

likely place them into the 2% of patients who have a "high" annual effective dose of radiation. Diagnostic cardiac catheterization has an average effective dose of 7 mSv and a percutaneous coronary intervention an average of effect of 15 mSv. It is obvious vascular surgical patients may be among those most intensively exposed to radiation through medical imaging procedures.

Fluvastatin and Perioperative Events in Patients Undergoing Vascular Surgery

Schouten O, Boersma E, Hoeks SE and the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. *N Engl J Med* 2009;361:980-9.

Conclusion: Perioperative fluvastatin therapy is associated with an improvement in post-operative cardiac outcome in patients undergoing vascular surgery.

Summary: To investigate the effects of statin medications on patients undergoing vascular surgery the authors conducted the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography III trial (DECREASE III). The hypothesis was that perioperative statin therapy would reduce post-operative incidents of cardiac events in patients undergoing elective vascular surgery.

This was a double blind placebo controlled trial where patients not previously treated with a statin were, in addition to a beta blocker, randomized to either 80 mg of extended-release fluvastatin, or placebo, once daily prior to undergoing vascular surgery. Lipid levels, interleukin-6 levels, and C-reactive protein were measured at randomization, before surgery and in follow-up. The primary endpoint was the occurrence of myocardial ischemia defined as a release of troponin-T, transient electrocardiographic abnormalities, or both, within 30 days of surgery. Secondary endpoint was a composite of death from cardiovascular causes and myocardial infarction.

There were 250 patients assigned to the fluvastatin group and 247 to the placebo group. Randomization was a median of 37 days before vascular surgery. In the fluvastatin group levels of low-density lipoprotein cholesterol, total cholesterol, C-reactive protein and interleukin-6 were significantly reduced but were unchanged in the placebo group. Myocardial ischemia postoperatively occurred in 27 patients (10.8%) of the fluvastatin group, and 47 patients (19.0%) of the placebo group (hazard ratio 0.55; 95% CI, 0.34 to 0.88; $p=0.01$). Death from myocardial infarction or cardiovascular causes occurred in 12 patients (4.8%) in the fluvastatin group and in 25 patients (10.1%) in the placebo group (hazard ratio, 0.47; 95% CI, 0.24 to 0.94; $p=0.03$). There was no increase in adverse events in the fluvastatin group compared to the placebo.

Comment: This paper provides the strongest evidence to date of the benefits of statin therapy in patients undergoing vascular surgery. Statins were beneficial in patients undergoing carotid endarterectomy, lower extremity revascularization and in patients undergoing both open and endovascular aortic surgery. For several years vascular surgeons have thought that whenever possible their patients should be on a statin medication prior to operation. The type of medication and dosage was unknown. The current study provides us at least some guidelines for one particular drug and one particular dosage for patients undergoing primarily elective vascular surgery. We still need additional data as to the minimal time preoperatively that patients can be treated with statins to achieve what appears to be a plaque stabilization effect.

High-Dose B Vitamin Supplementation and Progression of Subclinical Atherosclerosis: A Randomized Controlled Trial

Hodis HN, Mack WJ, Dustin L, the BVAIT Research Group. *Stroke* 2009;40:730-6.

Conclusion: Dietary supplementation with high-dose B vitamins reduces progression of carotid intima media thickness in individuals with a fasting total homocysteine $\geq 9.1 \mu\text{mol/L}$ and who are at low risk for cardiovascular disease.

Summary: Both meta-analysis and observational studies have indicated that elevated total plasma homocysteine (tHcy) is an independent risk factor for cardiovascular disease with risk increasing 40-60% for each 3-5 $\mu\text{mol/L}$ increase in tHcy. However, clinical trials have failed to show reduction of cardiovascular events with homocysteine lowering therapy. The B-vitamin atherosclerosis intervention trial (BVAIT) assessed the impact on subclinical atherosclerosis, in a population presumably free of cardiovascular disease, of reducing total plasma homocysteine with B-vitamin supplementation.

This was a randomized double-blind placebo controlled trial conducted from November 2000 to June 2006. Subjects were men and postmenopausal women more than 40-years of age with fasting total homocysteine levels $\geq 8.5 \mu\text{mol/L}$. All subjects had no clinical signs or symptoms of cardiovascular disease. Patients with diabetes, systolic blood pressures $> 160 \text{ mmHg}$, diastolic blood pressure $> 100 \text{ mmHg}$ and creatinine clearance $< 70 \text{ mL/min}$ were excluded. There were 506 participants randomized to high-dose of B-vitamin supplementation (5 mg folic acid + 0.4 mg vitamin B₁₂ + 50 mg vitamin B₆) or matching placebo for 3.1 years. Subclinical atherosclerosis was assessed using carotid artery intima media thickness

values obtained with duplex scanning, the primary outcome measure. Measurements of aortic and coronary artery calcification with multidetector spiral CT scanning were secondary outcome measures. At follow-up there was no statistical significant difference in the primary or secondary outcomes comparing the patients with B-vitamin supplementation to those treated with the placebo. A post-hoc analysis showed that subjects with baseline tHcy's $\geq 9.1 \mu\text{mol/L}$ and randomized to B-vitamin supplementation had statistically significant lower average rates of carotid intima media thickness progression compared to the placebo group, $p = 0.02$. Subjects with baseline total homocysteines $< 9.1 \mu\text{mol/L}$ had no treatment effect.

Comment: The authors contend that despite this being a post-hoc analysis, their findings that vitamin-B supplementation can decrease carotid intima media thickness in individuals with fasting total homocysteine $> 9.1 \mu\text{mol/L}$ is "highly relevant". Perhaps this is true for the basic biology of atherosclerosis but it is unlikely to have any clinical effect. Patients who had decreases in carotid intima media thickness were an average age of 61-years and had no signs of cardiovascular disease, no decrease in cardiovascular events, and "benefitted" only by reduction in a subclinical marker of atherosclerosis. The public health impact of these findings is likely to be nothing.

High Risk of Early Neurologic Recurrence in Symptomatic Carotid Stenosis

Ois A, Cuadrado-Godia E, Rodriguez-Campello A, et al. *Stroke* 2009;40:2727-31.

Conclusion: Patients with first mild stroke or TIA and significant carotid stenosis are at high risk for neurologic recurrence, especially within the first 72 hours of presentation.

Summary: Data from sub analysis of the European Carotid Surgery Trial and the North American Symptomatic Carotid Endarterectomy Trial have been evaluated to assess the risk of early stroke, defined as within two weeks, after TIA or a mild stroke. These trials recruited only patients with non-disabling stroke and therefore the number of patients who were not included because of early recurrence or subsequent disability before time of randomization is unknown. Recent studies have suggested a high recurrence risk of neurologic events after a TIA or minor stroke (*Stroke* 2004; 35:2855-2861, *Brit Med J* 2004; 328:326-328, and *Neurology* 2004; 62:569-573). The authors of this paper sought to analyze recurrence risk for ischemic events 72 hours, 7 days and 14 days in an unselected series of patients with symptomatic, $>50\%$ carotid stenosis and a first ever, non-disabling stroke or TIA evaluated within the first 6 hours from onset of symptoms. There were 163 patients evaluated. Of these, 121 had an initial mild stroke and 42 had a TIA. All were evaluated within 6 hours from onset of symptoms at a tertiary care hospital. Neurologic recurrence was defined as a new neurologic event (TIA or stroke) or an increase of 4 points in the initial National Institutes of Health Stroke Scale. Neurology recurrence rates were determined at 72 hours, 7 days and 14 days. Patients were defined as disabled from their stroke if they had a Rankin scale at 14 days of 3 to 6.

There were 45 patients (27.6%) that had a new neurologic event. Six patients had two episodes at different time periods. Thirty-four events (20.9%) occurred within the first 72 hours; 11 events (6.9%) occurred between 72 hours and 7 days, and 6 events (3.7%) occurred at 14 days. Carotid stenosis of $>70\%$ was associated with neurologic occurrence. Diabetes was marginally associated. At 2 weeks there were 19 patients (11.7%) who had disability. Fourteen of these 19 patients had experience neurologic recurrence within the first 72 hours.

Comment: Traditionally surgeons have been reluctant to intervene acutely in a patient with a new stroke. In this study, however, only 2 patients experienced non-disabling neurologic recurrence beyond 72 hours of symptoms. The results suggest the necessity of testing pharmacologic or interventional strategies to use in the hyperacute phase in patients with their first-ever TIA or non-disabling stroke. Urgent endovascular/surgical procedures in the first hours following presentation, which is clearly accepted in other vascular pathologies such as coronary disease, needs to be evaluated in a rigorous fashion in patient with acute neurologic events.

Multiligamentous Injuries of the Knee and Associated Vascular Injuries

McDonough EB, Wojtys EM. *Am J Sports Med* 2009;37:156-9.

Conclusion: Physical examination alone is not sufficient to detect the majority of vascular surgery injuries after suspected knee dislocation.

Summary: The rate of injury to the popliteal artery from knee dislocation varies widely from 7 to 80%. Evaluation of a patient with multiligament damage of the knee and/or knee dislocation for the presence of vascular injury is somewhat controversial. Traditionally, routine arteriography had been advocated but more recently elective arteriography basing the decision to proceed on arteriography on an abnormal physical examination or an abnormal ankle-brachial index has been advocated. The authors sought to report the frequency of vascular injuries in their patients with multiligament injured knees and examine the role of arteriography in their treatment protocol. This was a retrospective analysis of 71 patients over a 12 year period of patients who had a diagnosis of multiligamentous injury of the

knee with tibial-femoral dislocation documented by physical examination and MRI.

There were 72 knee injuries involving multiple ligaments. In these 72 injured extremities, 12 vascular injuries were identified. Four of these were identified by physical examination and 5 by routine arteriography. There were 3 additional vascular injuries not identified by either preoperative physical examination or arteriography. In the 4 patients who had an abnormal physical examination at presentation, all underwent immediate revascularization. The remaining 8 patients had normal pulses on initial examination. All underwent arteriography and 5 had vascular injuries detected by arteriography and underwent successful repair. There were 3 patients who had a normal physical examination and an arteriogram interpreted as normal but who subsequently proved to have a popliteal artery injury. Two of the 3 patients who had normal pulses and angiograms interpreted as normal had their popliteal artery injury discovered during release of the tourniquet following the repair of their ligamentous injuries. The third patient developed a pseudoaneurysm that bled following arthroscopic repair of the knee injury.

Comment: This is a selective series. There were no limb losses reported with popliteal artery injury in this group of patients, suggesting significant referral bias. However, it is important to note that both physical examination and arteriography may not detect a popliteal artery injury occurring in the setting of a knee dislocation. Despite normal arteriography and a normal physical examination, delayed presentation of a popliteal artery injury does happen. The take-home message here is that a single arteriogram or a single physical examination is not sufficient to rule out popliteal artery injury in a patient with a knee dislocation. Patients with knee dislocation should, at the very least, be followed by serial physical examinations.

Prehospital HMG Co-A Reductase Inhibitor Use and Reduced Mortality in Ruptured Abdominal Aortic Aneurysm

Feeney JM, Burns K, Staff I, et al. *J Am Coll Surg* 2009;209:41-6.

Conclusion: In patients with ruptured abdominal aortic aneurysms prehospital statin use appears to be associated with increased survival.

Summary: One of the pleiotropic effects of statins appears to be reduction of inflammatory mediators. These mediators include heat shock proteins, tumor necrosis factor α , multiple interleukins, nuclear factor κ b, as well as nitric oxide. Statins likely have free radical scavenger activity. Statins also appear to exert anti-inflammatory and antioxidant effects that improve mortality in septic shock populations and patients with severe sepsis who were taking statins appear to develop septic shock less frequently. Theoretically, similar shock mechanisms could be active in the setting of a ruptured abdominal aortic aneurysm (rAAA).

The authors performed a retrospective review of their patients with rAAAs from January 2000 to December 2008. They compared hospital and ICU lengths of stay, cardiac morbidity, and number of cardiac events per patient between survivor groups with and without pre hospital statin use. Mortality, cardiac morbidity, and gender were also compared. The Physiologic Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) was also calculated for all patients analyzed.

There are 121 records screened with 40 patients excluded due to the presence of active cancer, chronic immune suppression or living wills or advanced directives against live sustaining treatment. There were no statistically significant differences between statin users and non-users with respect to age, gender and POSSUM scores. Mortality in the group without pre hospital statin use was 63.8%. In the group with pre hospital statin use mortality was 34.8% ($p=0.018$, odds ratio 0.30 to 0.11). Hospital and ICU lengths of stay, cardiac morbidity, and number of cardiac events per patient were not statistically different among survivors.

Comment: This study provides further evidence for the ever-widening pleiotropic effects of statin medications. It does have several limitations including its small sample size and the fact that endovascular repair of ruptured aneurysms and the use of statins increased over the study period. Patients were included in this study if they used any statin at any dose for any period of time up to their time of admission for rAAA. What is now needed is prospective studies on dose related response and time delays in the generation of the pleiotropic effects of statin medications.