nary endothelial dysfunction assessed by cold pressor test is predictive of long-term cardiovascular event in type 2 diabetic patients with angiographically normal coronary arteries and without other coronary risk factor.

### 1131-140 Hemodynamic Effects of Aqueous Nitric Oxide Solutions Applied Directly into Human Coronary Circulation

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**Background:** Nitric oxide (NO) has been shown to dilate vessels and to inhibit platelet function, both effects having hitherto desirable during percutaneous intervention in patients with coronary artery disease (CAD). Whether or not NO applied directly into human coronary circulation exerts biological effects is unknown so far. Therefore, the aims of our study were: (i) to develop a method for reproducible production of sterile solutions containing aqueous NO (NO), and (ii) to find a safe and practical pre-coronary (in.) approach to and to characterize potential dilatory effects in conduit and resistance coronary arteries.

**Methods:** Changes in coronary blood flow (CBF) were quantified by quantitative coronary angiography (QCA) and intraoperative Doppler guide wires (IGW) in 13 patients without out-flow limiting CAD after application of either saline controls, aqueous NO solutions (NO1, 6 µmol), adenosine (ADO, 2.4gm/min) or isosorbiddinitrate (ISDN, 0.3 mg) in random order.

**Results:** NO diluted epicardial arteries in a dose-dependent manner up to 10% (p<0.05, equivalent to that seen upon ISDN). In parallel average peak velocity (APV) increased from 21 to 51±4cm/s. NO diluted coronary microvasculature to almost the same degree as seen after infusion of adenosine, whereas ISDN increased APV only slightly. Consequently, coronary blood flow increased according to the following rank order: NO and ADO > ISDN, whereas saline controls were without effect. NO induced increases in CBF lasted much longer than expected from its biochemical life span in human blood. Heart rate or blood pressure remained unaffected.

**Conclusions:** Aqueous NO solutions can be applied directly into human coronary circulation and dilate both coronary epicardial and resistance arteries increasing coronary blood flow several fold. I determined offers the avenue to selectivelly increase local NO stores within the coronary circulation without exerting systemical side effects.

### 1131-141 Coronary Endothelial Function: The Impact of Aging In a Matched Study Group With Normal Coronary Arteries

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**Background:** Coronary endothelial vasodilator function is attenuated with aging. It is unknown whether this finding is simply related to greater prevalences of risk factors and/or subclinical atherosclerosis among the elderly or alternatively to a direct or indirect effect of aging. Methods: Using graded coronary infusions of acetylcholine (ACh), endothelial function was tested in 25 patients between the ages of 20 and 45 years (defined as young) and in 25 matched patients aged 60 or older (defined as old). All patients had angiographic normal coronary arteries and were matched for gender, race, body mass index (BMI), indexed left ventricular mass (LVMH), low density lipoprotein cholesterol (LDL-C), and mean arterial pressure. Results: The study included 14 women and 11 men in each of the young and old groups. Age was 38 ± 1.2 years in the young group and 64.6 ± 0.7 in the old. Both groups were moderately overweight but not obese. Both were in normal range in their serum homocysteine levels, left ventricular hypertrophy (LVMH) and LDL-C was less than 19 mg/dl in both. Dose response curves relating % increase in coronary blood flow (CBF) to ACh dose were significantly attenuated among the elderly subjects (p<0.013 by ANOVA) despite similar BMI, LVMH, LDL-C, and blood pressure. Peak increase in CBF after ACh was 253 ± 18% in the young and 165 ± 23% among the old (p<0.01). After intracoronary adenosine, peak increase in CBF was also depressed among the old (211 ± 11% vs 173 % ± 16%, p<0.06). Among the young cohort, 16 of 25 (64%) had greater than 11% vs 17% vs 0.026) and 0.026, respectively). With simultaneous administration of vitamin C and methionine to the older group, there was no change in either the mean ACh-induced flow response or in the mean peak velocity response (2.9 ± 0.86 to 83.3 ± 21.3cm/sec and 3.9 ± 0.87, N.S. and N.S., respectively) in spite of an elevation of the plasma homocysteine level (from 11.7 ± 6.4 nmol/ml to 30.6 ± 8.6 nmol/ml, p<0.0001). Moreover, there was a significant negative correlation between plasma homocysteine level and CFVR (r=-0.542, p=0.0092). Conclusion: Elevation in homocysteine level would impair coronary endothelial function by increasing superoxide production. We studied 11 healthy volunteers 23.4 ± 0.9 years of age on average. Coronary flow velocity was measured by transthoracic-Doppler echocardiography performed every 30 minutes and the peak velocity response was presented in a nomogram (oxygenation or aging loss, or, oral methionine plus vitamin C (2g), on separate days in random order.

**Results:** In methionine group, plasma homocysteine level increased from 7.9±0.09mmol/l to 30.6±0.04mmol/l (p<0.0001), while the averaged diastolic peak velocity under hyperxyenic conditions (ADHP-vfp) and CFVR decreased significantly (from 77.2±4.1cm/sec and 4.1±0.7 to 75.5±2.1cm/sec and 3.5±0.5, p<0.028 and 0.025, respectively). With simultaneous administration of vitamin C, however, ADHP-vfp and CFVR did not decreased (from 84.4±2.0cm/sec and 3.9±0.9 to 86.3±3.1cm/sec and 3.9±0.7, N.S. and N.S., respectively). In spite of an elevation of the plasma homocysteine level (from 11.7±6.4mmol/l to 30.6±8.6mmol/l, p<0.0001), moreover, there was a significant negative correlation between plasma homocysteine level and CFVR (r=-0.54, p=0.028). Conclusion: Elevation in homocysteine concentration induced an acute impairment of coronary vessel resistance, and this was completely reversed by vitamin C. Oxidative stress was suggested to play a major role in the deleterious effects of homocysteine on the endothelium of coronary vessels.

### 1131-145 Differential Antiplatelet Effects of Angiotensin Converting Enzyme Inhibitors: Ex Vivo and In Vitro Studies Using Whole Blood Aggregometry

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**Background:** Increasing evidence suggests that angiotensin converting enzyme (ACE) inhibitors have antithrombotic effects. Therefore, we sought to evaluate the coagulative ex vivo activity of cardiovascular (CV) patients grouped for treatment with either captopril, enalapril, ramipril, or enalapril, aspirin (ASA) and/or clopidogrel or none of these medications and, in addition, the in vivo effects of these ACE inhibitors on platelet aggregation of healthy study participants.

**Methods:** Blood samples from 303 CV patients and from 10 strong correlation between FORM and HsCRP (n=0.72, p<0.004). The subjects were also stratified based on their FORM results into those with < 391 and those < 391 Carr Units. The results of the various markers of vascular health are shown below.