bypass surgery (CABG) were randomized into either a training (T) or an inactive control (C) group. At study begin (B) and after 4 weeks (4 wks) average peak velocity in response to different dosages of acetylcholine (Ach) was measured invasively using Doppler velocimetry, vessel diameter of the LIMA was determined by quantitative angiography. LIMA rings not used for bypass grafting during CABG were removed and suspended in an organ chamber to determine endothelial function in vitro. Additionally, expression of the subunit gp91phox of the NAD(P)H oxidase was measured in samples of the LIMA by real time PCR and expressed as ratio over van Willebrand factor.
ET was associated with a clear increase in APV at the highest dosage of Ach (7.2 mg/min) from 47±5% to 91±10% ($p<0.05$ vs. C). In vitro the concentration of Ach which was necessary to induce 50% relaxation (ED50) of the preconstricted LIMA rings was significantly lower in T as compared to C (7.49±0.10 [-log mol/L Ach] vs. 6.82±0.10 [-log mol/L Ach], $p<0.05$). A considerable reduction of the NAD(P)H oxidase subunit gp91phox mRNA expression was observed in T as compared to C (0.47±0.15 vs 1.93±0.60 arb.units; $p<0.05$).
Conclusions: In patients with CAD regular exercise training is associated with an enhanced endothelial function in vivo and in vitro. The improvement of endothelial function due to ET is paralleled by an attenuated mRNA expression of the subunit gp91phox of the NAD(P)H oxidase. These results imply that ET exerts its beneficial effects on the endothelial level at least partially by an attenuation of local oxidative stress.

1080-86 Does Folic Acid Supplementation Improve Endothelial Function in Coronary Patients Independent of Homocysteine Lowering?

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Hyperhomocysteinemia is an emerging risk factor for arterial endothelial dysfunction in coronary patients (CAD), which can be improved with folic acid supplementation (FA). To evaluate whether FA could improve endothelial function independent of homocysteine-lowering, 37 CAD with high homocysteine (total fasting homocysteine >12µmol/l)(HHC) and 39 CAD with normal homocysteine (Normal HC) were studied. FA (5mg/day) or placebo were given for 8 weeks to both groups in double blind cross over fashion, with 10 weeks placebo-washout before crossing over. Flow-mediated dilation (endothelium-dependent, FMD) were measured by high resolution ultrasound before and after each treatment period. The 2 groups were matched in age, gender, blood pressures, glucose, lipid profiles and coronary scores, but blood creatinine was slightly higher in HHC-CAD (108.3±25.7 vs 86.1±17.6µmol/l, $p<0.0001$). FA was associated with significant reduction in HC and improvement of FMD in both HHC and Normal HC groups. On multivariate analysis, changes in folate but not homocysteine or lipid (LDL-C), baseline creatinine nor coronary score, were correlated to changes in FMD, ($R=0.4$; F value=5.5; $p<0.001$)
In conclusion, folic acid supplementation has beneficial effect on endothelial function in coronary patients, independent of homocysteine-lowering.

	HIGH HC-CAD		NORMAL HC-CAD	
	FA	Placebo	FA	Placebo
LDL-C(mmol/l)	3.0±1.1	2.9±1.0	2.9±1.0	3.0±1.0
HC (µmol/l)	11.8±2.5*	13.6±3.0	8.8±2.1*	9.8±1.8
Folate (µmol/l)	83.6±10.9*	27.5±11.8	82.6±8.7*	34.0±14.7
FMD (%)	6.1±1.3**	5.4±1.8	5.9±1.6**	4.9±1.0

Compared with placebo : *$P<0.0001$; **$P<0.005$

1080-87 Vascular Reactivity and Carotid Intimal-Medial Thickness in Children With Insulin-Dependent Diabetes Mellitus

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Background: Endothelial dysfunction is a precursor of clinically detectable atherosclerosis. Diabetes mellitus is an established risk factor for atherosclerosis. Although vascular complications of diabetes are not clinically evident in diabetic children, the timing of onset of endothelial dysfunction in diabetic children is unknown.
Objective: The objective of this study was to test the hypothesis that endothelium- dependent vasodilation is impaired in children with insulin-dependent diabetes mellitus compared to age-matched controls.
Methods: We studied 31 diabetic teenagers (age 15.0 ± 2.4 years, duration of diabetes 6.8 ± 3.9 years) and 29 age-matched healthy children (age 15.4 ± 2.9 years). Using high-resolution vascular ultrasound, we compared brachial artery responses to reactive hyperemia (endothelium-dependent vasodilation) and to sublingual nitroglycerine (endothelium-independent vasodilation). We also measured bilateral carotid intimal-medial thickness in the two groups of subjects.
Results: There was no difference in baseline brachial artery diameter or the degree of reactive hyperemia between the two groups. Endothelium-dependent vasodilation was significantly lower in diabetic children compared to healthy children (4.9 ± 3.4% vs. 7.9 ± 5.8%, P = 0.02). There was no difference in endothelium-independent vasodilation (16 ± 5% vs. 18 ± 8 %, P = NS) or mean carotid intimal-medial thickness between the groups (0.33 ± 0.10 vs. 0.32 ± 0.08 mm, P = NS). There was no relationship of brachial reactivity to the diabetic control (Hb A1C) or the duration of diabetes.
Conclusions: Endothelial function is impaired in children with diabetes mellitus within the first decade of its onset. Strategies to improve endothelial function in these children may have a therapeutic role in this high-risk group.

1080-88 Endothelial Function, Skin Capillary Density, and Plasma Endothelin Levels in Hypertensive and Normotensive Patients With Anginal Chest Pain and Normal Coronary Arteriograms

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Background: Patients with anginal chest pain and normal coronary arteries (CP-NCA) often have abnormal endothelium-dependent vasodilator responses, reduced coronary blood flow reserve, and higher levels of plasma endothelin-1. We recently showed that skin capillary density is lower in patients with CP-NCA.
Aims & Methods: The aim of this study was to examine the relationship between capillary density (measured by intra-vital microscopy before and after maximisation with venous congestion) and flow-mediated dilatation (FMD) measured by brachial artery Doppler ultrasound and plasma endothelin levels. We studied 19 patients With CP-NCA [11 were hypertensive (age 60yr, sitting BP on treatment 145/82mmHg) and 8 were normotensive (age 60yr, BP 128/75mmHg)] and 9 healthy controls (age 59yr, BP 125/78mmHg).
Results: Mean capillary density was significantly lower in patients with CP-NCA independent of their BP compared to healthy controls, both at baseline [55±5 in hypertensives, 61±3 in normotensive versus 73±4 in controls, $p=0.001$ ANOVA], and after maximisation [60±5, 67±3 versus 86±4 respectively, $p<0.0001$]. FMD was higher in controls than in normotensive CP-NCA who in turn had higher values than hypertensive CP-NCA (5.561 versus 4.329 versus 3.646%, $p=0.056$. Capillary density was markedly lower with higher plasma endothelin-1 levels in subjects with CP-NCA ($r= - 0.7$, $p=0.01$).
Conclusions: We confirmed a significant reduction in baseline and maximal skin capillary density in patients with CP-NCA independent of blood pressure. Our findings suggest that plasma endothelin-1 may be implicated in the pathogenesis of capillary rarefaction in this syndrome.

1080-89 ACE Inhibitors Improve Endothelial Function of Coronary Arterioles From Patients With Atherosclerosis by Influencing Local Kinin Release

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ACE-inhibitors attenuate endothelial dysfunction by increasing the availability of NO in human coronary arterioles from patients with atherosclerosis. The release of NO by the coronary circulation is, in part, regulated by local kinin production in resistance vessels. We, therefore, hypothesized that the effect of ACE inhibitors on endothelial dysfunction is mediated via influencing local kinin metabolism.
Methods: In isolated perfused coronary arterioles (<80µM; videomicroscopy) from atrial appendage of patients with and without (control) atherosclerosis, dose-responses to the endothelium-dependent agonists histamine (His), serotonin (5-HT) and acetylcholine (ACh) as well as to the endothelium-independent vasodilator sodium nitroprusside (SNP) were obtained under control conditions and following incubation with the ACE-inhibitor lisinopril (lisi; 10-5M) alone or in combination with L-NAME (NO-inhibitor), HOE 140 (bradykinin B2-receptor antagonist) or dichloroisocoumarin (DCI; blocker of kinin-forming enzymes).
Results: In control vessels (n=6), there was maximal vasodilation to His and SNP (96±6% and 97±8%, respectively), a diverse effect of 5-HT (19±19%) and predominantly vasoconstriction to ACh (-15±21%). Lisi, HOE and DCI did not significantly influence the effects of the different agonists. In atherosclerotic vessels (n=6), the vasodilatory effect of His was significantly ($p<0.05$) attenuated (80±2%), 5-HT caused vasoconstriction (-20±10%) and constriction to ACh was increased (-27 ±25%), whereas the effect of SNP was unaltered (100±3%). Lisi significantly improved the vasodilatory effect of His (98±4%) and diminished constriction to 5-HT and ACh (3±11% and -20±18%, respectively) without altering the response to SNP (100±1%). Co-treatment with L-NAME, HOE or DCI attenuated the effect of lisi.
Conclusions: These results indicate that in coronary arterioles from patients with atherosclerosis, treatment with lisinopril acutely increases the effects of endothelial vasodilators. ACE-inhibitors improve endothelial dysfunction in coronary resistance vessels via activation of local kinin production.

POSTER SESSION

1081 Pulmonary Hypertension: New Insights and Therapies

Monday, March 18, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1081-77 Augmented Gene Transfer in Lungs From Patients With Scleroderma

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The goal of this study was to examine the potential differences in the expression of adenovirus-mediated gene transfer to pulmonary arteries from patients with scleroderma and normal donor pulmonary arteries. We used 2 different adenoviral vectors, driven by a CMV promoter. Pulmonary arteries were removed from explanted lungs and cut into rings. The arteries were incubated with an adenoviral vector that expresses the reporter gene (beta-galactosidase or endothelial nitric oxide synthase (eNOS). Arteries were incubated with virus for 2 hours, and then incubated in medium for 24 hours to allow