

Abstracts

Gregory L. Moneta, MD, Section Editor

Outcomes and survival in surgical treatment of the descending thoracic aorta with acute dissection

Bozinovski J, Coselli JS. *Ann Thorac Surg* 2008;85:965-71.

Conclusion: Open replacement of the descending thoracic aorta or thoracoabdominal aorta for acute type B dissection carries substantial morbidity and mortality rates.

Summary: In a large majority of cases, acute type B aortic dissection is managed medically with a favorable outcome. Certainly, aortic rupture in the setting of acute type B dissection is an indication for emergency intervention. Some centers also used continued pain or a large diameter aortic dissection as an indication for urgent repair. In this article the authors describe the results of open urgent or emergency repair of the descending thoracic aorta or the thoracoabdominal aorta for acute dissection in 76 consecutive patients (72% male). The patients were acquired during a 16-year period from 1989 to 2004 and therefore represent a relatively small component of patients treated for thoracic dissection at this center during that time. The average age of the patients who underwent surgery for acute type B aortic dissection was 64.1 ± 12.2 years (range, 36-86 years), and 22% presented with rupture. A variety of surgical adjuncts were used without a specific protocol, including hypothermic circulatory arrest in eight patients and left carotid bypass in 15. Spinal fluid drainage was used in only five patients. Aortic clamp time was 38.4 ± 17.3 minutes.

One patient died intraoperatively. The overall 30-day operative mortality was 22.4%. Paraplegia occurred in 6.6%, and hemodialysis was required in 19.7%, with about half of these patients requiring permanent hemodialysis. Cardiac complications occurred in 43.4%, and 10 patients had prolonged respirator dependence necessitating tracheostomy. The hospital stay was 26.0 ± 29.7 days. Rupture was not associated with an increased risk of operative mortality or perioperative complication.

Comment: The article highlights why it is best to avoid an operation in acute type B dissections. Even in a center with acknowledged expertise in thoracic aortic surgery, mortality is high and morbidity is also very high. Because mortality and morbidity rates were the same for patients with and without rupture, it is important to reassess indications for emergency or urgent open thoracic aortic repair in patients with acute type B dissection. We need better natural history data to know whether continued pain predicts rupture or if a larger initial diameter of the dissection predicts actual rupture. One can also see this article as providing justification for endovascular repair of ruptured or severely symptomatic acute type B dissections. Given the results here, most centers are likely to do better with endovascular repair rather than open repair of an acute type B dissection.

Telmisartan, ramipril, or both in patients at high risk for vascular events

ONTARGET Investigators. *N Engl J Med* 2008;358:1547-59.

Conclusion: The angiotensin-receptor blocker (ARB) telmisartan is equivalent to the angiotensin-converting enzyme (ACE) inhibitor ramipril in preventing cardiovascular events in patients with vascular disease or diabetes.

Summary: It is well known that ACE inhibitors reduce mortality and morbidity from cardiovascular causes in patients with vascular disease or high-risk diabetes who do not have heart failure. ARBs have also been shown to reduce fatal and nonfatal cardiovascular events, but have not been previously compared with ACE inhibitors in patients with peripheral arterial disease or high-risk diabetes. In this study, the ACE inhibitor ramipril was compared with the ARB inhibitor telmisartan and with the combination of the two drugs in patients with vascular disease or high-risk diabetes. This was a noninferiority study. Patients underwent a three-way, single-arm, run-in period and then were randomized using double-blind techniques so that 8576 patients received 10 mg of ramipril daily, 8542 received 80 mg of telmisartan daily, and 8502 received both drugs as a combination therapy. The primary composite outcome was myocardial infarction, stroke, hospitalization for heart failure, or death from cardiovascular causes.

Median follow-up was 56 months. The mean blood pressure was lower in both the telmisartan group and the combination therapy group compared with the ramipril group. The difference was 0.9/0.6 mm Hg in the telmisartan group and 2.4/1.4 mm Hg in the combination therapy group compared with the ramipril group. The primary endpoint occurred in 1412 patients (16.5%) in the ramipril group and in 1423 (16.7%) in the telmisartan group (relative risk, 1.05; 95% confidence interval, 0.95-1.09). The telmisartan group had lower rates of cough than the ramipril group (1.1% vs 4.2%, $P < .001$). The telmisartan group also had a lower rate of angioedema than the ramipril group (0.1% vs 0.2%, $P = .01$) but a higher rate of

hypotensive symptoms (2.6% vs 1.7%, $P < .001$). Syncopal rate was the same in the two groups (0.2%). In the combination therapy group, the primary endpoint occurred in 1386 patients (16.3%; relative risk, 0.99; 95% CI, 0.92-1.07) compared with the ramipril group. The combination therapy group had an increased risk of hypotensive symptoms (4.8% vs 1.7%, $P < .001$), syncope (0.3% vs 0.2%, $P = .03$), and renal dysfunction (13.5% vs 10.2%, $P < .001$) than the ramipril group.

Comment: The data indicate that the ARB telmisartan is equivalent to the ACE inhibitor ramipril in patients with vascular disease or high-risk diabetes in reducing cardiovascular events. This is the fourth trial indicating the ARBs are equivalent to ACE inhibitors in reducing cardiovascular events. The clinical role of ARBs is still being defined. These drugs are more costly than ACE inhibitors and generally have more side effects. At this point their primary value seems to be patients who cannot tolerate ACE inhibitors because of cough.

Long-term results of carotid stenting vs endarterectomy in high-risk patients

Grum HS, Yadava JS, Fayad P, and the SAPPHERE Investigators. *N Engl J Med* 2008;358:1572-9.

Conclusion: There is no significant difference in long-term outcomes in patients with severe carotid artery stenosis and increased surgical risk treated with carotid stenting and an embolic protection device vs those undergoing carotid endarterectomy (CEA).

Summary: The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHERE) trial was designed as a noninferiority trial and reported 1-year results in 2004, finding carotid artery stenting with an embolic protection device was not inferior to CEA (*N Engl J Med* 2004;351:1493-501). The 3-year results are reported here. Originally, 334 patients were entered in the trial. The patients were considered at increased risk for complications for CEA and had to have had at least 50% stenosis of the internal carotid artery to be included. Eighty percent of the patients were asymptomatic. Prespecified major secondary endpoints at 3 years were a composite of death, stroke, or myocardial infarction ≤ 30 days after the procedure, or death or ipsilateral stroke between 31 days and 1080 days (3 years).

At 3 years, data were available for 260 patients, 85.6% of the patients in the stented group and 70.1% of patients in the CEA group. Prespecified major secondary endpoints occurred in 41 patients in the stented group (cumulative index, 24.6%; Kaplan-Meier estimate, 26.2%) and in 45 patients in the endarterectomy group (cumulative index, 26.9%; Kaplan-Meier estimate, 30.3%; absolute difference in cumulative incidence for the stenting group, -2.3%; 95% CI, 11.8-7.0). There were 15 strokes in each of the two groups, with 11 in the stenting group and nine in the CEA group being ipsilateral to the treated artery.

Comment: This trial has a number of significant limitations, all of which, to the authors' credit, are indicated on the last page of the article, before the references. These include the absence of a medical therapy group, the fact that many of these patients in many practices would not be treated with any intervention, the small size of the randomized cohort that prevents meaningful subgroup analysis, incomplete follow-up at 3 years, the use of only one type of embolic protection device, and the lack inclusion of moderate- or low-risk patients for CEA. Finally, 10 of the 12 named authors are financially linked to Cordis, the sponsor of the trial, or had patents linked to the cerebral protection device used in the trial.

Significance of postoperative cross cerebellar hypoperfusion in patients with cerebral hyperperfusion following carotid endarterectomy: SPECT study

Ogasawara K, Kobayashi M, Suga Y, et al. *Eur J Nucl Med Mol Imaging* 2008;35:146-52.

Conclusion: Postoperative crossed cerebellar hypoperfusion (CCH) in patients with cerebral hyperperfusion after carotid endarterectomy (CEA) results in postoperative cognitive impairment even when asymptomatic.

Summary: Cerebral hyperperfusion after CEA is defined as an increase in ipsilateral cerebral blood flow that exceeds the metabolic demands of brain tissue. The occurrence of the cerebral hyperperfusion syndrome is characterized by headache, face and eye pain, seizure, and focal symptoms. Symptomatic cerebral edema or intracerebral hemorrhage occurs less often than cerebral hyperperfusion after CEA, much of which may be asymptomatic. There are data to suggest post-CEA cerebral hyperperfusion, as measured by a single-photon emission computed tomography (SPECT) scanning, can be associated with development of postoperative cognitive impairment without

the occurrence of clinically evident cerebral hyperperfusion. Crossed cerebellar hypoperfusion (CCH) is a reduction in blood flow in the cerebellar hemisphere contralateral to a supratentorial lesion. This phenomenon can be seen after CEA. The authors sought to clarify the significance of postoperative CCH in patients with cerebral hyperperfusion using SPECT scanning and tests of cognitive impairment.

Brain perfusion was measured using SPECT scanning before and immediately after CEA and on postoperative day 3 in 80 patients who underwent CEA for >70% stenosis. Postoperative CCH was determined by differences between asymmetry of perfusion in the cerebellar hemispheres before and after CEA. Patients also underwent neuropsychologic testing preoperatively and at 1 month after CEA.

The authors used a definition of a 100% increase in cerebral blood flow for cerebral hyperperfusion and found that it had developed in 11 of 80 patients after CEA. SPECT scans were performed immediately after CEA and on postoperative day 3. Of the 11 patients in whom cerebral hyperperfusion developed, CCH was observed in seven on postoperative day 3. Three patients had cerebral hyperperfusion syndrome and exhibited cerebral hyperperfusion and CCH on postoperative day 3, and postoperative cognitive impairment developed. Four of eight patients with asymptomatic cerebral hyperperfusion exhibited CCH. Three of these patients exhibited postoperative cognitive impairment. The four patients with asymptomatic cerebral hyperperfusion who did not have CCH did not experience postoperative cognitive impairment.

Comment: Cerebral hyperperfusion after CEA is more complicated than most are aware. The article points out that it occurs more frequently than is generally thought, has different patterns of hyperperfusion, and can result, at least when measured using sophisticated neuropsychiatric testing, in cognitive impairment even in the absence of clinical hyperperfusion syndrome.

Use of multiple biomarkers to improve the prediction of death from cardiovascular causes

Zethelius B, Berglund L, Sundstrom J, et al. *N Engl J Med* 2008;358:2107-16.

Conclusion: In elderly men, use of biomarkers of cardiovascular and renal abnormalities increases risk stratification for death from cardiovascular causes beyond that of a predictive model using traditional risk factors only.

Summary: The authors sought to evaluate the utility of multiple biomarkers from different disease pathways to predict the risk of death from cardiovascular causes in elderly men. Data were acquired from the Uppsala Longitudinal Study of Adult Men (ULSAM). This community-based cohort study was initiated in 1970 of 50-year-old men born from 1920 to 1924 and living in Uppsala, Sweden. This analysis is based on the third examination cycle of this cohort when participants were approximately 71 years of age (1991 to 1995). Established risk factors for cardiovascular disease analyzed included age, systolic blood pressure, use or nonuse of antihypertensive treatment, total cholesterol levels, high-density lipoprotein cholesterol, use or nonuse of lipid-lowering treatment, presence or absence of diabetes, smoking status, and body mass index. Additional biomarkers evaluated reflected those that mirrored myocardial cell damage, left ventricular dysfunction, renal failure, and inflammation (troponin I, N-terminal pro-brain natriuretic peptide, cystatin C, and C-reactive protein). Follow-up was for a median of 10.0 years.

There were 1135 participants (mean age, 71 years at baseline). Of these, 315 died during follow-up, and 136 of the deaths were the result of cardiovascular disease. All the biomarkers predicted risk of death from cardiovascular causes according to Cox proportional hazard models and adjusting for established risk factors. The predictive value increased significantly when the biomarkers were incorporated into a model with established risk factors in the entire cohort and in the group of 661 patients who did not have cardiovascular disease at baseline (C statistic with biomarkers vs without biomarkers, 0.766 vs 0.664, $P < .001$; C statistic with biomarkers vs without biomarkers, 0.748 vs 0.688, $P = .03$).

Comment: Previous studies evaluating the combination of multiple biomarkers in predicting cardiovascular risk (*N Engl J Med* 2006;355:2631-9) have not shown as dramatic results as the current study. The authors point out that this may be because participants in the present study were an average of 10 years older than the participants in previous studies, and that the combination of biomarkers used in the current study were not used in previous studies. Biomarkers used in this study may identify patients with functional or structural abnormalities of their cardiovascular systems that have not yet led to overt cardiovascular disease but place the patients at risk for the development of cardiovascular disease during follow-up.

Risk of new aneurysms after surgery for popliteal aneurysm

Ravn A, Wanhainen A, Bjorck M. *Br J Surg* 2008;95:571-5.

Conclusion: In patients treated surgically for popliteal artery aneurysm, the development of new aneurysms at other sites during follow-up is common.

Summary: Patients with popliteal artery aneurysms (PAA) are known to have a high incidence of concurrent aneurysmal degeneration of the

opposite popliteal artery or the abdominal aorta, or both, at the time of discovery of the index PAA. The risk of developing new aneurysms in previously apparently normal arterial segments after PAA repair is, however, unknown. This study sought to determine the incidence of development of new aneurysms in previously nonaneurysmal popliteal arterial segments after repair of an index PAA. The study was based on analysis of the Swedish Vascular Registry. (Every citizen in Sweden has a unique personal identity code that can be used in vascular surgical research.)

Between 1987 and 2002, 571 patients (717 legs) in Sweden had a primary operation for PAA. Analysis for this study began in January 2005. Data were crosschecked against the national population registry and indicated 337 patients had undergone PAA repair during the study period and were alive in January 2005. Patients were then assessed for the presence of additional aneurysms at the time of their index PAA repair and were asked to participate in a telephone interview and a re-examination. Of these, 240 patients agreed, and 190 were re-examined by ultrasonography at a medium of 7 years (range, 2.9-18.7 years) after their index PAA repair.

At the time of the PAA repair, the number of patients with at least one aneurysm, in addition to the index PAA, was 108 (56.8%) at the index operation, and 131 (68.0%) at re-examination. The number of additional aneurysms increased from 244 to 346 (an increase of 41.8%). Among the 82 patients who had an isolated PAA at the index operation, a new aneurysm was detected in 23 at the time of their follow-up ultrasound study. Patients in whom new aneurysms developed tended to be older ($P = .004$). The presence of bilateral PAA at the index operation was associated with a later development of an abdominal aortic aneurysm ($P = .004$). Increased age and hypertension at the time of the index operation were associated with multianeurysmal disease at any time ($P = .004$ and $P = .012$ respectively).

Venous bypass grafts were used to treat 138 of the legs, and six (4.3%) developed aneurysm degeneration of the venous bypass graft. Within 3 years of the initial PAA repair, no normal arterial segments had developed sufficient aneurysmal degeneration that required surgery. Overall, an additional 102 aneurysms developed in 74 patients, and only 59 of the 190 subjects re-examined did not develop an additional aneurysm.

Comment: This study indicates new aneurysm development in patients with PAA is frequent. Because no patient developed a new aneurysm that required surgery ≤ 3 years of the index operation, it would seem that a practical plan for follow-up would be to reinvestigate patients with PAAs for new aneurysms every 3 years, beginning 3 years after the initial popliteal aneurysm repair.

Do current outcomes justify more liberal use of revascularization for vasculogenic claudication? A single-center experience of 1000 consecutively treated limbs

Taylor SM, Kalbaugh CA, Healy NG, et al. *J Am Coll Surg* 2008;206:1053-64.

Conclusions: In contemporary practice, treatment of claudication is safe, effective, and predominantly endovascular.

Summary: This is a retrospective review of 1000 limbs in 669 patients treated for what was determined to be medically refractory vasculogenic claudication. The authors assess procedural complication rates, patency of reconstructions, maintenance of ambulatory status, maintenance of independent living, survival, symptom resolution, symptom recurrence, and limb salvage. Of the 1000 limbs treated, aortoiliac disease was treated in 70.1% and infrainguinal occlusive disease in 29.9%. Endovascular therapy was used in 64.3% of the limbs treated and open surgery in 35.7%. The 30-day complication rate was 7.5%. The authors noted no difference in complication rates comparing types of treatment or level of disease. At 1 and 5 years, reconstruction primary patency was 87.7% and 70.8%, secondary patency was 97.8% and 93.9%, survival was 94.4% and 76.9%, and limb salvage was 100% and 98.8%, respectively. Symptom resolution occurred in 78.8% and recurrence in 18.1%. There was slightly higher resolution and recurrence noted in patients treated with endovascular therapy.

Comment: You have to admire the fact that this group of surgeons keeps track of what they do and tries to report their results. Unfortunately, the way they report their results is not all that useful. Patients were not stratified by degree of claudication, TransAtlantic Inter-Society Consensus lesions, prehemodynamic and posthemodynamic status, or the occurrence of single-level or multilevel disease. We also have no idea about who was not treated. Nevertheless, it does appear that if you are willing to spend a lot of money, you can treat a lot of patients with claudication and you won't hurt many of them very much.

Fistula elevation procedure: Experience with 295 consecutive cases during a 7-year period

Bronder CM, Cull DL, Kuper SG, et al. *J Am Coll Surg* 2008;206:1076-82.

Conclusion: Elevation of an autogenous fistula that is otherwise too deep or tortuous for access is a valuable adjunct that improves ultimate utilization of autogenous arteriovenous fistulas in hemodialysis access.