ORAL CONTRIBUTIONS

848FO

Featured Oral Session...Peripheral Arterial Disease

Tuesday, March 09, 2004, 2:00 p.m.-3:30 p.m.
Morial Convention Center, Room 260

2:15 p.m.

848-2 Utilizing of the Fibrin Meshwork to Induce Neovascularization in Patients With Chronic Limb Ischemia: Long-Term Follow-Up

Nicholas N. Kipshidze, Kote Kipiani, Nutsa Beridze, Gary Roubin, Mykola Tsapenko, Mohammad Shehzad, Jeffrey W. Moses, Nodar N. Kipshidze, Lenox Hill Heart and Vascular Institute and CRF, New York, NY, National Center of Angiology and Vascular Surgery, Tbilisi, Georgia

Objectives: We assessed the feasibility and efficacy of fibrin as an angiogenic substance alone and/or as a carrier for vascular endothelial growth factor (VEGF) in patients with chronic limb ischemia.
Methods: 23 patients with chronic limb ischemia were randomized for treatment: Group 1(control): 7 patients received only a saline injection; Group 2: 9 received intramuscular injection of fibrin and Group 3: 7 received the fibrin composition with Deferoxamine and added $VEGF_{165}$, The fibrin meshwork was introduced into the popliteal area of the diseased limbs using a dual syringe system (one contained thrombin solution [1mg, 5000U] and one contained fibrinogen [1 mg, Baxter Hyland Immuno] solution). In group 3, Deferoxamine (100 µg) and 500 µg of $VEGF_{165}$ were added to the fibrinogen solution.
Results: The ankle-brachial index (ABI) in the Group 1 was 0.46 ± 0.12 before beginning the trial and was 0.41 ± 0.16 at the 3 month follow-up (FU). The ABI in patients treated with fibrin only increased from 0.43 ± 0.20 to 0.73 ± 0.12 at six months FU ($p<0.05$ vs. baseline data and vs. control group). In the Group 3 the ABI increased from 0.49 ± 0.12 to 0.78 ± 0.19 ($p<0.05$ vs. control). Transcutaneous oxygen pressure ($Tc0_2$) increased in the Group 2 from 20.1 ± 4.4 mmHg to 41.5 ± 3.2 mmHg and in the Group 3 from 19.8 ± 4.5 mmHg to 47.8± 2.6 mmHg at 3 months FU as compared to it decrease from 19.1 ± 3.6 mmHg to 16.3±4.7 mmHg in the control group. In the control group 5 patients had undergone below the knee amputation at 3-6 month FU. Only 1 patient from the Group 2 had amputation at 5 months FU. At 3 year FU 1 more patient from the Group 2 underwent below knee amputation. Thus, at 3 year FU clinical improvement was sustained in 6 patients from the Group 2 and in 6 patients from the Group 3.
Conclusion: IM injection of Fibrin is safe and appears to be an efficient method to treat chronic limb ischemia. These findings indicate that use of fibrin may be a novel and simple method for inducing therapeutic angiogenesis.

2:30 p.m.

848-3 Estrogen Plus Progestin and the Risk of Peripheral Arterial Disease

Judith Hsia, Michael Criqui, Rebecca Rodabough, Helaine Resnick, Jane Kotchen, Denise Bonds, Matt Allison, Pat Caralis, Lawrence Phillips, Kamal Masaki, Robert D. Langer, George Washington University, Washington, DC

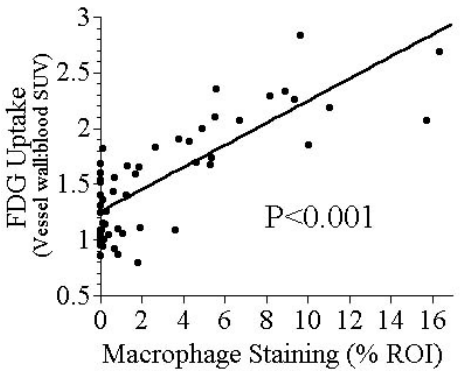
Background: In randomized trials, postmenopausal hormone therapy has had variable effects on peripheral arterial intima-media thickness. Combination therapy with estrogen plus progestin (E+P) did not affect peripheral arterial events in women with prior coronary heart disease. This analysis evaluates the impact of E+P on peripheral arterial events among generally healthy women in the Women's Health Initiative randomized trial.
Methods: The Estrogen Plus Progestin trial assigned 16,608 postmenopausal women, age 50-79 years, to daily conjugated estrogens 0.625 mg with medroxyprogesterone acetate 2.5 mg or to placebo. Peripheral arterial disease was a prespecified secondary outcome.
Results: During 5.6 years of follow up, carotid artery disease (0.08%/y), lower extremity arterial disease (0.06%/y) and abdominal aortic aneurysm (0.02%/y) requiring hospitalization were infrequent, and did not differ between treatment groups (HR 0.89, 95% CI 0.63, 1.25). In the two years following randomization, risk of peripheral arterial events was slightly greater among women assigned to active E+P (HR 1.33 in year 1, HR 1.27 in year 2), but this difference subsided thereafter (HR 0.85 and 0.87 in years 5 and ≥6, respectively); p for trend 0.39. In multivariate analysis, independent predictors of incident peripheral arterial disease among women assigned to placebo included age, diabetes (HR 3.96, 95% CI 1.93, 8.10; $p<0.001$), current smoking (HR 4.65, 95% CI 2.38, 9.09; $p<0.001$) and prior peripheral arterial disease (HR 20.26, 95% CI 9.13, 44.97; $p<0.001$). Among women assigned to combination hormone therapy, associations were similar except that prior coronary heart disease, which was reported by 2.4% of women at baseline, also independently predicted peripheral arterial events (HR 4.13, 95% CI 1.81, 9.41; $p<0.001$). Subgroup analysis identified no significant interactions between E+P and baseline characteristics with regard to peripheral arterial disease risk.
Conclusions: Estrogen plus progestin does not confer protection against peripheral arterial disease among generally healthy postmenopausal women.

2:45 p.m.

848-4 Noninvasive Characterization of Carotid Plaque Inflammation in Humans With FDG-Positron Emission Tomography

Ahmed Tawakol, Raymond Q. Migrino, Henry Gewirtz, James E. Muller, Thomas Brady, Alan J. Fischman, Massachusetts General Hospital, Boston, MA

Introduction: Atherosclerotic plaques that cause MI and stroke are inflamed. We previously demonstrated that that positron emission tomography (PET) with 18F-fluorodeoxyglucose (FDG) characterizes plaque inflammation in an animal model of atherosclerosis. **Methods:** To test the hypothesis, in humans, that plaque inflammation can be characterized using FDG-PET, 6 patients with moderate to high-grade carotid stenoses underwent PET imaging 3 hours after FDG administration (25 mCi). Local uptake of FDG was determined non-invasively by measuring Standardized Uptake Values (SUV) within the vessel wall. Thereafter, subjects underwent carotid endarterectomy (CEA), at which time carotid specimens were collected and examined for macrophage staining. Carotid FDG uptake (determined by PET, prior to CEA) was subsequently compared to macrophage density (determined histologically). **Results**: Moderate to severe carotid inflammation was observed in the histologic specimens of 3/6 patients. Moreover, FDG uptake, determined non-invasively prior to CEA (plaque:blood SUV) correlated with histologic evidence of inflammation, ($r=0.80$, $p<0.001$, figure). **Conclusions**: These preliminary findings support the hypothesis that carotid plaque inflammation can be characterized non-invasively by FDG PET. Such metabolic information has potential to contribute to the assessment of stroke risk from carotid plaques and underscores the utility of metabolic imaging to characterize vascular inflammation in humans.



3:00 p.m.

848-5 The Impact of Percutaneous Renal Artery Revascularization on QT Dispersion in Patients With Hypertensive Heart Disease

Adam E. Berman, Patty Uber, Mandeep R. Mehra, Ochsner Clinic Foundation, New Orleans, LA

Objective: To evaluate the efficacy of percutaneous renal artery revascularization (PRAR) on the reduction of indices of ventricular repolarization in homogeneity in patients with underlying hypertensive heart disease (HHD).
Methods: We retrospectively analyzed all patients who underwent percutaneous renal artery intervention for angiographically proven renal artery stenosis > 70% over a 4 year period. We evaluated predictors of benefit from renal artery intervention including age, CHF, LVH, LVEF, and prior MI. Patients with electrocardiographic evidence of HHD were compared to similar patients undergoing renal artery intervention without evidence of HHD. Baseline and follow-up intervals including QRS, QT, QTc, and QT dispersion (QTd) were measured manually. Patients taking Class I or III antiarrhythmic or angiotensin converting enzyme inhibitor therapy were excluded from the study.
Results: 39 patients were identified with underlying HHD at the time of percutaneous renal artery intervention (13 males, mean 68±8 yrs). 41% had evidence of prior MI, 33% had prior CABG, LVEF = .46 ± .16, and 56% had a history of CHF. Mean baseline values were QRS 105±21 ms, QTc 445 ±33 ms, and QTd 94±32. At 24 month follow up mean QTd was 46±16 ms ($p<.0001$).
Conclusions: PRAR in the presence of HHD and renal artery stenosis is associated with benefits beyond blood pressure control and renal preservation. PRAR may alter indices of ventricular refractoriness with a greater magnitude than the decrease in LVH would suggest.

	P value	R value
Age	0.05	
Absolute QTd	< 0.0001	0.9
LVH @ baseline	0.02	0.4
CHF	0.05	0.3