(23%). Over the two study periods, a smaller proportion of patients on bosentan than on placebo required epoprostenol therapy (2.8% versus 4.3%), additional therapy for PAH (28.6% versus 38.5%), or hospitalization (4.2% versus 13.0% for PAH-related and 16.0% versus 23.2% for all causes of hospitalization).
Conclusion: The benefit achieved in exercise capacity, dyspnea, and reduced need for additional therapy or hospitalization demonstrated in the initial 16-week BREATHE-1 study appears to be sustained when patients are followed for 28 weeks.

5:15 p.m.

825-6 **Long-Term Secondary Prevention With Folic Acid: No Effects on Clinical Outcomes (the GOES Extension Study)**

A. Liem, G. H. Reynierse-Buitenwerf, A. H. Zwinderman, J. W. Jukema, D. J. van Veldhuisen, Oosterschelde Hospital, Goes, The Netherlands

Purpose: Folic acid has favourable effects on vascular endothelium and lowers plasma homocysteine levels. In addition, homocysteine appears to be an independent risk factor for atherosclerotic disease. However, the value of folic acid in secondary prevention had seldom been tested. Two yr folic acid treatment in the randomized GOES study showed no reduction in clinical endpoints despite a 18% homocysteine reduction in patients on folic acid. Suggested was that the follow up could have been too short, therefore the study was extended with another 18 months Tx. Here we report results of the extended Goes trial, an open-label trial with folic acid 0.5 mg per day in a patient population with stable coronary artery disease (CAD).
Methods: 593 Patients were included in this study; 300 were randomized to folic acid and 293 served as controls. Mean follow-up time was 42 months. At baseline all patients had been on statin therapy for a mean of 3.2 years.
Results: In patients treated with folic acid plasma homocysteine levels decreased with 18% from 12.0 ± 4.8 to 9.4 ± 3.5 µmol/L, while these levels remained unaffected in the control group (p <0.001 between groups). The primary endpoint (all-cause mortality and a composite of vascular events) was encountered in 75 (25.0%) patients in the folic acid group and in 75 (25.6%) patients in the control group (RR 0.98; p=NS). Also in the quartile of patients with the highest baseline homocysteine levels (>13.7 micromol/L) no salutary effects of folic acid Tx could be demonstrated. In a multifactorial survival model with adjustments for clinical factors the most predictive laboratory parameters were, in order of significance, levels of creatinine clearance, and homocysteine.
Conclusions: Within 3.5 years folic acid does not seem to reduce clinical endpoints in patients with stable CAD while on statin treatment. Homocysteine might therefore merely be a marker of disease than a causal risk factor. Thus, until more trials will become available, low dose folic acid supplementation should be treated with reservation.

ORAL CONTRIBUTIONS

831

Atherosclerotic Plaque, Inflammation, and Oxidative Stress: Clinical Studies

Tuesday, March 09, 2004, 8:30 a.m.-10:00 a.m.
Morial Convention Center, Room 265

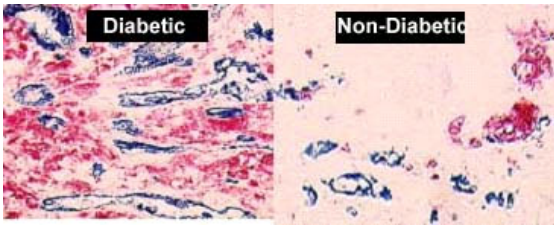
8:30 a.m.

831-1 **Ruptured Diabetic Atherosclerotic Plaques Have More Inflammation and Neovascularization Than Ruptured Plaques From Patients Without Diabetes**

K. Raman Purushothaman, William N. O'Connor, Dario Echeverri, Chikezie Amadi, Juan J. Badimon, Valentin Fuster, Pedro R. Moreno, Mount Sinai Medical Center, New York, NY, University of Kentucky, Lexington, KY

Background: Plaque rupture may be asymptomatic or precipitate acute thrombotic events, and patients with diabetes mellitus (DM) are at higher risk for acute events than patients without DM. To evaluate if this difference is related to plaque composition, we quantified inflammation and neovascularization in ruptured aortic plaques from patients with/without DM.
Methods: Neovessels and macrophages/T cells were identified by CD34 (blue) and CD68/CD3 (red) bicolor immunohistochemistry (Figure) in 41 DM ruptured and compared to 34 non-DM ruptured plaques.
Results: See table.
Conclusion: Ruptured plaques from DM have increased inflammation and neovascularization supporting plaque composition as a contributor for the increased incidence of atherothrombotic complications among DM population.

Neovessel Unit (Total Count)	**Diabetic Ruptured Plaques (n=41)**	**Non-Diabetic Ruptured Plaques (n=34)**	***P* Value**
Neovessels in the outer media	173 ± 61	104 ± 42	0.0001
Neovessels in the inner media	124 ± 52	48 ± 24	0.0001
Neovessels in the intima	27 ± 20	13 ± 10	0.0001
Inflammation score (0-2)	1.8 ± 0.5	1.5 ± 0.5	0.0001

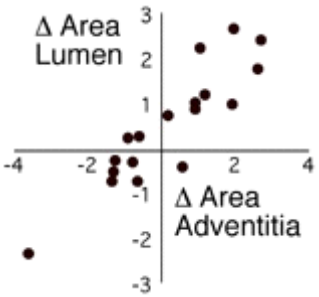


8:45 a.m.

831-2 **Coronary Lumen Change Is Determined Primarily by Adventitial Remodeling Rather Than Plaque Change During Therapy**

David T. Linker, B. Greg Brown, University of Washington, Seattle, WA

Background: Remodeling of coronary arteries has been demonstrated during plaque regression, but the contribution to lumen change is unclear.
Methods: Intracoronary ultrasound automated pull-backs were recorded on S-VHS tape both before and after twelve months of lipid-lowering therapy in a target coronary artery in 18 subjects with known coronary artery disease. The pullbacks were digitized and calibrated, and identical segments with plaque in the target artery were identified on the pre- and post-therapy images. The lumen and adventitia-media borders were manually traced on all images in the segment that allowed image interpretation, with the longitudinal position noted. The plaque and adventitial volumes were calculated by a numerical integration of the area over the longitudinal length. The mean plaque adventitial, and lumen areas in sq. mm were calculated based on plaque and adventitial volume and segment length.
Results: The change in mean lumen area was poorly correlated with the change in mean plaque area (R = 0.256, p = 0.306). Lumen area change was strongly correlated with adventitial area change (R = 0.903, p <0.001, see figure below) The relationship was Change in mean lumen area = 0.712 x Change in mean adventitial area + 0.347 mm2.
Conclusions: The changes in lumen area after one year of lipid-lowering therapy are better correlated with adventitial change than with plaque change, indicating that arterial remodeling is an important determinant of lumen change.



9:00 a.m.

831-3 **Circulating Endothelial Progenitor Cells Predict Coronary Artery Disease Severity**

Geoffrey A. Kunz, Grace Liang, Florim Cuculoski, David Gregg, Korkut Vata, Linda Shaw, Pascal Goldschmidt-Clermont, Chunming Dong, Doris Taylor, Eric Peterson, Duke University, Durham, NC

Background: Circulating endothelial progenitor cell (EPC) counts are hypothesized to play an important role in preventing atherosclerosis. EPC counts have been found to be inversely related to traditional coronary artery disease (CAD) risk factors, yet their association to CAD severity remains unknown.
Methods: We measured EPC counts by quantitative cell culture in 122 patients undergoing diagnostic cardiac catheterization. The association between patients' EPC count and the presence of multi-vessel CAD and of traditional cardiac risk factors was assessed using logistic regression analysis. **Results:** The median age of the study population was