

863-3

Comparison of Medical Treatment With Percutaneous Closure of Patent Foramen Ovale for Secondary Prevention of TIAs and Strokes: A Case-Control Study

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Background: Patients with transient ischemic attack (TIA) and stroke related to patent foramen ovale (PFO) are at risk for recurrence. The best treatment for secondary prevention is not known. The purpose of this study was to compare the risk of recurrence between medical treatment and percutaneous PFO closure in patients with TIA and stroke related to PFO.

Methods: A total of 311 patients with TIA or stroke related to PFO were retrospectively included in a case-control study. 161 patients received medical treatment (oral anticoagulation: n=80, platelet inhibitors: n=81), and 150 patients underwent percutaneous PFO closure. The actuarial risk of recurrence was calculated and compared between the two groups.

Results: The mean age of the study population was 50±13 years. The two groups were matched for age, sex and presence of an associated atrial septal aneurysm. The overall mean follow-up was 2.3±1.8 years, 2.4±1.9 years in the medical treatment group and 2.2±1.5 years in the percutaneous PFO closure group. The average annual TIA and/or stroke rate was 6.6% in the medical and 4.5% in the endovascular group (p=0.08). There were no recurrent major strokes in the percutaneous PFO closure group compared with 7 recurrent events in the medically treated patients (p<0.02). Patients with 2 or more events before enrollment were at higher risk for recurrence when treated medically (11% per year) compared to percutaneous PFO closure (5% per year; p=0.01). Multivariate logistic regression analysis identified arterial hypertension, and more than one embolic event at baseline as significant predictors for recurrence (OR 2.2, 95% CI 1.1-4.9).

Conclusions: Our results indicate a non-significant trend towards decreased recurrence for the combined endpoint of TIA and stroke, and a significant decrease in recurrent major strokes in patients with PFO and presumed paradoxical embolism undergoing percutaneous PFO closure compared with medical treatment. The subgroup of patients with 2 or more events before enrollment had a significantly lower recurrence rate after percutaneous PFO closure compared with medical treatment. Confirmation of these results by a prospective randomized trial with longer follow-up is needed.

2:45 p.m.

863-4

Effect of Vitamin C on Atherosclerosis Progression and Cardiovascular Events in a Ten-Year Randomized Study (San Valentino)

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Background: subclinical carotid-femoral atherosclerotic lesions evolution and cardiovascular events in 10 years have been defined by ultrasound in a sample of 10000 subjects. **Methods:** Four classes were considered (by high resolution ultrasound of the carotid-femoral bifurcations) at inclusion: I= normal wall; II= wall thickening and granulation; III non-stenosing (50%) plaques. **Results:** In the main group the event rate in class I at 10 years was <1%; in II it was 8.6%; in III, 39% and in IV, 81%. A separate, comparable subgroup of 1032 subjects was randomised for Vitamin C (1g/day) and no-treatment to evaluate effect on cardiovascular events and on progression. When 855 subjects (444 in the treatment group and 411 in the control group) completed the 10-year follow-up the analysis of the differences between the two groups indicated that in class I there were no differences between groups; in II there was an event rate of 3% in the Vit C group vs 8% in controls; in III 6% vs 36% in controls; in IV 44% vs 82% in controls (P<0.02). Progression (class increase) was observed in class II in 3% in the Vit C group vs 13% in controls; in class III in 6% vs 34% in controls and in class IV in 21% vs 67% in controls (P<0.022). In conclusion Vit C supplements, in a 10-year follow-up, significantly reduce the incidence of cardiovascular (including coronary) events and the progression rate of carotid-femoral bifurcation atherosclerotic lesions. Also the number of cardiovascular deaths is reduced (43% less in the Vit C group) (P<0.01).

3:00 p.m.

863-5

The Ankle-Brachial Index: A Predictor of Cardiovascular Mortality. The San Valentino Vascular Screening Study

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The prognostic value of alterations in the ankle-brachial index (ABI) is not well known in our population. This study was conducted to know whether ABI predicts morbidity and mortality in a population of subjects aged > 55. **METHODS:** The study was planned as a large population study based on non-invasive vascular tests; 16,700 subjects (48% men, mean age 60.2, SD 6) were studied evaluating the presence of peripheral arterial disease (PAD) and intermittent claudication (IC). **RESULTS:** During the 8 years (mean 5.5) of follow-up 11.6 subjects died (2.5% of defined cardiac causes; 0.92% suddenly). According to the Rotterdam study model, compared to subjects with ABI>0.9 and no IC: a) subjects with IC and ABI < 0.9 had an age and sex adjusted increased risk of 2.2 for all causes mortality (hazard ratio = HR 2.1, 95% Conf Int = CI 1.3-3.2); b) subjects with ABI<0.9 and non IC had a risk of 1.5% (HR 1.5, 95% CI 1.2-2.0); c) subjects with ABI>0.9 and IC had a risk of 1.4 (HR 1.3, 95% CI 0.5-3.3) not significantly different from those

with ABI> 0.9 without IC. Additional adjustments for the presence of stroke, myocardial infarction, diabetes, hypolipidemia, smoking at baseline slightly reduced the risk. The same pattern was observed for the risk of cardiovascular mortality. **CONCLUSIONS:** ABI is an important predictor of cardiovascular and all-cause mortality and cardiovascular events. Our results, in a different population, are comparable to data from the Rotterdam Study and therefore ABI value is comparable in different population/countries.

3:15 p.m.

863-6

Secular Trends and Long-Term Survival in Thromboangiitis Obliterans

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Background: Thromboangiitis obliterans (TAO) is an unusual disorder of medium and small arteries. Secular trends and long term prognosis in TAO have not been described. **Methods:** We reviewed the medical records of all TAO patients (n=343) registered at Mayo Clinic from 1/1/1976 to 12/31/1999. The inclusion criteria were: Age >50, tobacco use, objective evidence of medium or small arterial disease (angiography 45%, biopsy 11%, noninvasive tests 44%), and no other cause. 108 patients were excluded. **Results:** The mean age of the 235 TAO patients was 33.5 ± 8.5 yrs. The percentage of female patients increased from 1976 to 2000 (Table, p=.003 for trend). Four patients had a family history of TAO and 120(51%) had a family history of cardiovascular disease. 153 (65%) patients presented with intermittent claudication, 170 (73%) had rest pain, 92 (39%) patients had Raynauds phenomenon, and 82 (35%) had superficial thrombophlebitis. Ischemic ulceration or gangrene was present in 164 (70%). By Kaplan-Meier analysis the rate of any amputation was 61.5% at 17 years. The rate of amputation per person year was similar before and after 1990 (.077 vs .087), 5.1% of TAO patients died during follow-up. **Conclusions:** These data suggest that the percentage of women diagnosed with TAO is increasing. The rate of amputation in the past decade remains high despite advances in medical therapy; nonetheless, the mortality rate is low at 5.1%.

Gender by Year of Onset of TAO

Year of Onset

| Gender | 1976-80 | 1981-85 | 1986-90 | 1991-95 | 1996-99 | Total |
|--------|------------|------------|------------|------------|-----------|-------------|
| Female | 6 (15.8%) | 11 (26.8%) | 18 (40.9%) | 15 (50.0%) | 4 (36.4%) | 54 (32.9%) |
| Male | 32 (84.2%) | 30 (73.2%) | 26 (59.1%) | 15 (50.0%) | 7 (63.6%) | 110 (67.1%) |

POSTER SESSION

1199 Coronary Calcification, Thrombosis, and Vascular Inflammation

Tuesday, March 19, 2002, 3:00 p.m.-5:00 p.m.

Georgia World Congress Center, Hall G

Presentation Hour: 3:00 p.m.-4:00 p.m.

1199-69

Activation of Toll-like Receptor 4 in Adventitial Cells by Lipopolysaccharide Induces Neointima Formation in a Mouse Model

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Background: Previously, we demonstrated that the gram negative bacterium *Chlamydia pneumoniae* is frequently present in the adventitia of atherosclerotic coronary arteries. The toll-like receptor 4 (TLR4) is identified as the transmembrane receptor of lipopolysaccharide (LPS) and heat shock protein 60, which are both components of *Chlamydia pneumoniae*. We recently demonstrated that the TLR4 is expressed in adventitial fibroblasts. Activation of this receptor induced the release of chemokines and other cytokines, like IL-6. The aim of the present study was to determine whether activation of the TLR4 in the adventitia by LPS induces neointima formation in an in vivo situation.

Methods: BALB/C mice were used. In 18 mice, a non-constrictive polyethylene cuff (ID 4mm, OD 8mm) was placed loosely around the right femoral artery. In 9 control mice 2% gelatin was injected in the peri-adventitial space between the cuff and the artery. In the other 9 mice 2% gelatin with LPS (4 µg) was injected between cuff and artery. The mice were sacrificed after 3 weeks.

Results: The intimal area in the LPS treated group was significantly larger compared to the controls (9133 ± 5143 versus 2353 ± 3228 µm², respectively, p=0.003). Intima to media ratio was larger in the LPS treated group compared to the controls (0.95 ± 0.51 versus 0.23 ± 0.27, respectively, p=0.002).

Conclusion: Adventitial lipopolysaccharide application augmented neointimal formation induced by a cuff. This result implies that activation of adventitial cells via toll-like receptor 4 might participate in arterial obstructive diseases.