# Abstracts

## Greogry L. Moneta, MD, Section Editor

### Population-Based Study of Incidence and Outcome of Acute Aortic Dissection and Premorbid Risk Factor Control: 10-Year Results From the Oxford Vascular Study

Howard DPJ, Banerjee A, Fairhead JF, et al. Circulation 2013;127:2031-7.

**Conclusions:** Hospital-based registries likely underestimate not only the incidence of acute aortic dissection but also its association with premorbid hypertension. The most significant treatable condition leading to acute aortic dissection remains uncontrolled hypertension.

**Summary:** Even with well-established treatment guidelines, acute aortic dissection can have a high case fatality rate. However, little data on risk factors, incidence, or outcome of acute aortic dissection are available, and there is no prospective population-based study. Although abdominal aortic aneurysm incidence of rupture appears to be declining (Darwood R et al, J Vasc Surg 2012;56:8-13), trends with respect to acute aortic dissection are uncertain (Thrumurthy SG et al, BMJ 2012;344:d8290). The authors note there have only been two studies of the epidemiology of aortic dissection since 1980, and both were retrospective and used only routinely collected diagnostic or mortality coding data. Neither study assessed premorbid risk factors or functional outcome (Clouse WD et al, Mayo Clin Proc 2004;79:176-80; and Olsson C et al, Circulation 2006;114:2611-8). This study used the 92,728 patient population of Oxfordshire in the United Kingdom to prospectively determine event rates, incidence, risk factors, early case fatality, and long-term outcome of all cases of acute aortic dissection from 2002 to 2012. Data were collected as part of the Oxford Vascular Study. Among 155 patients with 174 acute aortic events, there were 54 patients (31 men; mean age, 72.0 years) with 59 thoracoabdominal aortic dissections (52 incident events: 6/100,000; 95% confidence interval, 4-7) comprising 37 Stanford type A and 15 Stanford type B. Of the patients with type A incident events, 18 (48.6%) died before hospital assessment (61.1% women). The 30-day fatality rate was 47.4% for patients with type A dissections who survived to hospital admission and 13.3% for patients with type B dissections. Subsequent 5-year survival rates were, however, high (85.7% for type A; 83.3% for type B). Although 67.3% of patients were taking antihypertensive drugs, 46.0% had at least one systolic BP >180 mm Hg in their primary care records during the preceding 5 years. The proportion of blood pressures in the hypertensive range (>140/90 mm Hg) averaged 56.0%. Premorbid blood pressure in the type A dissection patients was higher in those patients where the dissection was immediately fatal than in those who survived to admission (mean/standard deviation pre-event systolic blood pressure was 151.2 ± 19.3 vs 137.9 ± 17.9; $P < .001$).

**Comment:** The data suggest that the incidence of acute aortic dissection is higher than previously reported. The authors speculate this is likely due to more complete inclusion of deaths before hospital admission. If one does the numbers in the report, it appears there are ~44 ruptured abdominal aortic aneurysms per year and 24 acute aortic dissections per year in the Oxford population of ~93,000 patients. The Oxford population is 94% Caucasian, whereas that of the United States is about 72.4% Caucasian, and thus, the incidence rates of acute aortic events in this study are not directly applicable to all populations. Nevertheless, the epidemiologic data provided here allow one to estimate the burden of acute aortic events in many regions of Europe, Australia, and the United States.

### Cilostazol Reduces Angiographic Restenosis After Endovascular Therapy for Femoropopliteal Lesions in the Sufficient Treatment of Peripheral Intervention by Cilostazol Study

Iida O, Yokoi H, Soga Y, et al., and the STOP-IC investigators. Circulation 2013;127:2307-15.

**Conclusions:** Cilostazol reduces angiographic restenosis for femoropopliteal lesions after percutaneous transluminal angioplasty with provisional nitinol stenting.

**Summary:** Use of nitinol stents has improved long-term outcomes of endovascular therapy for femoropopliteal lesions compared with balloon angioplasty alone (Schillinger M et al, N Engl J Med 2006;354:1879-88; and Laird JR et al, Circ Cardiovasc Interv 2010;3:267-76). However, even with the use of stents, there remains a 20% to 50% incidence of restenosis at 1 year. The present study was designed to determine, using angiographic follow-up, whether treatment with cilostazol reduces restenosis at 12 months after percutaneous transluminal angioplasty with provisional nitinol stenting. The Sufficient Treatment of Peripheral Intervention by Cilostazol study enrolled 200 patients with femoropopliteal lesions. Patients were treated from March 2009 to April 2011 at 13 centers and randomly assigned 1:1 to receive oral aspirin with or without cilostazol. The primary end point was 12-month angiographic restenosis of ≥50%. Secondary end points were restenosis rates on duplex ultrasound imaging (peak systolic velocity >200 cm/s), rates of major adverse cardiac events, and target lesion event-free survival. End points were assessed in a blinded fashion. The mean lesion length and reference vessel diameter at the treated segment were 128 ± 86 mm and 5.4 ± 1.4 mm, respectively. Frequency of stent use was similar between groups (88% vs 90% in the cilostazol and noncilostazol groups, respectively; $P = .82$). Eleven patients died, and 152 (80%) had evaluable angiographic data at 12 months of follow-up. Angiographic restenosis at 12 months was 20% (15 of 75) in the cilostazol group vs 49% (38 of 77) in the noncilostazol group ($P = .0001$) by intention-to-treat analysis. There was also a significantly higher event-free survival in the cilostazol group at 12 months (83% vs 71%, $P = .02$). Cardiovascular event rates were similar in both groups.

**Comment:** The data indicate cilostazol, in combination with aspirin, can significantly reduce angiographic restenosis after endovascular therapy for femoropopliteal disease. This study is limited by the fact that, strictly speaking, the data apply only to a Japanese population. At the start of the study, the S.M.A.R.T. stent was the only one available for this study. Newer-generation stents and drug-eluting stents were not included. Certainly, restenosis rates with the use of cilostazol and newer stents or clopidogrel, or both, in more varied populations will also be of interest. Until such data are available, routine addition of cilostazol as an adjunct to femoropopliteal stenting is not likely to occur.

### Home-Based Walking Exercise Intervention in Peripheral Artery Disease a Randomized Clinical Trial

McDermott MM, Liu K, Guralnik JM, et al. JAMA 2013;310:57-65.

**Conclusions:** Home-based walking exercise programs can significantly improve walking endurance, physical activity, and patient-perceived walking endurance and speed in patients with peripheral arterial disease (PAD), with and without classic claudication symptoms.

**Summary:** Few patients with PAD participate in supervised treadmill exercise therapy (Regensteiner JG, Curr Drug Targets Cardiovasc Haematol Disord 2004;4:233-9). There may be many reasons why supervised exercise therapy is not used in the PAD patient, including that it requires regular transportation to an exercise center and that supervised exercise is not generally covered by medical insurance. Although home-based walking exercise would seem a promising alternative to supervised exercise, trials have yielded conflicting results with respect to the efficacy of home-based exercise in the PAD patient. Indeed, most physicians do not recommend home-based walking exercise to patients with PAD (Hirsch AT et al, Vasc Med 2001;6:87-96; and McDermott MM et al, J Gen Intern Med 2002;17:895-904). Here, the authors report the result of the Group Oriented Arterial Leg Study, a randomized, controlled, clinical trial designed to assess if an intervention to increase home-based walking exercise would improve walking performance at the 6-month follow-up in patients with PAD. A group-mediated cognitive behavioral intervention incorporating group support and self-regulatory skills was used to help participants adhere to a home-based exercise program. The authors' hypothesis was that the intervention group would have greater improvement in objective and subjective measures of walking performance and physical activity compared with a control group that received health education alone. The study included 194 patients with PAD, 72.2% of whom did not have classic symptoms of intermittent claudication. The study took place in Chicago between July 22, 2008, and December 14, 2012. Randomization was to one of two parallel groups, a home-based group-mediated cognitive behavioral walking intervention or an attention control condition. The primary outcome was the 6-month change in 6-minute walk performance. The secondary outcomes included the 6-month change in treadmill walking, physical activity, Walking Impairment Questionnaire, and Physical and Mental

Health Composite Scores from the 12-item Short-Form Health Survey. Those randomized to the intervention group increased their 6-minute walk distance in meters significantly (357.4 to 399.8 vs 353.3 to 342.2 for those in the control group; mean difference, 53.5; $P < .001$). There were also increases in maximum treadmill walking time (intervention, 7.91 to 9.44 minutes vs control, 7.56 to 8.09 minutes; mean difference, 1.01 minutes; $P = .04$). Accelerometer-measured physical activity over 7 days also increased in the intervention group vs the control group ($P = .03$). There were also significant improvements in the Walking Impairment Questionnaire distance score ($P = .003$) and Walking Impairment Questionnaire speed score ($P = .004$).

**Comment:** The study indicates that home-based exercise can be effective in patients with PAD. It does not indicate that home-based exercise has equal effectiveness to supervised exercise programs, because the two were not directly compared. Nevertheless, until supervised exercise becomes a benefit of insurance coverage, the data should encourage physicians to recommend home-based exercise therapy in their patients with PAD.

### Use of Glucocorticoids and Risk of Venous Thromboembolism: A Nationwide Population-Based Case-Control Study

Johannesdottir SA, Horvath-Puho E, Dekkers OM, et al. JAMA Intern Med 2013;173:743-52.

**Conclusions:** Glucocorticoid use increases the risk of venous thromboembolism (VTE).

**Summary:** It is known that excess endogenous cortisol increases VTE risk. Whether this risk applies to exogenous use of glucocorticoids is unclear, however, potentially clinically important. The authors point out that in Denmark, the country of origin of this study, 3.5% of the population redeemed a prescription for systemic glucocorticoids in 2010 (Danish Medicines Agency). Given the incidence of VTE and the prevalence of glucocorticoid use, any association between VTE and glucocorticoid use has important implications. The authors therefore decided to examine the association between exogenous glucocorticoid use and VTE. This was a population case-control study using a nationwide database from Denmark. The authors identified 38,765 VTE cases from the period of January 1, 2005, through December 31, 2011. Risk matched sampling by birth year and sex was used to select 387,650 controls from the general population. The VTE diagnosis date for the case was the index date for cases and matched controls. Patients who had filled a glucocorticoid prescription were classified by the time the prescription was filled, ≤90 days, 91 to 365 days, and >365 days before the index VTE date. Such patients were classified as present, recent, and former users of glucocorticoids, respectively. Present users were subdivided into new (first-ever prescription <90 days before the index date) and continuing users (others). Analysis was performed using conditional logistic regression adjusted for VTE risk factors to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for glucocorticoid users vs nonusers. VTE risk was increased by systemic glucocorticoids in present (adjusted IRR, 2.31; 95% CI, 2.18-2.45), new (3.06; 2.77-3.38), continuing (2.02; 1.88-2.17), and recent (1.18; 1.10-1.26) users but not in former users (0.94; 0.90-0.99). Adjusted IRR increased from 1.00 (95% CI, 0.93-1.07) for a prednisolone-equivalent cumulative dose of ≤10 mg to 1.98 (95% CI, 1.78-2.20) for >1000 to 2000 mg, and to 1.60 (95% CI, 1.49-1.71) for doses >2000 mg. New use of inhaled (adjusted IRR, 2.21; 95% CI, 1.72-2.86) and intestinal-acting (adjusted IRR, 2.17; 95% CI, 1.27-3.71) glucocorticoids also increased VTE risk.

**Comment:** Of course, many of the disease processes for which glucocorticoids are prescribed may, in themselves, increase VTE risk. However, this extensive analysis found increased risk for not only systemic glucocorticoids but also inhaled and intestinal-acting glucocorticoids, and a causal link is further suggested by higher risk with new users, and with higher doses. These observations, along with adjustment for confounding variables, strongly suggest that the authors' conclusion is correct that glucocorticoid use increases the risk of VTE.

### Ambulatory Blood Pressure Changes After Renal Sympathetic Denervation in Patients with Resistant Hypertension

Mahfoud F, Ukena C, Schmieder RE, et al. Circulation 2013;124:132-40.

**Conclusions:** Office blood pressures are reduced and relevant aspects of ambulatory blood pressure (BP) monitoring (APBM) are improved after renal sympathetic denervation in patients with true-treatment resistant hypertension.

**Summary:** Hypertensive patterns and methods of assessing BP appear to be important in the relationship between hypertension and cardiovascular morbidity and mortality. Guidelines recommend ABPM for patients with resistant hypertension. This is to exclude pseudohypertension and accurately assess BP control according to treatment. ABPM, with 24-hour day-and-night average BP values, correlates better than office BP values with hypertensive or diabetic end-organ damage (Mancia G et al, Hypertension 2000;36:894-900). In addition, nighttime BP correlates more closely with cardiovascular morbidity and mortality than daytime BP (Fagard RH et al, Hypertension 2008;51:55-61). Finally, high nighttime BP and nondipping patterns of hypertension have been associated with increased sympathetic activity in hypertensive patients (Grassi G et al, Hypertension 2008;52:925-31). Renal sympathetic denervation (RDN) reduces office systolic and diastolic BPs in patients with resistant hypertension (Esler MD et al, Lancet 2010;376:1903-9). The purpose of this study was to investigate the effects of RDN on out-of-office BP using 24-hour ABPM. The study represents the largest cohort of patients with true resistant and pseudoresistant hypertension analyzed thus far. A total of 346 uncontrolled hypertensive patients were separated according to daytime ambulatory BP monitoring into 303 with true resistant BP (office systolic BP [SBP] 172 ± 22 mm Hg; 24-hour SBP 154 ± 16 mm Hg) and 43 with pseudoresistant hypertension (office SBP 161 ± 20.3 mm Hg; 24-hour SBP 121 ± 20 mm Hg). Patients were from 10 centers and were studied at 3, 6, and 12 months of follow-up after RDN. In follow-up, office SBP was reduced by 21.5/23.7/27.3 mm Hg, office diastolic BP by 8.9/9.5/11.7 mm Hg, and pulse pressure by 13.4/14.2/14.9 mm Hg (n = 245/236/90; *P* for all <.001), respectively, at 3, 6, and 12 months. In patients with true treatment resistance, there was a significant reduction with RDN in 24-hour SBP (−0.1/−10.2/−11.7) and minimum SBP (−6.0/−9.4/−13.1 mm Hg; $P < .001$) at 3, 6, and 12 months, respectively. In pseudoresistant patients, RDN had no effect on ambulatory BP; however, office BP was reduced to a similar extent. RDN was equally effective in reducing BP in different subgroups of patients. Office SBP at baseline was the only independent correlate of BP response.

**Comment:** The study addressed concerns that RDN might not as effectively reduce ambulatory BP as it does office BP. Results of the study are not entirely unexpected. The Symplicity study of resistant hypertension and RDN did not specifically exclude pseudoresistant hypertension (Esler MD et al, Lancet 2010;376:1903-9). However, only ~12% of the patients in the Symplicity study apparently had pseudoresistant hypertension. As treatment with RDN for resistant hypertension potentially moves toward application out of clinical trials, it will be important for clinicians to be aware that only patients with truly resistant hypertension, and not those with "white-coat syndrome," be considered for RDN.

### Endovascular Repair Versus Open Repair of Ruptured Abdominal Aortic Aneurysms: A Multicenter Randomized Controlled Trial

Reimerink JJ, Hoornweg LL, Vahl AC, and the Amsterdam Acute Aneurysm Trial Collaborators. Ann Surg 2013;258:248-56.

**Conclusions:** There is no difference in outcome of treatment of ruptured abdominal aortic aneurysm (RAAA) in rates of death and severe complication for those patients treated with endovascular (EVAR) or open repair (OR).

**Summary:** In recent years, treatment of RAAA with EVAR has emerged as an alternative to OR. Support for the hypothesis that EVAR reduces mortality in patients with RAAA vs those treated with OR comes from observational and population-based studies (Veith FJ, Ann Surg 2009;250:818-24; and Giles KA, J Endovasc Ther 2009;16:554-64). However, to date, no significant randomized trial data has been available comparing EVAR vs OR for RAAA. A single previous trial was terminated after randomizing 32 patients (Hinchliffe RJ et al, Eur J Vasc Endovasc Surg 2006;32:506-13). The Amsterdam Acute Aneurysm Trial was designed with the hypothesis that EVAR would reduce mortality and severe complications compared with OR for treatment of RAAA. The study was conducted in the greater Amsterdam area (1.24 million inhabitants and 10 hospitals). Three hospitals, consisting of two academic medical centers and a teaching hospital, were trial centers for this study. The trial centers provided alternating around-the-clock RAAA service. The other seven regional hospitals agreed to participate in the trial by transferring patients with suspected RAAA to one of the trial centers if possible. They also provided data on all patients who presented with an RAAA. After diagnosis, anatomic suitability for EVAR based on computed tomography angiography and clinical suitability for OR was documented by the vascular surgeon and the radiologist. Patients suitable for both were then randomized. All patients in the trial region with proven RAAA were included in a prospective parallel cohort. The primary end point of the study was the composite of death and severe complications at 30 days. Between April 2004 and February 2011, 520 patients were identified with RAAA. Of these patients, 365 were excluded from potential randomization because of anatomy unfavorable for EVAR, another 71 were not evaluated by computed tomography scan, and 54 were not referred to a trial center. This left 155 with favorable anatomy who could potentially be randomized. An additional 39 patients, however, were excluded as unfit for OR (n = 16),