Usefulness of Plasma Fibrin D-Dimers for Differentiation of Acute Versus Chronic Aortic Dissection

Holler Egggebrecht, Christoph K. Naber, Axel Schmermund, Clemens von Birgelen, Marc Wichert, Thomas Bartel, Klaus Mann, Raimund Erbel, University Essen, Essen, Germany

Background: Discrimination between acute and chronic aortic dissection (AD) has important prognostic and therapeutic implications, but is frequent difficult in the clinical setting. This study evaluated the usefulness of plasma fibrin D-dimer levels and biomarkers of inflammation to differentiate between acute and chronic AD.

Methods and Results: Blood samples from 38 consecutive patients with acute (group 1, n=12) and chronic (group 2, n=26) AD were tested for plasma fibrin D-dimers, while blood cell (WBC) count, C-reactive protein (CRP), and fibrinogen. White blood cell count and CRP levels were significantly higher in group 1 compared to group 2 (15.4±7 x 10^9/L vs. 8.1±2.2 x 10^9/L, p<0.001; and 88±74 mg/L vs. 24±38 mg/L, p<0.001, respectively), with considerable overlap between both groups. Group 1 patients had significantly higher levels of plasma D-dimers compared to group 2 patients (209±146±162 µg/L vs. 275±170 µg/L, p<0.001). ROC curve analysis yielded an optimal cutoff value of 627 µg/L for D-dimer levels with a sensitivity of 100% and specificity of 96% for the presence of an acute dissection state of AD.

Conclusion: Measurement of D-dimers is a widely available laboratory test which allows to discriminate between acute and chronic AD with high accuracy once the diagnosis has been made.

Prevalence and Clinical Correlates of Symptomatic Peripheral Arterial Disease in Italy

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Background. Epidemiology of peripheral arterial disease (PAD) was studied almost exclusively in Northern European and Northern American populations. Thus, it is unclear what is the magnitude of the problem in other countries. We report the first survey in Italy to describe the prevalence of symptomatic PAD and its relationship with cardiovascular risk factors and other diseases.

Methods. From the lists of 7 general practitioners, all subjects living in a well defined area of Southern Italy were identified who were aged 40-80 years (n=4352). All of them received a Rose questionnaire (RQ) which was completed by 3699 subjects. In those referring a pain in the calf that began while walking and did not disappear continuing to walk, regardless of whether the other Rose criteria were met (n=760), ankle/brachial index (ABI) was measured, and the presence of PAD defined by ABI < 0.90.

Results. The prevalence of symptomatic PAD was 1.6% (2.4% in men, 0.9% in women). For each PAD patient, 3 controls matched for sex and age were selected randomly from the listing for each general practitioner. At the multivariate analysis, smoking (OR 3.7, 95% CI 1.7-8.0; p < 0.01), diabetes mellitus (OR 3.6, 95% CI 1.7-7.6; p < 0.01) and hypertension (OR 3.3, 95% CI 1.4-7.8; p < 0.01) were associated with PAD. A consistent cardiovascular disease was found in 48% of patients and 17% of controls (OR 4.6, 95% CI 2.4-8.8; p < 0.01). At the multivariate analysis, only PAD was significantly associated with a previous cardiovascular event (OR 7.8, 95% CI 2.8-21.4; p < 0.01). Of all cases of symptomatic PAD, 45% were unaware of their condition. No significant difference was observed between known and unknown cases.

Conclusion. This study seems to indicate that both prevalence and cardiovascular comorbidity of symptomatic PAD in Italy are lower than in Northern European and Northern American countries. Moreover, the finding that, PAD was unrecognized in about 50% of affected individuals suggest that many patients accept leg complaints as a normal feature of ageing, and imply that a large proportion of PAD population is not given preventive therapy, so remaining at high cardiovascular risk. Thus, there is need to alert general practitioners to this topic.

The Pivotol Link Between Hepatitis C Virus Infection and Increased Arterial Stiffness in Patients With End Stage Renal Failure

Nobuyuki Oake, Toshio Shimada, Yu Murakami, Yuta Ishibashi, Harumi Kato, Shin-ichi Horui, Yuki Ohra, Shimane Medical University, Izumo, Japan

Background: Recent reports have emphasized a link between infection with microorganisms such as Chlamydia pneumoniae and cytomegalovirus, and an increased risk of cardiovascular and cerebrovascular diseases. Although the high prevalence of hepatitis C virus (HCV) infection in patients with end stage renal failure (ESRF) has been well-known, the role of these atherosclerotic diseases is unclear. It has been recently reported that aortic pulse wave velocity (PWV), a marker of arterial stiffness, is a major predictor of mortality in ESRF patients. In this study, we evaluate the relationship of aortic PWV and HCV infection in patients with ESRF. Methods: Seventy-five patients (mean age: 64 years, 57% male, 46% hypertensive, 41% on dialysis treatment for <3657 days) undergoing chronic dialysis treatment in single center were examined. We measured their blood pressure and aortic PWV by VaSera VS-1000 (FUKUDA DENSHI, Japan), left ventricular mass index (LVMl) by echocardiography, serum HCV-RNA by RT-PCR, and plasma brain natriuretic peptide (BNP) by highly sensitive RIA. Determinants of aortic PWV were analyzed by multiple stepwise regression analysis. Results: Twenty patients (26%) were seropositive for HCV, and twelve patients (16%) had HCV viremia. Aortic PWV was significantly higher in patients with HCV viremia than those without it (11.3±5.0 vs. 7.7±3.2 m/sec, p = 0.01). Serum transaminase indicated that independent determinants of aortic PWV were age (p=0.08, p<0.001), HbA1c (p=0.09, p<0.001), mean blood pressure (p=0.05, p<0.001), and the presence of HCV-RNA (p=0.03, p<0.001) (multiple R=0.88). Conclusion: These data show that for the first time HCV infection is strongly associated with the progression of atherosclerosis in patients with ESRF.

Severe Renal Artery Stenosis Is Common in Patients With Severe Thoracic Aortic Plaque

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Background: Atherosclerotic renal artery stenosis (RAS) is an underdiagnosed disorder, and is potentially treatable etiology of hypertension and renal insufficiency. RAS may be a manifestation of generalized atherosclerosis. This study investigates the association of RAS, as detected by abdominal duplex ultrasonography, and thoracic aortic plaque, as detected by transesophageal echocardiography.

Methods. All pts were referred for transesophageal echocardiography for various clinical indications. Abdominal duplex ultrasound was performed on 67 patients: 42 with severe thoracic aortic plaque (> 4 mm) and 25 controls. The prevalence of RAS was determined in both groups. Severe RAS (n=60%) was defined as flow velocity > 1.8 m/sec and renal clinical velocity ratio > 3.5. Clinical data regarding a history of hypertension, coronary artery disease, diabetes mellitus, smoking, dyslipidemia, stroke and peripheral embolization were recorded.

Results: The overall average age of the pts was 72.6 ± 9.7 yrs (57% male). There were 8 cases of RAS identified (all severe), all of them in the group with severe thoracic aortic plaque (19% vs. 0% with <= 2 mm plaque; P = 0.02). In a paired analysis, matched for age and sex (McNemar), severe plaque was highly significantly associated with RAS (P = 0.008). On univariate analysis, severe plaque (P = 0.001) and hypertension (P = 0.05) were correlated with severe RAS (with plaque, hypertension, dyslipidemia and smoking in the model), severe plaque (P = 0.001) and hypertension (P = 0.05) remained independently correlated with RAS. Conclusions: 1. Severe thoracic aortic plaque is strongly associated with RAS. 2. Pts found to have severe thoracic aortic plaque on TEE should be screened for RAS.

Preoperative Hemodynamic Status as a Predictor of Surgical Mortality in Acute Type A Aortic Dissection

Santi Tramarinchi, Rosella Fattori, Christoph A. Nienaber, Jeanne V. Cooper, Dean E. Smith, Vincenzo Rampoldi, Giuseppe Sangioni, Trus Myrmei, Toru Suzuki, Jai K. Oh, Eric M. Isselbacher, Kim A. Eagle, Istituto Policlinico S. Donato, S. Donato Milanese, Italy, University of Michigan Medical Center, Coordinating Center for IRAD Investigators, Ann Arbor, MI

Background: Pre-operative hypertension or shock are known to predict adverse surgical outcomes in patients with acute type A aortic dissection (AAD). However, data evaluating preoperative hemodynamic status from onset of symptoms to surgery in large numbers of patients in the modern era are limited.

Methods: We categorized 526 patients (pts) submitted to surgery for AAD among 1032 pts enrolled in the IRAD between 1996 to 2001. Preoperative hemodynamic status was assessed at the clinical presentation of AAD, after hospitalization in the referral center and at surgery using standard Chi-square test or Student’s T-test. These were correlated with in-hospital mortality.

Results: Data are showed in the table. Our study highlights the importance of hypoten-
sion as a major preoperative risk factor for mortality in AAD pts. Pts bearing severe hypotension from the onset of symptoms to surgery have a worse mortality rate than those who do not (42.3% vs 13.5%, p<0.0001).

Conclusions: Our study provides information regarding the importance of preoperative hemodynamic status, from symptom onset to surgery, as a predictor of mortality in AAD pts. Knowledge about temporal variations of these parameters may help surgeons in making treatment decisions among high-risk patients being considered for potentially heroic surgical attempts.

Table: Pre-operative Hemodynamic Status of Surgical Type A Acute Aortic Dissection Patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall (n=526)</th>
<th>Survived (n=394)</th>
<th>Dead (n=132)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BLOOD PRESSURE AT PRESENTATION</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (SBP &gt; 150 mmHg)</td>
<td>160 (32.4)</td>
<td>128 (32.4)</td>
<td>32 (26.7)</td>
<td>0.124</td>
</tr>
<tr>
<td>Normotension (SBP 100-149 mmHg)</td>
<td>213 (42.9)</td>
<td>176 (46.9)</td>
<td>37 (30.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hypotension (SBP &lt; 100 mmHg)</td>
<td>66 (12.6)</td>
<td>50 (13.3)</td>
<td>16 (12.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Shock or tamponade (SBP &lt; 80 mmHg)</td>
<td>62 (16.1)</td>
<td>47 (12.3)</td>
<td>15 (11.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>BLOOD PRESSURE AFTER HOSPITALIZATION</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital pre-op. hypotension (SBP &lt; 100 mmHg)</td>
<td>123 (24.7)</td>
<td>73 (19.5)</td>
<td>50 (40.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypotension from onset to surgery</td>
<td>213 (40.6)</td>
<td>123 (31.3)</td>
<td>90 (68.2)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**HEMODYNAMICS AT SURGERY**

- Hypotension/Shock at surgery: 153 (29.0) vs 79 (21.4) vs 74 (59.2), p<0.001
- Normotension at surgery: 262 (53.9) vs 219 (60.5) vs 43 (34.7), p<0.001
- LV dysfunction at surgery: 63 (13.0) vs 34 (9.3) vs 29 (24.2), p<0.001
- RV dysfunction at surgery: 31 (6.4) vs 10 (2.8) vs 21 (17.5), p<0.001

**Characteristic** (% or median) **Males** **Females** **Total**

| Age ≥65 years | 42% | 38% | 41% |
| Current smoker | 10% | 8% | 9% |
| BMI ≥30 kg/m² | 42% | 60% | 48% |
| Diabetes duration (years) | 7.2 | 6.7 | 7.0 |
| History of hypertension | 52% | 64% | 57% |
| Prior cardiovascular disease | 20% | 15% | 18% |
| Receiving insulin | 14% | 13% | 13% |

**Total cholesterol (mmol/L)**: 5.0 ± 1.3 ± 5.1

**HDL-C (mmol/L)**: 1.0 ± 1.2 ± 1.1

**TG (mmol/L)**: 1.7 ± 1.8 ± 1.7

**Urinary albumin >20 mg/L**: 36% ± 27% ± 33%

**HbA1c**: 6.9% ± 6.9% ± 6.9%

Poster Session

**1047**

The Answer Is in the Lipid Fractions

Sunday, March 07, 2004, 3:00 p.m.-5:00 p.m.
Moira Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

**1047-177**

Significant Lipid Changes in a Large-Scale Trial of Fenofibrate to Prevent Cardiovascular Disease in Type 2 Diabetes

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Background: The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) trial is a randomized controlled trial designed to test the effects of a long-term increase in high-density lipoprotein cholesterol (HDL-C) and decrease in triglycerides (TG) with fenofibrate therapy on coronary heart disease (CHD) events and mortality in diabetes.

Methods: The FIELD trial included 9,795 type 2 diabetic patients (50-75 years; total cholesterol 3.0-6.5 mmol/L), who received either micronized fenofibrate 200 mg or placebo over 5 years. Total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, and apolipoprotein subfractions were measured in 586 randomly selected students from grades 2, 5, 8 and 11, using a magnetic resonance method (LipoScience®). PB was defined as mean particle size <20.6nm. IR was assessed in 2nd and 11th graders by the homeostasis model assessment of insulin resistance (HOMA-IR). Overweight was defined as age and sex adjusted BMI >85th centile based on 2000 CDC norms. PB increased nearly 4-fold across the 4 tested grades (2.2% in 2nd grade, 5.6% in 5th grade).

Results: PB increased nearly 4-fold across the 4 tested grades (2.2% in 2nd grade, 5.6% in 5th grade).

Conclusions: The frequency of PB increases with age. As seen in adults, PB in youth is associated with age and sex adjusted body mass index (BMI), IR, HDL and triglyceride levels.

**1047-178**

Low-Density Lipoprotein Subfractions in a Random Sample of Children and Adolescents

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Background: The Wausau SCHOOL Project is a community-based effort to assess the frequency of cardiovascular risk factors in students in the Wausau School District. Lipoprotein sub-fraction studies in adults have demonstrated that a preponderance of small dense LDL particles (Pattern B) is associated with obesity, increased HOMA-IR, lower HDL and increased risk of heart disease. Limited information is available on lipoprotein subfractions in children and young adults.

Methods: Lipid profiles and lipoprotein subfractions were measured in 586 randomly selected students from grades 2, 5, 8 and 11, using a magnetic resonance method (LipoScience®). PB was defined as mean particle size <20.6nm. IR was assessed in 2nd and 11th graders by the homeostasis model assessment of insulin resistance (HOMA-IR). Overweight was defined as age and sex adjusted BMI >85th centile based on 2000 CDC norms.

Results: The incidence of PB increased nearly 4-fold across the 4 tested grades (2.2% in 2nd grade, 5.6% in 5th grade).

Conclusions: The frequency of PB increases with age. As seen in adults, PB in youth is associated with IR, higher triglycerides, decreased HDL levels and high BMI.

**1047-179**

Serum Triglycerides and the Risk of Cardiovascular Disease in the Asia Pacific Region: An Individual Participant Data Meta-Analysis of Cohort Studies Including 96,130 Individuals

Arundhika Patel, Mark Woodward, Federica Barzi, Dongfeng Gu, Hirotsugu Ueshima, for the Asia Pacific Cohort Studies Collaboration, Institute for International Health, University of Sydney, Sydney, Australia

Background: The importance of serum triglyceride levels as an independent risk factor for cardiovascular diseases is controversial.

Methods: We performed an individual participant data meta-analysis of prospective studies conducted in the Asia-Pacific region. Cox models were applied to the combined data from 26 studies to estimate the overall and region-, sex-, and age-specific hazard ratios for major cardiovascular diseases by quintiles of triglyceride values.

Results: During 796,929 person-years of follow-up among 96,130 individuals, 638 deaths due to coronary heart disease and 667 stroke deaths were recorded. After adjustment for major cardiovascular risk factors and correction for regression dilution, each 1 mmol/L higher level of usual triglyceride level was associated with a 34% (95% CI 14-58%) greater risk of coronary death. There was clear evidence of an association between triglycerides and ischaemic stroke risk, but not with risk of haemorrhagic stroke. The association between triglycerides and coronary death was similar when stratified by age or sex, but there was a trend towards a stronger association in Australia / New Zealand compared with Asian cohorts (hazard ratio for 1 mmol/L higher usual triglyceride level 1.54 [95%CI 1.26-1.89] vs. 1.12 [95%CI 0.86-1.45], p=0.06).

Conclusions: In the largest study examining this question to date, triglycerides were found to be an independent risk factor for cardiovascular diseases in the Asia-Pacific region. The value of incorporating triglycerides into clinical algorithms for prediction of individual risk of cardiovascular disease and the specific role of therapy aimed at lowering serum triglyceride levels should be further investigated.