI, hypothyroidism, and chronic obstructive pulmonary disorders (COPD) were similar (P=NS for all three conditions). Once admitted, patients with PMIC stayed an average of 7.6 days longer in hospital than patients without PMIC (p<0.0001). Both U.S. and Canadian patients experiencing PMICs Lad a significantly higher cost of treatment compared with those without PMICs (U.S.: median \$22,823 vs \$12,786, mean \$45,770±7,205 vs \$19,441±990, p<0.0001; Canada: median \$14,850 vs \$1,2,785, mean \$20,862±1,802 vs \$10,868±541, p<0.0001). After controlling for clinical and demographic differences, there was a 68% increase in cost among U.S. patients with PMICs and a 56% increase among Canadian patients.

Conclusion: PMIC following AAA repair leads to substantially higher in-hospital costs of treatment and should be prevented.

#### 1034-145 Hospital Readmissions Following Abdominal Aortic Aneurysm Repair

Laura C. Gioia, Kristian B. Filion, Seema Haider, Louise Pilote, Mark J. Eisenberg, Jewish General Hospital/McGill University, Montreal, PQ, Canada

Background: In-hospital outcomes associated with abdominal aortic aneurysm (AAA) repair are well-described. However, little is known about post-discharge readmission rates, subsequent mortality, and cost.

Methods: We examined 206 consecutive patients who underwent AAA repair at 2 Ameri-

can hospitals between 1997 and 2001. Index hospitalization and 6-month readmission data were extracted from a resource and cost accounting system used by both hospitals. Results: Among the 206 patients, 183 survived until discharge (mortality rate 11.2%; 10 deaths after elective repair (6.4%) and 13 after non-elective repair (26.5%)). Among the 147 elective patients who survived until discharge, 21.1 % (31/147) were readmitted within the subsequent 6 months. Among the 36 non-elective patients, 36.1% (13/36) were readmitted. Age and gender distribution were similar among readmitted patients and non-readmitted patients (72.5  $\pm$  9.5 vs. 73.0  $\pm$  10.1 years, p=NS and 68.2% vs. 69.1% male, p=NS, respectively). More than two-thirds of the readmissions occurred during the first month following discharge (mean 36.3 ± 46.7 days, median 15.5). The mortality rate among readmitted patients was 11.4%: 6.5% among elective patients and 23.1% among non-elective patients. For each readmission, the mean cost was \$10.547 ± 1,993 (median \$4,464.8) and mean length of stay was  $8.5 \pm 12.6$  days (median 4.0). The mean number of readmissions per patient was  $2.2 \pm 1.8$  times (median 1.0). The total per-patient cost for all readmissions during the first 6 months following AAA repair was \$19,460 ± 4,863 (median \$6,895.5); the total length of stay was 15.5 ± 21 days (median 8). Overall, readmissions during the 6 months following AAA repair accounted for a cost >50% over and above the cost of the index hospitalization (mean \$32,217.9 ± 7,015.9, median 18.229.5)

Conclusions: Hospital readmissions within the 6 months following AAA repair occur commonly and are associated with high mortality rates, high length of stays, and high costs.

#### POSTER SESSION

## 1035 Pharmacologic Modulation of Endothelial Function

Sunday, March 30, 2003, Noon-2:00 p.m. McCormick Place, Hall A

Presentation Hour: 1:00 p.m.-2:00 p.m.

#### 1035-146 Metformin Improves Endothelial Function in Patients With Metabolic Syndrome X

Cristlana Vitale, Giuseppe Mercuro, Antonello Silvestri, Massimo Fini, <u>Giuseppe M.</u> <u>Rosano</u>, San Raffaele, Roma, Italy, University of Cagliari, Cagliari, Italy

Metabolic Syndrome X (SX, hyperinsulinemia, hypertension, hyperlipemia) is associated with impaired endothelial function and increased risk of cardiovascular events. Insulin resistance plays an important role in the pathogenesis of endothelial dysfunction. The effects of metformin, an antidiabetic agent that improves insulin sensitivity, on endothelial function have not been reported.

The present study was designed to assess the effect of metformin on endothelial function in 65 patients with SX.

Subjects with SX were allocated to receive metformin 500 mg twice daily (n = 32) or placebo (n = 33) for 3 months. Before and after treatment endothelial function was assessed using flow mediated dilatation of the brachial artery using a high resolution vascular ultrasound machine Whole-body insulin resistance was assessed on both occasions using the homeostasis model (HOMA-IR).

Subjects who received metformin demonstrated statistically significant improvement in endothelium-dependent vasodilation compared with those treated with placebo (p = 0.0012 by 2-way analysis of variance), whereas no significant effect was seen on endothelium-independent response to sublingual GTN (p = 0.41). A significant improvement in insulin resistance after metformin was observed (27% reduction in HOMA-IR, p < 0.01), and improvement in insulin resistance was associated with improvement in endothelial function (r = -0.56, p < 0.01).

In conclusion metformin improves both insulin resistance and endothelial function in patients with SX. This supports the concept of the central role of insulin resistance in the development of endothelial dysfunction in SX and the role of metformin for the treatment of these patients

## 1035-147 R

# Raloxifene Effect on Endothelial Function Depends on Duration of Menopause and Previous Hormone Use

<u>Giuseppe M. Rosano</u> Otavio Gebara, Cristiana Vitale, Mauricio Wajngarten, Antonello Silvestri, Josè Antonio F. Ramires, San Raffaele, Roma, Italy, INCOR, Sao Paulo, Brazil

Ovarian hormone deficiency reduces endothelial function in post-menopausal women (PMW).

This effect is reversed by hormone and estrogen replacement therapy. Recent studies however have questioned the cardioprotective effect of hormone therapy in PMW. Recently a new class of agents the selective estrogen receptor modulators have been proposed for the treatment of PMW and one of these drugs (Raloxifene, R) is currently being tested in a multicenter study in order to assess its cardioprotective effect. The effect of R on endothelial function of PMW is controversial, studies in younger PMW showed an improvement of flow mediated dilatation (FMD) while other studies in older PMW failed to find such an effect on FMD suggesting that the effect of R is age-dependent. The aim of the present study was to evaluate: 1) if the effect of R on endothelial function is age-dependent; 2) if the vasodilator effect of R is related to a previous exposure to estrogen replacement therapy.

To this end we studied endothelial function by means of FMD in 39 PMW aging from 49 to 75 years before and after 3 months of therapy with R 60 mg. R administration improved FMD ( $35\pm12\%$ , p<0.05 compared to baseline). In never estrogen users an inverse correlation was found between time from menopause and the effect of R on FMD (r=-58, p<0.01).

In PMW >60 years who received estrogen replacement therapy in the past R increased