

Abstracts

Gregory L. Moneta, MD, Section Editor

Family History of a Risk Factor for Carotid Artery Stenosis

Khaleghi M, Isseh IN, Jouni H, et al. *Stroke* 2014;45:2252-6.

Conclusions: Family histories of stroke and coronary heart disease are associated with carotid artery stenosis suggesting shared genetic and environmental factors contribute to the risk of carotid artery stenosis.

Summary: Multiple studies have shown family history is a significant risk factor for coronary heart disease and stroke. However, the association between family history of atherosclerotic vascular disease and presence of carotid artery stenosis is largely unknown. In the Tromso study, a family history of coronary heart disease was marginally associated with carotid artery stenosis in men but not in women (Mathiesen EB et al, *Cerebrovasc Dis* 2001;12:44-51). In the present study the authors sought to determine whether a family history of stroke or coronary heart disease was associated with the presence of carotid artery stenosis. The study cohort included 864 patients (72 ± years; 68% men) with carotid artery stenosis and 1698 controls (61 ± 11 years; 55% men) referred for noninvasive vascular testing. Carotid artery stenosis was defined as ≥70% stenosis in the internal carotid artery on ultrasound or history of carotid revascularization. Controls did not have carotid artery stenosis or history of cerebrovascular disease or coronary heart disease. Family history of stroke and coronary heart disease was defined as having ≥1 first-degree relative who had a stroke or coronary heart disease before age 65 years. Logistic regression analysis was used to evaluate whether family history of stroke or coronary heart disease was associated with presence of carotid artery stenosis, independent of conventional risk factors. Both family history of stroke and coronary heart disease were present more often in patients with carotid artery stenosis than in controls. Odds ratios (95% CI) were 2.02 (1.61-2.53) and 2.01 (1.70-2.37), respectively. After adjustments for age, sex, body mass index, smoking, diabetes, hypertension and dyslipidemia, the associations remain significant. Odds ratios were 1.41 (1.06-1.90) and 1.69 (1.35-2.10), respectively. More affected relatives with stroke or coronary heart disease was associated with higher odds ratios of CAS; adjusted odds ratios, 1.25 (0.91-1.72) and 1.46 (1.14-1.89) vs 2.65 (1.35-5.40) and 2.13 (1.57-2.90) for patients with 1 and ≥ 2 affected relatives with stroke and coronary heart disease, respectively.

Comment: While seemingly obvious, the data for the first time documents family history of stroke or coronary heart disease as independently associated with the presence of carotid artery stenosis. In addition, siblings' histories of stroke or coronary heart disease confers an even greater risk and the magnitude of association is greater in those with more affected relatives. The underlying reasons for these associations are likely due to both genetic susceptibility to carotid artery stenosis and lifestyle and environmental factors shared by family members. While currently screening for carotid artery stenosis is not broadly recommended the study may help identify certain subgroups of patients where the yield for screening would be sufficiently increased to potentially provide benefit for these patients. Targeted screening for carotid artery stenosis may be a subject for both efficacy and cost-effectiveness analyses in the future.

Persistent Cognitive Impairment After Transient Ischemic Attack

Van Rooij FG, Schaapsmeeders P, Maaijwee NAM, et al. *Stroke* 2014;45:2270-4.

Conclusions: More than a third of patients with TIA have impairment of ≥1 cognitive domains within 3 months after their TIA and these cognitive domains fit the vascular cognitive impairment profile.

Summary: Cytotoxic edema beyond the point of symptom resolution can be found in more than 30% of patients with TIA using diffusion-weighted imaging techniques (Pendlebury ST et al, *Lancet Neurol* 2009;8:1006-18). Permanent cerebrovascular damage, both with and without clinical signs of brain infarction can lead to cognitive decline. That decline has a so-called vascular cognitive impairment pattern, characterized by deficits in executive function and attention with relatively intact memory function (Gorelick PB et al, *Stroke* 2011;42:2672-713). However, since most TIAs occur in older patients cognitive impairment secondary to a TIA could potentially be obscured by age or Alzheimer pathology-related

cognitive decline. The authors sought to determine the cognitive performance of patients within 3 months after TIA in a single center cross-sectional study. They sought to minimize the effects of aging concomitant cognitive disorders by restricting the research population to those within an age range of 45 to 65 years. The hypothesis was that cognitive function after TIA would be impaired and would have a vascular profile. Patients with TIA within the age range of 45 to 65 years, without prior stroke or dementia underwent comprehensive neuropsychological testing within 3 months of the TIA. Z scores per cognitive domain were obtained based on the mean of a control group within the same age range. Cognitive impairment was defined as a domain z score ≤ -1.65. Patients underwent either computed tomography or MRI brain imaging. There were 107 patients with TIA 63% women, mean age 56.6 years included in the study who were compared with 81 controls (56% women, mean age, 52.9 years). TIA patients performed worse on all cognitive domains except episodic memory. Working memory (25%), attention (22%), and information processing speed (16%) were most frequently impaired and often more than in the control group (age- and sex-adjusted odds ratios, respectively, 22.5 [95% CI, 2.9-174.3], 6.8 [1.9-24.3], and 7.1 [1.5-32.5]). More than 35% of patients with TIA had impairment of ≥1 cognitive domain. Presence of silent brain infarcts was related to worse executive functioning but did not explain the whole relationship between TIA and cognitive impairment.

Comment: The cause of cognitive function decline after TIA is not elucidated by this study. However, the so-called nonamnestic cognitive impairment found in this study is compatible with vascular cognitive impairment and is primarily driven by subcortical brain damage disrupting subcortical frontal connections (O'Brien JT et al, *Lancet Neuro* 2003;2:89-98). The author's data clearly show a likelihood of cognitive impairment after TIA in relatively young adults. Clinicians need heightened clinical awareness of this problem and future studies with more advanced brain imaging techniques to localize sites of functional cerebrovascular damage, as well as longitudinal assessment of cognitive function after TIA are needed.

PICC-Associated Bloodstream Infections: Prevalence, Patterns, and Predictors

Chopra V, Ratz D, Kuhn L, et al. *Am J Med* 2014;127:319-28.

Conclusions: Peripheral-inserted central catheter (PICC)-associated bloodstream infection is most associated with hospital length of stay, intensive care unit (ICU) status, and number of lumens of the device.

Summary: PICCs have been perceived as posing a lower-risk of bloodstream infection than standard central venous catheters. However, a recent systematic review and meta-analysis of 57,250 patients from 23 studies, found PICCs placed in hospitalized patients were associated with infection rates not statistically different than those related to other central venous catheters (incidence rate ratio, 0.91; 95% confidence interval [CI], 0.46-1.79; Chopra V et al, *Infect Control Hosp Epidemiol* 2013;34:908-18). Based on this it appears PICC-associated bloodstream infection may be more common than previously realized. The authors therefore conducted a retrospective study to examine patterns, incidence, timing, and predictors of PICC-associated bloodstream infection, with the goal of trying to better inform clinical practice and safeguard patient safety with the use of these devices. This was a retrospective cohort study of consecutive adults who underwent PICC placement from June 2009 to July 2012. Multivariable logistic and Cox-proportional hazards regression models, with covariates specified a priori were analyzed for their association with PICC-associated bloodstream infection. Odds ratios (ORs) and hazard ratios (HRs) with corresponding 95% CIs were used to express the association between each predictor and outcome of interest. During the study period, 966 PICCs were inserted in 747 unique patients. This gave a total of 26,887 catheter days. Indications for PICC insertion were long-term antibiotic administration (52%), venous access (21%), total parenteral nutrition (16%), and chemotherapy (11%). With bivariate analysis, intensive care unit status (OR, 3.23; 95% CI, 1.84-5.65), mechanical ventilation (OR, 4.39; 95% CI, 2.46-7.82), length of hospital stay (OR, 1.04; 95% CI, 1.02-1.06), and ICU stay (OR, 1.03; 95% CI, 1.02-1.04), Power PICCs (C. R. Bard Inc, Murray Hill, NJ; OR, 2.58; 95% CI, 1.41-4.73), and

devices placed by interventional radiology (OR, 2.577; 95% CI, 1.41-4.68) were associated with PICC-bloodstream infection. Catheter lumens were strongly associated with this event (double lumen, OR 5.21; 95% CI, 2.46-11.04, and triple lumen, OR, 10.84; 95% CI, 4.38-26.82). With multivariable analysis only hospital length of stay, ICU status, and number of PICC lumens remained significantly associated with PICC-bloodstream infection. In fact, the HR for PICC lumens increases substantially over time suggesting earlier time to infection among patients with multi-lumen PICCs (HR, 4.08; 95% CI, 1.51-11.02, and HR, 8.52; 95% CI, 2.55-28.49 for double- and triple-lumen devices, respectively).

Comment: Assuming patients are in the hospital and in the intensive care unit only because they need to be, the only modifiable risk factor for PICC-associated bloodstream infection appears to be the number of lumens in the catheter placed. The data suggests the number of lumens should be kept as low as possible and multilumen catheters should only be used when absolutely necessary.

Pressure Control During Preparation of Saphenous Veins

Li FD, Eagle S, Brophy C, et al. *JAMA Surg* 2014;149:655-62.

Conclusions: During preparation of vein grafts, limiting vein graft distension with a pressure release valve preserves endothelial integrity, and reduces intimal hyperplasia.

Summary: Long-term patency of vein conduits in the arterial system is limited because of vein graft failure largely secondary to loss of endothelial coverage and intimal hyperplasia. LoGerfo in the early 1980's identified that integrity of vein grafts is at least partially a function of initial intimal and neointima preservation in preparation of the vein graft (LoGerfo FW et al, *Surgery* 1981;90:1015-24). Flushing vein grafts during preparation with uncontrolled pressure can result in high intraluminal pressure which can exceed 600 mm Hg, and result in denudation of the endothelium and a subsequent inflammatory response that may lead to intimal hyperplasia (Khaleel MS et al, *Ann Thorac Surg* 2012;93:552-8). In this study the authors sought to investigate if pressure distension during vein graft preparation leads to endothelial injury and intimal thickening. The hypothesis was that by limiting pressure during distension, neointimal thickening would be reduced and would result in preservation of vascular function of the grafts. A pressure limiting device that potentially can be integrated into current distension techniques was utilized in this study. The authors collected segments of human saphenous veins (HSVs) in a university hospital from 13 patients undergoing CABG procedures immediately after harvest (unmanipulated [UM]), after pressure distension (after distension [AD]), and after typical intraoperative surgical graft preparation (after manipulation [AM]). Porcine saphenous veins (PSVs) from 7 healthy research animals were subjected to manual pressure distension with or without an in-line PRV that prevented pressures of 140 mm Hg or greater. Endothelial function of the HSVs and PSVs was determined in a muscle bath and endothelial integrity was assessed and intimal thickening in PSVs evaluated after 14 days in organ culture. The primary outcome measures were endothelial function measured in force, converted to stress, and defined as the percentage relaxation of maximal phenylephrine-induced contraction. Endothelial integrity was assessed by immunohistologic examination. Neointimal thickness was measured by histomorphometric analysis. Pressure distension of HSVs led to decreased mean (SEM) endothelial-dependent relaxation (5.3% [2.3%] for AD patients vs 13.7% [2.5%] for UM patients; $P < .05$) and denudation. In the AM group, the function of the conduits was further decreased (-3.2% [3.2%]; $P < .05$). Distension of the PSVs led to reduced endothelial-dependent relaxation (7.6% [4.4%] vs 61.9% [10.2%] in the control group; $P < .05$), denudation, and enhanced intimal thickening (15.0 [1.4] μm vs 2.2 [0.8] μm in the control group; $P < .05$). Distension with the PRV preserved endothelial-dependent relaxation (50.3% [9.6%]; $P = .32$ vs control, prevented denudation, and reduced intimal thickening (3.4 [0.8] μm ; $P = .56$ vs controls) in PSVs.

Comment: In its entirety the data appears to demonstrate a causal relationship between manual distension, endothelial, and medial injury, and intimal hyperplasia. Assuming endothelial injury and intimal hyperplasia have adverse effects on vein graft patency, it is possible the use of this simple pressure regulating valve employed in this study may help contribute to long-term vein graft patency in both coronary and peripheral vascular procedures.

Hemodynamic-Guided Fluid Administration for the Prevention of Contrast-Induced Acute Kidney Injury: The POSEIDON Randomized Controlled Trial

Brar SS, Aharonian V, Mansukhani P, et al. *Lancet* 2014;383:1814-23.

Conclusions: Left ventricular end-diastolic pressure-guided fluid administration is a safe and effective method to prevent contrast-induced kidney injury in patients undergoing angiography.

Summary: A common cause of acute kidney injury is contrast-induced. This is associated with both increased morbidity, mortality and health-care costs. There are no known treatments available after acute kidney injury has occurred. Primary focus is therefore to identify preventative therapies. Currently, although many interventions have been assessed to prevent contrast-induced acute kidney injury, none are universally embraced with the exception of intravascular volume expansion. However, the rate and duration of fluid administration around the time of contrast exposure that could optimally prevent acute kidney injury is unclear. In this study, the Prevention of Contrast Renal Injury with Different Hydration Strategies (POSEIDON) trial the authors investigated different rates of fluid administration guided by left ventricular end-diastolic pressure in patients undergoing cardiac catheterization. This was a randomized, parallel-group, comparator-controlled, single-blind phase 3 trial. The trial investigated the efficacy of a new fluid protocol based on left ventricular end-diastolic pressure for the prevention of contrast-induced acute kidney injury in patients undergoing cardiac catheterization. The primary outcome was the occurrence of contrast-induced acute kidney injury, which was defined as an increase in serum creatinine concentration of greater than 25% of baseline or greater than 0.5 mg/dL. Between October 10, 2010 and July 17, 2012, 396 patients aged 18 years or older undergoing cardiac catheterization with an estimated glomerular filtration rate of 60 mL/min per 1.73 m² or less and one or more of several risk factors (diabetes, history of congestive heart failure, hypertension, or age older than 75 years) were randomly allocated in a 1:1 ratio to left ventricular end-diastolic pressure-guided volume expansion (n = 196) or the control group (n = 200) who received a standard fluid administration protocol. Four computer-generated concealed randomization schedules, each with permuted block sizes of 4, were used for randomization and participants were allocated to the next sequential randomization number by sealed opaque envelopes. Patients and laboratory personnel were masked to treatment assignment, but the physicians who did the procedures were not masked. Both groups received intravenous 0.9% sodium chloride at 3 mL/kg for 1 hour before catheterization. Analyses were by intention to treat. Adverse events were assessed at 30 days and 6 months and all such events were classified by staff who were masked to treatment assignment. Findings concluded that contrast-induced acute kidney injury occurred less frequently in patients with left ventricular end-diastolic pressure-guided fluid administration (6.7% [12/178]) than in the control group (16.3% [28/172]; relative risk, 0.41, 95% CI, 0.22-0.79; $P = .005$). Hydration treatment was terminated prematurely because of shortness of breath in three patients in each group. The total mean (SD) volume of normal saline administered was 1727 (583) mL in the left ventricular end-diastolic pressure-guided group vs 812 (142) mL in the control group ($P < .001$).

Comment: The study is possible because left ventricular end-diastolic pressure is a haemodynamic parameter routinely obtained during cardiac catheterization. Obviously that is not the case in angiographic procedures performed for other reasons. Nevertheless, the fact patients who had end-diastolic monitoring to guide their fluid administration received larger volumes of fluid and had decreased levels of acute kidney injury compared to the control group, implies that more aggressive hydration of patients at the time of administration of contrast than is routinely performed could be an effective strategy to reduce contrast-induced acute kidney injury.

Sex Differences in the Association Between Smoking and Abdominal Aortic Aneurysm

Stackelberg O, Björck M, Larsson SC, et al. *Br J Surg* 2014;101:1230-7.

Conclusions: There are sex differences in the association between smoking status and abdominal aortic aneurysm (AAA) risks. Further investigation of targeted AAA screening among women who smoke is indicated.

Summary: Ultrasound screening for AAA among men has been demonstrated by randomized trials to be an effective strategy to prevent rupture and aneurysm associated death. AAA is considered more dangerous in women than men, but thus far there's no randomized data supporting ultrasound screening among women for AAA. However, the Society for Vascular Surgery and the European Society for Vascular Surgery have both suggested that ultrasound screening in women as an effective strategy to prevent aneurysm related death in women. It is known that smoking and the risk of AAA is widely correlated and that smoking cessation is one of the few medical strategies that can decrease the expansion and rupture rate of small screen detected AAA (Sweeting MJ et al, *Br J Surg* 2012;99:655-65). In this study the authors sought to investigate sex specific, dose response associations between smoking (smoking status, pack-years smoked, and smoking cessation) and risk of developing AAA in two large, comparable, population-based prospective cohorts of women and men from central Sweden. Women in the Swedish Mammography Cohort and men in the Cohort of Swedish Men were followed up from 1998 to 2011. AAA was identified through linkage of the cohorts to the Swedish