Abstracts

Gregory L. Moneta, MD, Section Editor

Abdominal Aortic Aneurysm Events in the Women’s Health Initiative: Cohort Study

Conclusion: There are no significant differences between endovascular and open repair of blunt aortic injury with respect to morbidity or mortality. Summary: Endovascular stent grafting has nearly become the standard of care for treatment of blunt thoracic aortic injury. This is despite the lack of any randomized data to support this paradigm change in the treatment of blunt thoracic aortic injury. The authors sought to determine whether the use of endovascular stent grafting has actually improved outcome of treatment of blunt thoracic injury. This was a retrospective review of the patients from single institution trauma registry and included in this study if they had computed tomography angiography during their hospitalization. More data are clearly needed, as the trend for ER of blunt thoracic aortic injury will continue.

Blunt Thoracic Aortic Injury: Open or Stent Graft Repair?

Conclusion: There are no significant differences between endovascular and open repair of blunt aortic injury with respect to morbidity or mortality. Summary: Endovascular stent grafting has nearly become the standard of care for treatment of blunt thoracic aortic injury. This is despite the lack of any randomized data to support this paradigm change in the treatment of blunt thoracic aortic injury. The authors sought to determine whether the use of endovascular stent grafting has actually improved outcome of treatment of blunt thoracic aortic injury. This was a retrospective review of the patients from single institution that were treated for blunt thoracic aortic injury from October 1999 to May 2007. Patients were identified from the University of Wisconsin’s level I trauma registry and included in this study if they had computed tomography or angiography evidence of a thoracic aortic injury distal to the left subclavian artery after blunt trauma. Patients were separated into those who underwent open repair (OR) and those who underwent endovascular repair (ER). Patients were assessed for demographics, mechanism of injury, injury severity score (ISS), associated injuries, known comorbid conditions, intraoperative findings, postoperative complications, and hospital stay. Outcomes in patients treated with OR and ER were compared. During this 8-year period, 26 consecutive patients (20 men) were treated for blunt aortic injury, of which 12 were treated with OR and 14 with ER. The mean age was 36 years. There were no differences between the OR and ER groups with respect to mechanism of injury, ISS, or number of associated injuries upon presentation. ER was technically successful in 100% of patients. There was no mortality in the OR group. There were four deaths in the ER group. Patients in the ER group tended to have delayed repair vs those in the OR group, with an average time from injury to repair of 0.8 days for the OR group and 12.2 days for the ER group. Comment: ER of thoracic aortic injury has its problems, but most articles on this subject have concluded ER of blunt thoracic injury has advantages over OR. This report will not significantly detract from the trend for ER of blunt thoracic aortic injury. The number of patients treated here was relatively small, averaging only about three patients per year. In addition, the patients treated with OR had a mean cross-clamp time of 27 minutes (these are quick surgeons), and half of the patients could be treated with primary repair (favorable injuries). Overall survival of the OR group was higher than is usually seen in reports of OR of thoracic aortic injury. This suggests a relatively favorable group of patients treated with OR for blunt thoracic injury at the University of Wisconsin. More data are clearly needed, but despite this report, the trend for ER of blunt thoracic aortic injury will continue.

Cytchrome P 450 Polymorphisms and Response to Clopidogrel

Conclusion: Persons with a reduced function of the CYP2C19 allele have significantly lower levels of active metabolite of clopidogrel, with diminished platelet inhibition and higher rates of major cardiovascular events than noncarriers of the CYP2C19 allele. Summary: Clopidogrel is a thienopyridine inhibitor of the platelet P2Y12 adenosine diphosphate (ADP) receptor. It is a “prodrug” that requires biotransformation to an active metabolite by a cytochrome P 450 enzyme. Esters of mcllodogrel to an inactive pathway, with the remaining prodrug requiring two separate CYP-dependent oxidative steps. Genes encoding CYP enzymes are polymorphic, with some alleles conferring reduced enzymatic function. Therefore, it is possible CYP polymorphisms can effect conversion of clopidogrel to active metabolite and hence affect the degree of clopidogrel induced platelet inhibition.

In this study the authors tested the association between functional variance in CYP genes, plasma concentration of active clopidogrel drug metabolite, and platelet inhibition in response to clopidogrel. There were 162 healthy subjects analyzed as well as 1477 individuals with acute coronary syndromes treated with clopidogrel in a trial to assess improvement in therapeutic outcomes by optimizing platelet inhibition in patients with myocardial infarction (TRITON-TIMI 38). Approximately 30% of the healthy participants were carriers of at least one CYP2C19 reduced-function allele. These individuals had a reduction of 32–42 % in plasma exposure to the active metabolite of clopidogrel compared with noncarriers (P < .001). Carriers also had reduced reduction in maximal platelet aggregation compared with noncarriers (P < .001). Among clopidogrel-treated patients in TRITON-TIMI 38, carriers of reduced-function alleles had a relative increase of 53% in the composite primary end point of death due to cardiovascular causes, myocardial infarction, or stroke compared with noncarriers (12.1% vs 8%; hazard ratio [HR] for carriers, 1.52; 95% confidence interval [CI] 1.07–2.19; P = .01). Carriers had an increase by a factor of three in the risk of stent thrombosis (2.6% vs 0.8%; HR, 3.09; 95% CI, 1.19–8.00; P = .02).

Conclusion: This study, along with the similar study also appearing in the same issue of the New England Journal of Medicine (2009;360:363–75), provides strong evidence linking genetic variations in CYP genes to reduced exposure to active drug metabolite in patients treated with clopidogrel. These polymorphisms are seen in approximately 30% of white patients, 40% of African Americans, and >55% of people of East Asian origin. Of course multiple other genetic and environmental factors can also contribute to platelet aggregation. Nevertheless, the data are quite convincing that genetic variation in the genes encoding CYP enzymes can result in meaningful and profound clinical effects.

Effect of Statins Alone Versus Statins Plus Ezetimibe on Carotid Atherosclerosis in Type 2 Diabetes

Conclusion: Reducing low-density lipoprotein cholesterol (LDL-C) to aggressive target levels results in similar regression of carotid intimal medial thickness (CIMT) in patients achieving equivalent LDL-C reductions using either a statin or statin plus ezetimibe. CIMT increases in patients achieving only standard target levels for LDL-C. Summary: This is a secondary analysis from the SANDS (Stop Atherosclerosis in Native Diabetics Study). The goal was to examine the effects