# ABSTRACTS

## Gregory L. Moneta, MD, Abstracts Section Editor

**Inhibition of annexin V binding to cardiolipin and thrombin generation in an unselected population with venous thrombosis**

Hanly JG, Smith SA, Anderson D. J Rheumatol 2003;30:190-3.

**Conclusion:** Abnormalities in annexin V may contribute to the procoagulant state in patients with idiopathic venous thrombosis.

**Summary:** The authors evaluated 111 patients who came to an emergency room with symptoms suggestive of venous thromboembolism (VTE). In 34 patients the diagnosis of lower extremity deep venous thrombosis or pulmonary embolism was confirmed (VTE-positive group). Seventy-seven patients with normal findings at diagnostic workup for VTE composed the control group (VTE-negative group). Plasma samples were collected before beginning anticoagulation, and were examined for immunoglobulin G (IgG) anti-cardiolipin, IgG anti-$_{\beta 2}$-glycoprotein1, and IgG anti-prothrombin antibodies with an enzyme-linked immunosorbent assay. They also examined the effect of individual patient variables on control plasma samples of annexin V binding to anti-cardiolipin and on in vitro thrombin generation determined with a competitive enzyme-linked immunosorbent assay and a chromogenic assay.

Prevalence and levels of IgG anti-cardiolipin, anti-$_{\beta 2}$-glycoprotein 1, and anti-prothrombin antibodies were similar in the groups with and without VTE. Plasma samples from the VTE-positive group, however, caused a significant inhibition of in vitro thrombin generation, and concurrent, less impressive inhibition of annexin V binding to aCL. Only age and inhibition of thrombin generation were significantly associated with VTE.

**Comment:** Despite improvement in detection of hypercoagulable states, many patients with unprovoked VTE have, as yet, no identifiable hypercoagulable abnormality. The study suggests that annexin V abnormalities may result in a minor hypercoagulable state. It is still unclear whether annexin V abnormalities can act in isolation to produce VTE.

**A prospective registry of carotid angioplastine and stenting**

Theiss W, Hermanek P, Mathias K, et al. Radiology 2004;35:2134-9.

**Conclusion:** Carotid angioplasty and stenting (CAS) may be performed with similar results in the community setting, as has been reported by highly specialized centers and in clinical studies.

**Summary:** The German Societies of Angiology and Radiology instituted a prospective registry of CAS to limit its uncontrolled use and collect data about technique and results of CAS outside of clinical trials. The registry is open to investigators in Germany, Austria, and Switzerland who are active in CAS. Thirty-eight centers participate. Patients are prospectively interviewed before CAS is performed. At discharge from the hospital, technical details, periprocedural medications, and clinical course are reported on a standardized form.

After 4 years, 3853 planned interventions were recorded in the registry. CAS was attempted in 3267 patients. Of these, 56% had symptomatic disease and 44% had asymptomatic disease. In 98% of patients stents were used, 89% of which were self-expanding. Other technical aspects of CAS, including cerebral protection devices and methods of periprocedural monitoring, varied widely among centers. Periprocedural medications generally included aspirin and clopidogrel before and after CAS, and high-dose heparin and atropine during CAS. CAS was technically successful in 3207 patients (98%). In-hospital mortality was 0.6% (n = 18). In-hospital major stroke rate was 1.2% (n = 38), and in-hospital minor stroke rate was 1.3% (n = 41). Combined stroke and death rate was 2.8% (n = 90).

**Comment:** There are ongoing trials to evaluate the efficacy of CAS versus carotid endarterectomy. These trials will determine the relative utility of the 2 procedures. In the meantime, studies such as this one can be used to justify randomized trials of carotid endarterectomy versus CAS. Because of the limitations of a registry format, and the very short-term follow up (in-hospital only) of registry patients, this trial should not, and cannot, be used to justify performance of CAS in the community setting.

**Elevated plasma factor VIII and D-dimer levels as predictors of poor outcome of thrombosis in children**

Goldenberg NA, Knapp-Clevenger R, Manco-Johnson MJ, and Mountain States Regional Thrombophilia Group. N Engl J Med 2004;351:1081-8.

**Conclusion:** Elevated levels of plasma factor VIII, D-dimer, or both at diagnosis and during follow-up after the standard duration of anticoagulation therapy predict poor outcomes in children with thrombosis.

**Summary:** Elevated levels of plasma factor VIII and D-dimer predict recurrent venous thromboembolism in adults (N Engl J Med 2000;343: 457-62; Thromb Haemost 2002;87:7-12). The authors investigated whether elevated levels of factor VIII, D-dimer, or both at diagnosis, and persistence of these laboratory abnormalities after anticoagulation therapy correlated with poor outcome of thrombosis in children, defined as those from birth to age 21 years. Data analyzed were from Children's Hospital in Denver and hospitals participating in the Mountain States Regional Hemophilia and Thrombosis Center. The study included 144 children with radiologically confirmed acute thrombotic events. All initially received heparin therapy, followed by warfarin sodium for 3 to 6 months. Follow-up was at 3, 6, and 12 months, and then annually. Repeat thrombophilia testing was performed in children with previously abnormal factor VIII and D-dimer levels.

Complete data were available for analysis in 82 children. Of these 82 children, 67% had factor VIII levels greater than 150 IU/dL, D-dimer levels greater than 5 ng/mL, or both, at diagnosis. In the 75 patients in whom thrombophilia testing was performed after 3 to 6 months of anticoagulation therapy, 43% had persistent elevation of at least 1 of these 2 laboratory values at a median follow-up of 12 months (range, 3 months–5 years), and 51% of the 82 patients had a poor outcome, such as lack of thrombus resolution, recurrent thrombosis, or postthrombotic syndrome. Elevated levels of factor VIII, D-dimer, or both at diagnosis predicted a poor outcome, with an odds ratio of 6.1 ($P$ = .008). Persistence of at least 1 laboratory abnormality at 3 to 6 months also predicted poor outcome, with an odds ratio of 4.7 ($P$ = .002). A combination of factor VIII level greater than 150 IU/dL and D-dimer level greater than 5 ng/mL at diagnosis was predictive of poor outcome, with 91% specificity. After 3 to 6 months of standard anticoagulation this combination predicted poor outcome with 88% specificity.

**Comment:** Children with thrombosis should not be considered just small adults. Children have lower concentrations of physiologic inhibitors of the coagulation system and a more limited fibrolytic capacity than adults do. These differences in the coagulation systems between adults and children are particularly prominent in the first year of life and at puberty and adolescence (Thromb Haemost 1995;74:415-25). This study's identification of specific levels of factor VIII and D-dimer in children with thrombosis should help guide anticoagulation therapy in children and, it is hoped, reduce the burden of late thrombosis-related complications in pediatric patients.

***N*-acetylcysteine vs fenoldopan mesylate to prevent contrast agent–associated nephrotoxicity**

Birguori C, Colombo A, Airoldi F, et al. Am J Cardiol 2004;44:762-5.

**Conclusion:** *N*-acetylcysteine (NAC) is more effective then fenoldopan in preventing contrast agent–induced nephrotoxicity.

**Summary:** Both fenoldopan mesylate, a specific antagonist of the dopamine-1 receptor, and NAC are thought to prevent contrast agent–associated nephrotoxicity. The authors randomly assigned 192 consecutive patients with chronic renal insufficiency who were referred for coronary or peripheral procedures involving administration of contrast agents to receive intravenous hydration with 0.45% saline solution and NAC (1200 mg orally twice daily) or fenoldopan (0.10 μg/kg/min) before and after nonionic iso-osmolar contrast dye administration. There were 97 patients in the NAC group, and 95 patients in the fenoldopan group.

Creatinine concentration was similar in the 2 groups of patients. The amount of contrast medium administered was similar in the 2 groups ($P$ = .54). An increase in creatinine concentration of at least 0.5 mg/dL 48 hours after the procedure occurred in 4 of 97 patients (4.1%) in the NAC group and in 13 of 95 patients (13.7%) in the fenoldopan group ($P$ = .019; odds ratio, 0.27; 95% confidence interval, 0.08-0.85).

**Comment:** Fenoldopan is thought to potentially selectively increase blood flow to the renal medulla. The findings of this study, however, indicate that fenoldopan is ineffective in preventing further deterioration in renal function in patients with chronic renal insufficiency receiving an iodinated contrast agent. On the basis of these data, and considering the high cost of fenoldopan, hydration plus fenoldopan should not be used as prophylaxis to prevent contrast agent–associated neuropathy.

**Endoluminal stent-graft placement for acute rupture of the descending thoracic aorta**

Scheinert D, Krankenberg H, Schmidt A, et al. Eur Heart J 2004;25:694-700.

**Conclusion:** Stent-graft placement is an effective option for emergency repair of descending thoracic aortic perforations.

**Summary:** The authors evaluated 31 consecutive patients who underwent catheter-based treatment of perforating lesions of the descending aorta. Twenty-one patients received treatment of rupture of a descending thoracic aneurysm or descending thoracic aortic dissection, and 10 patients received treatment of traumatic disruption of the descending aorta. A total of 32 endographs were implanted.

Endograft placement was successful in all patients. In 1 patient a second prosthesis was necessary, because of type I endoleak. The mortality rate at 30 days was 9.7%. One of 3 deaths occurred secondary to type I endoleak and aortic rupture. All 3 deaths occurred in patients with rupture of a descending thoracic aneurysm or thoracic dissection. Other complications associated with placement of the endograft were also more common in patients who received treatment of a descending thoracic aneurysm or dissection, compared with those who received treatment of traumatic transection of the descending aorta (28.6% vs 10%). The left subclavian artery was intentionally covered in 6 patients, without a major acute adverse event. No complications were noted secondary to placement of endograft struts into the aortic arch. There was no paraplegia and no further deaths or ruptures during a mean follow-up of 17 months.

**Comment:** Clearly, endograft repair of thoracic aortic disruption is feasible with excellent short-term results in selected patients. It is still unclear the percent of patients with acute thoracic disruption who will be eligible for endograft therapy. Nevertheless, as these devices become more available, endograft therapy for acute thoracic aortic disruption will be the preferred treatment in selected patients.

**Randomized clinical trial of distal anastomotic interposition vein cuff and infrainguinal polytetrafluoroethylene (PTFE) bypass grafting**

Griffiths GD, Nagy J, Black D, et al. Br J Surg 2004;91:560-2.

**Conclusion:** Three-year patency rates for femoral to below-knee popliteal polytetrafluoroethylene (PTFE) bypasses are improved with use of a Miller cuff. Miller cuffs have no effect on patency rates for femoral to above-knee popliteal bypasses at 5 years, and do not improve limb salvage in either above-knee or below-knee PTFE bypasses.

**Summary:** The authors examined the effect of a Miller vein cuff at the distal anastomosis of a PTFE graft on median to long-term patency of femoral to above-knee and femoral to below-knee bypasses. Outcome measures were bypass graft patency and limb salvage. This was a prospective, randomized clinical trial with 261 bypass operations originally randomized. Data were available for 235 bypasses (120 with a Miller cuff, 115 without). Mean age of patients in the cuff group was 67.2 years, and in the non-cuff group was 69.3 years ($P = .72$). The indication for operation was limb salvage in 89% of each group. Cumulative 5-year patency for above-knee bypasses with a Miller cuff was 40%, compared with 42% for the non-cuffed bypasses ($P = .702$). Cumulative 3-year patency for below-knee bypasses with a Miller cuff was 45%, compared with 19% for non-cuffed bypasses ($P = .018$). The Miller cuff had no significant effect on limb salvage for either above-knee or below-knee bypasses.

**Comment:** When PTFE bypass is indicated to the below-knee popliteal artery in a primarily limb salvage population, a Miller cuff should be used. The results also suggest that PTFE bypass to the popliteal artery for limb salvage, whether above or below the knee, has relatively poor long-term patency.

**Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization**

Go AS, Chertow GM, Fan D, et al. N Engl J Med 2004;351:1296-1305.

**Conclusion:** Progressive levels of renal insufficiency substantially increase the risk for death or cardiovascular disease, and use of healthcare resources. The effect is more marked with end-stage renal disease than with milder levels of renal insufficiency.

**Summary:** The authors estimated longitudinal glomerular filtration rate (GFR) in 1,120,295 adults in the Renal Registry of Kaiser Permanente of Northern California. In patients in the registry, 1 or more outpatient determinations of serum creatinine levels were made between January 1, 1996, and December 31, 2000. Excluded were patients with kidney transplants and those receiving maintenance dialysis. Multivariable analysis was used to examine the association between estimated GFR and the risk for death, cardiovascular events, and hospitalization.

Median follow-up was 2.84 years. Mean patient age was 52 years; 55% of patients were women. After adjustment, risk for death increased as GFR decreased below 60 mL/min/1.73m$^2$ of body surface area. The adjusted hazard ratio for death was 1.2 with an estimated GFR of 45 to 59 mL/min/1.73m$^2$ (95% confidence interval [CI], 1.1-1.2), 1.8 with an estimated GFR of 30 to 45 mL/min/1.73m$^2$ (95% CI, 1.7-1.9), 3.2 with an estimated GFR of 15 to 29 mL/min/1.71m$^2$ (95% CI, 3.1-3.4), and 5.9 with an estimated GFR less than 15mL/min/1.73m$^2$ (95% CI, 5.4-6.5). Adjusted hazard ratios for cardiovascular events also increased inversely with estimated GFR: 1.4 (95% CI, 1.4-1.5), 2.0 (95% CI, 1.9-2.1), 2.8 (95% CI, 2.6-2.9), and 3.4 (95% CI, 3.1-3.8), respectively. Risk for hospitalization also correlated with reduced estimates of GFR.

**Comment:** Chronic renal disease, even when it does not necessitate dialysis, has considerable adverse effects. While prevention of end-stage renal disease is clearly important, more effective management of milder levels of renal insufficiency is also needed to reduce the adverse health effects of lesser levels of impaired renal function.

**Below-knee elastic compression stockings to prevent the postthrombotic syndrome: A randomized, controlled trial**

Prandoni P, Lensing AWA, Prins MH, et al. Ann Intern Med 2004;141: 249-56.

**Conclusion:** Below-knee elastic compression stockings reduce development of postthrombotic syndrome in almost half of patients with proximal deep venous thrombosis (DVT).

**Summary:** The authors sought to evaluate the ability of elastic compression stockings to prevent postthrombotic syndrome in patients with acute proximal DVT. This randomized, controlled trial, conducted in a university hospital in Italy, included 180 consecutive patients with a first episode of symptomatic proximal DVT treated with conventional anticoagulation therapy. Before discharge, patients were randomly assigned to use below-knee elastic compression stockings (30-40 mm Hg at the ankle) for 2 years. Follow-up extended up to 5 years. Presence and severity of postthrombotic syndrome was scored with a standardized scale.

Sequela of postthrombotic syndrome developed in 44 of 90 control patients, and was severe in 10. Sequela of postthrombotic syndrome developed in 23 of 90 patients wearing elastic stockings, and was severe in 3. The cumulative incidence of postthrombotic syndrome in the control group versus the elastic stocking group was 40.0% (95% confidence interval [CI], 29.9-50.1) versus 21.1% (95% CI, 12.7-29.5) after 6 months, 46.7% (95% CI, 36.4-57.0) versus 22.2% (95% CI, 13.8-30.7) after 1 year, and 49.1% (95% CI, 38.7-59.4) versus 24.5% (95% CI, 15.6-33.4) after 2 years. The hazard ratio for postthrombotic syndrome in the elastic compression stockings group compared with the control group was 0.49 (CI, 0.29-0.84; $P = .011$).

**Comment:** This study and a previous study by Brandjes et al (Lancet 1997;349:759-62) indicate a beneficial effect of prophylactic elastic compression stockings in preventing postthrombotic syndrome in patients with symptomatic proximal DVT. Patients with proximal DVT should use elastic compression stockings to reduce the incidence of postthrombotic syndrome.