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also quantified from each biopsy. Analysis was by enzyme-linked immunoabsorbent assay.

The biopsy specimens of the anterior sites showed no difference in MMPs or TIMPs concentrations in ruptured vs nonruptured aneurysms. MMP-8 and MMP-9 levels were elevated from the biopsy specimens of 12 ruptured sites compared with the 12 paired anterior wall biopsy sites (MMP-8, $P < .001$; MMP-9, $P = .01$). Other MMPs and TIMPs showed no difference. Expression of MMP-8 and MMP-9 was mediated by native mesenchymal cells. Expression was independent of inflammatory infiltrate.

Comment: The article suggests a final common pathway in the breakdown of extra cellular matrix in AAA rupture. The corollary, of course, is that inhibition of MMP-8 or MMP-9 activity could potentially decrease the risk of aneurysm rupture. Perhaps someday patients with aortic aneurysms unsuitable for repair will be treated with inhibitors of MMP-9 or MMP-8 in an attempt to prevent death from aneurysm rupture.

Asymptomatic central venous stenosis in hemodialysis patients

Levit RD, Cohen RM, Kwak A, et al. Radiology 2006;238:1051-6

Conclusion: In patients with a hemodialysis access graft and an asymptomatic central venous stenosis (CVS) of >50%, treatment of the CVS results in more rapid stenosis progression compared with a nontreatment approach.

Summary: The authors evaluated the natural history of >50% asymptomatic CVSs in hemodialysis patients. Outcome of serial treatment of CVS with percutaneous catheter-based techniques (PTA) was also evaluated. All patients in this study required maintenance procedures for their dialysis access.

Between 1998 and 2004, 35 patients (19 men, 16 women), with a mean age of 58.7 years, were found to have asymptomatic CVS of >50%. CVS was measured by using venograms obtained before and after PTA. Patients with arm swelling, multiple CVSs, or indwelling catheters, were excluded. CVS progression was calculated by comparing degrees of stenoses with serial venographic examinations.

The mean severity of CVSs before intervention was 71% (range, 50% to 100%), with 62% of lesions having associated collateral vessels. Twenty eight percent of CVSs were not treated. The mean degree of stenosis in the untreated group was 72% (range, 30% to 100%). Mean progression of stenosis in the untreated group was −0.8% point per day. No untreated CVS progressed to symptoms, stent placement, or developed additional CVS.

PTA was used to treat 62 CVS lesions (72%). The mean degree of stenosis in the treated group was 74% (range, 50% to 100%) before and 40% (range, 0% to 75%) after treatment. In the treated group, mean progression of CVS was 0.21% per day after treatment. Six of the 62 treated CVS lesions were monitored, with symptomatic escalation of the CVS as manifested by arm swelling, need for stent placement, or development of additional CVS lesions.

Comment: Treatment of an asymptomatic CVS in a dialysis patient is not a good thing. One is reminded of the old adage that it is wise to avoid poking a skunk. A major weakness of this study is that the patients were undergoing maintenance procedures for their dialysis access. We do not know if the CVS contributed to the need for the dialysis access maintenance. It would be interesting to know if there was a higher rate of repeat procedures for maintenance of dialysis access in patients with treated vs untreated CVS.

Balloon angioplasty versus implantation of nitinol stents in the superficial femoral artery

Schillinger M, Sabeti S, Loewe C, et al. N Engl J Med 2006;354:1879-88

Conclusion: At 6 months and 12 months, percutaneous angioplasty of superficial femoral artery stenoses with primary implantation of a self-expanding nitinol stent is superior to percutaneous angioplasty of superficial femoral artery stenoses with optional secondary stenting.

Summary: The authors evaluated whether primary implantation of a self-expanding nitinol stent in the superficial femoral artery yielded superior anatomic and clinical benefits compared with a policy of percutaneous transluminal angioplasty with stenting reserved as a secondary option. The study screened 252 patients for participation, of which 104 were eligible for randomization. These patients all had chronic limb ischemia and claudication due to stenosis or occlusion of the superficial femoral artery. Fifty-one patients underwent primary stent implantation, and 53 patients underwent angioplasty with secondary stent implantation.

The primary study end point was a rate of restenosis of at least 50% in the treated segment 6 months after intervention. Restenosis was determined by computed tomography angiography or digital subtraction angiography and was measured in the worst angiographic view of the narrowest stent segment or in the 10-mm segments proximal and distal to the treated superficial femoral artery segment. Secondary end points included restenosis as determined by duplex scanning at 3, 6, and 12 months. Rutherford's stage of peripheral arterial disease maximal walking capacity on the treadmill at 24 hours and at 3, 6, and 12 months were also determined. Amputation and death at 6 and 12 months were additional secondary end points. The ankle brachial index was measured at 24 hours, and at 3, 6, and 12 months.

The mean length of the treated arterial segment was 132 ± 71 mm in the primary stent group vs 127 ± 55 mm in the angioplasty/secondary stent group. In the secondary stent group, 17 patients (32%) had secondary stenting. At 6 months, the rate of restenosis on angiography was 43% in the angioplasty group and 24% in the primary stent group ($P = .05$). At 12 months, rates of restenosis were 63% in the angioplasty group and 37% in the primary stent group as determined by duplex scanning ($P = .01$). No amputations occurred in either group at 6 or 12 months, and one patient died in the primary stent group at 12 months. Patients in the stent group walked farther on the treadmill at 6 months (average distance, 363 vs 270 meters; $P = .04$) and at 12 months (average distance, 387 vs 267 meters; $P = .04$). At 12 months the ankle brachial index was higher in the stent group than in the angioplasty group ($P = .03$). The rate of stent fracture was 2%.

Comment: This study suggests that the primary use of nitinol stents may improve what is a relatively poor result of angioplasty and secondary stenting of the superficial femoral artery. Given that previous studies have suggested that an exercise program is as effective as or more effective than angioplasty of the superficial femoral artery, it is a shame that the authors did not include a control group in their trial. It would also have been nice to know whether the increased walking distance measured on the treadmill translated to an increased quality of life for the patients in this study. Nevertheless, it can be said that given the end points of this trial, the use of primary stenting with nitinol stents for angioplasty of the superficial femoral artery, was superior to selective stenting after angioplasty of the superficial femoral artery.

Homocysteine lowering with folic acid and B vitamins in vascular disease

The Heart Outcomes Prevention Evaluation (HOPE) Two Investigators. N Engl J Med 2006;354:1567-77

Conclusion: In patients with vascular disease, supplemental folic acid, vitamin B6, and B12 do not reduce the risk of major cardiovascular events.

Summary: In observational studies, higher homocysteine levels have been associated with increased rates of stroke and heart disease. It is known vitamins B6, B12, and folate can lower homocysteine levels. The purpose of this study was to determine whether the risk of major cardiovascular events in patients with vascular disease could be reduced with the use of supplemental vitamin therapy.

Patients who were aged ≥55 years and who had vascular disease or diabetes were randomly assigned either treatment with placebo or a combination of 2.5 mg of folic acid, 50 mg of vitamin B6, and 1 mg of vitamin B12. The study enrolled 5552 patients aged >55 years and monitored them for an average of 5 years. The primary end point was a composite of death from myocardial infarction, stroke, and other cardiovascular causes.

In the treatment group, mean plasma homocysteine levels decreased by 2.4 μm/L (0.3 mg/L). In the placebo group, mean plasma homocysteine increased by 0.8 μm/L (0.1 mg/L). Primary outcome end points occurred in 18.8% of the active therapy group (n = 519), and in 19.9% (n = 547) of the placebo group (relative risk [RR], 0.95; 95% confidence interval [CI], 0.84 to 1.07; P = .41). Compared with placebo, vitamin treatment did not decrease risk of death from cardiovascular causes (RR, 0.96; 95% CI, 0.81 to 1.13) or myocardial infarction (RR, 0.98; 95% CI, 0.85 to 1.14). More patients in the treated group were hospitalized for unstable angina (RR 1.24; 95% CI, 1.04 to 1.49). There were fewer strokes in the active treatment group than the placebo group (RR, 0.75; 95% CI, 0.59 to 0.97).

Subgroup analysis indicated no heterogenicity of treatment effect in patients from regions where food had mandatory supplementation of folate vs regions where food was not supplemented. There was no difference in treatment affects in patients with the top third of baseline homocysteine levels or in the patients with the top fifth of homocysteine levels. With adjustments for age, sex, and treatment assignment, baseline homocysteine level as a continuous measure was a predictor of cardiovascular events.

Comment: Multiple trials have now demonstrated a lack of efficacy of supplemental vitamin therapy to decrease cardiovascular events. This is despite documented lowering of homocysteine levels by the vitamin therapy. This discordance between epidemiology and results of clinical trials is similar to that noted for estrogen and antioxidant vitamins. It may be that the epidemiologic data of homocysteine are confused by confounding variables that cannot be completely adjusted for in multivariable analysis. It may, however, simply be that homocysteine is a marker but not a cause of vascular disease.

Massive pulmonary embolism

Kucher N, Rossi E, DeRosa M, et al. Circulation 2006;113:577-82

Conclusion: Mortality of pulmonary embolism in patients with massive pulmonary embolism (PE) is not reduced by thrombolysis or embolectomy. There does appear to be reduced mortality in patients with massive PE who have placement of inferior vena cava filters.

Summary: The International Cooperative Pulmonary Embolism Registry (ICOPER) enrolled 2454 consecutive patients with acute PE from January 1995 through November 1996. Fifty-two institutions in 7 countries were represented. There were 2392 patients with acute PE and known systolic blood pressure at presentation. Massive PE was defined as a systolic arterial pressure <90 mm Hg at presentation. Massive PE was present in 108 patients (4.5%), and 2284 patients (95.5%) had nonmassive PE. Sixteen patients with massive PE and 29 patients with nonmassive PE had the diagnosis of PE at autopsy ($P < .01$). For patients with massive PE, the 90-day mortality rate was 52.4% (95% confidence interval [CI], 43.3% to 62.1%). For patients with nonmassive PE, the 90-day mortality rate was 14.7% (95% CI, 13.3% to 16.2%). Within 90 days, recurrent PE occurred in 12.6% of patients with massive PE and in 7.6% with nonmassive PE ($P < .001$). In patients with massive PE, thrombolysis was performed in 33 patients, catheter embolectomy in one, and surgical embolectomy in three, for an overall active intervention rate for massive PE of 32%. These treatments were withheld in 68% (n = 73).

The 90-day mortality rate was not reduced with thrombolytic therapy: thrombolysis, 46.6% (95% CI, 31.1 to 64.8%) vs no thrombolysis, 55.1% (95% CI, 44.3% to 66.7%; hazard ratio 0.79; 95% CI, 0.44 to 1.43). The incidence of recurrent PE at 90 days was 12% in patients with and without thrombolytic therapy ($P = 0.99$). Eleven patients received an inferior vena cava filter. None of these patients had recurrent PE within 90 days, and 10 (90.9%) survived at least 90 days. Inferior vena cava filters were associated with a decreased 90-day mortality (hazard ratio, 0.12; 95% CI, 0.02 to 0.85).

Comment: It is probably wrong to conclude from these data that thrombolytic therapy cannot reduce mortality in patients with massive pulmonary embolism syndrome. ICOPER is a registry. Patients receiving thrombolytic therapy may have been the worst among the worst. The apparent significant reduction in mortality associated with inferior vena cava filters deserves further investigation, but it may also reflect those patients who are actually well enough to receive a filter. Clearly, improved and more standardized treatment of massive PE syndrome is needed.