1142-7 Determinants of Brachial Artery Endothelial Function In Women: Pilot Phase Results From the WISE Clinical Centers

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Background: While brachial artery (BA) endothelial dysfunction correlates with atherosclerotic risk factors in men, the influence of risk factors and menopause history on BA function in women is not clear. We hypothesized that menopausal status and atherosclerotic risk factors are determinants of BA endothelial function in women.

Methods: Women with chest pain [n = 106, mean age 58 years] in the NHLBI Women's Ischemic Syndrome Evaluation (WISE) had BA diameter measured before and after ischemia-induced hyperemia to assess flow-mediated dilatation (FMD), a marker of endothelial function. We assessed relation of FMD to menopausal status, risk factors for coronary artery disease (CAD), and presence of CAD.

Results: FMD was negatively correlated with age (Spearman correlation −0.28, $p < 0.01$) and systolic BP (−0.22, $p = 0.02$). Absence of FMD was associated with menopause ($p = 0.02$), diabetes ($p < 0.01$), prior PTCA ($p = 0.02$), and presence of 3 or more CAD risk factors ($p = 0.02$). Association of FMD with Core-Lab-assessed CAD (≥50% stenosis) was not significant ($p = 0.08$). Multivariate regression analysis found age and diabetes were independent significant predictors of FMD.

Conclusion: Menopause and diabetes history influence BA FMD in women with chest pain. In particular, older women with chest pain and multiple CAD risk factors are predisposed to brachial artery endothelial dysfunction.

1142-8 Endothelial Dysfunction of Coronary Artery in Subjects With Impaired Glucose Tolerance

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Backgrounds and Methods: To determine whether impaired glucose tolerance affects vasomotion of coronary artery, we evaluated maximal increases of the coronary blood flow induced by intracoronary infusion of adenosine triphosphoric acid or acetylcholine (FN or FE, respectively), using quantitative coronary arteriography and intracoronary doppler-tipped guidewire in 169 subjects, whose glucose tolerance was graded by oral 75 g-glucose tolerance test. We also evaluated the contributions of other coronary risk factors and diabetic variables upon the vasomotion in subjects with impaired glucose tolerance (IGT).

Table 1

	DM (n = 38)	IGT (n = 97)	N (n = 34)
FN	153 ± 85%	181 ± 77%	189 ± 79%
FE	51 ± 30%	60 ± 39%	77 ± 50%

Table 2

	nRF	smoking	sIRI
Standard coefficient (F value)	−0.29 (8.2)	−0.24 (5.4)	−0.19 (4.3)

Results: FN in IGT was not different from that in subjects with diabetes mellitus (DM) or in subjects with normal glucose tolerance test (N). FE in IGT was lower than that in N (IGT vs N; p = 0.04, Table 1). By multiple stepwise regression analyses in IGT, number of coronary risk factors (nRF) proposed by Framingham Heart Study, smoking, and summation of insulin levels (sIRI) on glucose tolerance test were determinants for FE (multiple coefficient 0.48, Table 2). In followed-up subjects achieving two or more reduction of the nRF, or cessation of smoking, FE was improved (from 34 ± 19 to 76 ± 40%, p < 0.01).

Conclusions: These results suggest endothelial dysfunction of coronary artery is present even in subjects with impaired glucose tolerance, and clustering of coronary risk factors, smoking, and hyperinsulinemia contribute to the endothelial dysfunction.

1142-9 Effect of Vitamin C on Acetylcholine-induced Epicardial Coronary Vasoconstriction

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Background: Vitamin C (VC) has been shown to improve abnormal vasomotion in the forearm circulation of diabetics and smokers. We hypothesized that acute VC administration would ameliorate coronary endothelial dysfunction in patients without obstructive coronary artery disease.

Methods: Following diagnostic angiography, a 0.018" Doppler guidewire was placed in a major left coronary artery branch, and an infusion catheter positioned proximally. Acetylcholine (ACh) at estimated final concentrations of 10^{-7} and 10^{-6}M was infused for 4 min each. VC (2 gm i.v.) was given over 10 minutes, and ACh infusions were repeated. Cine-based quantitative coronary angiography (Quinton) was performed at baseline and during each ACh infusion, before and after VC.

Results: Intracoronary ACh produced vasoconstriction in six patients (3 M, 3 F), aged 49 ± 9 (mean ± SD) years. Five were current smokers, 3 were hypertensive and 2 had elevated LDL cholesterol (>160 mg/dl). Peak epicardial constrictor response to ACh before VC was 19 ± 10%, and 11 ± 9% afterwards (p = 0.06). VC had no effect on systemic hemodynamics or ACh-induced changes in average peak coronary flow velocity, coronary blood flow or coronary resistance.

Conclusion: Parenteral VC attenuated epicardial coronary vasoconstriction caused by ACh in patients with risk factors but without obstructive coronary artery disease. VC had no effect on the coronary resistance vasculature.

1142-10 Combined Effects of Estrogen Replacement Therapy and Lovastatin on Brachial Artery Endothelial Function

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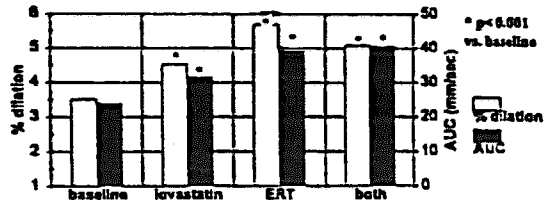
Background: Estrogen replacement therapy (ERT) and lipid-lowering drugs improve flow-mediated vasodilation (FMV). However, it is unclear if ERT plus lipid-lowering therapy is better than either therapy alone.

Methods: Twenty-three women (mean age 68 years) with coronary artery disease were enrolled in a randomized, blinded 3-period cross-over trial of Premarin 0.625 mg and Provera 2.5 mg, lovastatin 20 mg, or both. Brachial artery FMV (% dilation and area under diameter versus time curve (AUC)) were measured at baseline and after each 6-week treatment period.

Results: ERT plus lovastatin produced the greatest enhancement in FMV (% dilation: 46%; AUC 69%; p < 0.001 each). This improvement paralleled the reduction in LDL/HDL ratio (74%; p < 0.001) associated with combined therapy.



Conclusion: ERT plus lovastatin results in marked improvement in endothelium-dependent vasodilator capacity.

1143 Ventricular Shape, Response, and Remodeling

Tuesday, March 31, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 3:00 p.m.–4:00 p.m.

1143-23 The Onset of LV Failure in Pressure Overload Hypertrophy Is More Closely Related to Deleterious Chamber Remodeling Than to Myocardial Dysfunction

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To establish whether LV failure in pressure overload hypertrophy (POH) is due to the deleterious effects of progressive chamber remodeling or to alterations in intrinsic myocardial function, rats underwent aortic banding or sham surgery (S, n = 12). At 20 wk's after surgery, LV pressure-dimension (P-D) relations were constructed from echo measurements obtained during load manipulations *in vivo*. LV chamber and myocardial function were assessed *ex vivo* by the slopes of the LV pressure-volume (LV-Ees) or linearized LV stress-strain (Myoc.-Ees) relations, respectively. The extent of systolic chamber enlargment was assessed by the volume (V_0) and end-systolic diameter (ESD_0) intercepts of the pressure-volume and P-D relations, respectively. Rats were divided into those with LV failure (increased lung wt's), POH-F (n = 19), and those without failure, POH-NF (n = 25).