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Abstracts

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Comparative Determinants of 4-Year Cardiovascular Event Rates in Stable Outpatients at Risk of or With Atherothrombosis

Bhatt DL, Eagle KA, Ohman EM, and the REACH Registry Investigators. JAMA 2010;304:1350-7.

Conclusion: Patients with vascular events are those at highest risk for future cardiovascular death, myocardial infarction, and stroke.

Summary: Clinical trials of pharmacologic agents in patients with atherosclerosis often report event rates in placebo groups lower than projected (Bhatt DL, N Engl J Med 2009;361:2330-41; Sacco RL, N Engl J Med 2008;359:1238-51; and Topol EG, Lancet 2010;376:517-23). To increase likelihood that a particular therapy might demonstrate benefit, it is important to identify patients to participate in trials who are at high risk for cardiovascular events. The REACH (Reduction of Atherothrombosis for Continued Health) Registry consists of patients with various manifestations of atherosclerosis varying from asymptomatic adults with risk factors to those with stable atherosclerosis to those with prior ischemic events. In this study the authors analyze the effects of prior ischemic events, polyvascular disease, and diabetes mellitus with respect to future cardiovascular risk. Patients in the REACH Registry were followed for up to 4 years. Patients were from 3647 centers in 29 countries enrolled between 2003 and 2004 and followed up until 2008. The primary end point was a composite of cardiovascular deaths, myocardial infarction, and stroke. Main outcome measures were rates of cardiovascular death, myocardial infarction, and stroke.

There were 45,227 patients included in the 4-year analysis. During follow-up, 5481 patients experienced at least one event; 2315 cardiovascular deaths, 1228 myocardial infarctions, 1898 strokes, and 40 cases where myocardial infarction and stroke occurred on the same day. Those with a history of ischemic events at baseline (n = 21,890) had the highest rate of subsequent ischemic events (18.3%: 95% confidence interval [CI], 17.4%-19.1%). Patients with stable coronary, cerebrovascular, or peripheral artery disease (n = 15,264) had a lower risk (12.2%; 95% CI, 11.4%-12.9%). Patients with risk factors without established atherothrombosis (n = 8073) had the lowest risk (9.1%; 95% CI, 8.3%-9.9%; $P < .001$ for all comparisons). In multivariable modeling diabetes (hazard ratio [HR], 1.44; $P < .001$), an ischemic event in the previous year (HR 1.71; $P < .01$), and polyvascular disease (HR, 1.99; $P < .001$) all were associated with increased risk of the primary end point.

Comment: The data indicate polyvascular disease and a history of ischemic events, particularly in the last year, are strongly associated with cardiovascular death, myocardial infarction, and stroke. Many vascular surgical patients would fall in to the high-risk groups. This perhaps explains, in part, the high mortality rates of vascular surgical patients over time and somewhat cynically may explain why vascular surgery patients tend to be "repeat customers." Once a patient with vascular disease has a cardiovascular event they are much more likely to have additional events.

Standard Prophylactic Enoxaparin Dosing Leads to Inadequate Anti-Xa Levels and Increased Deep Venous Thrombosis Rate in Critically Ill Trauma and Surgical Patients

Malinoski D, Jafari F, Ewing T. J Trauma 2010;68:874-80.

Conclusion: Standard prophylactic dosing of enoxaparin leads to low anti-Xa levels in half of surgical intensive care unit patients with associated increased risk of deep venous thrombosis (DVT).

Summary: DVT rates of those untreated intensive care unit (ICU) patients range from 13% to 31% and up to 70% in severely injured patients. Standard prophylaxis in higher-risk trauma or surgical patients includes twice-daily dosing with enoxaparin (30 mg) but can still result in DVT rates of 10% to 15%. Some patients experience altered pharmacokinetics and pharmacodynamics of low-molecular-weight heparin (LMWH), reflected in low trough anti-Xa levels with standard prophylactic dosing of LMWH. The authors hypothesized that low anti-Xa levels would be found in critically ill, trauma, and surgical patients treated with standard prophylactic doses of LMWH and that such patients would have higher rates of DVT.

When there were no contraindications, surgical ICU patients were treated with prophylactic enoxaparin and prospectively monitored. Anti-Xa levels were drawn after the third dose. A trough level of ≤0.01 IU/mL was considered low. Screening venous duplex ultrasound exams were obtained at ≤48 hours of admission and then weekly. Excluded patients included those who did not receive an ultrasound study, those who had a prior DVT, or if anti-Xa trough levels were incorrectly obtained. Demographic data and DVT rates were compared between patients with low and normal anti-Xa levels. Fifty-four patients had a complete data set, of which 85% had an injury severity score of 25 ± 12. There were 74% men and 26% women, and 27 patients (50%) had low anti-Xa levels. Those patients with low anti-Xa levels had more DVTs than those with normal levels (37% vs 11%, $P = .026$). There were no differences between those with normal and low anti-Xa levels with respect to age, injury severity score, creatinine clearance, body mass index, prevalence of high-risk injuries, and ICU/ventilator days.

Comment: The data provide at least a partial explanation for the continued high rates of VTE complications in the injured patient despite protocols of chemical and mechanical VTE prophylaxis. It remains to be seen whether prophylactic dosing of LMWH stratified for anti-Xa levels would be both effective and cost effective in reducing VTE complications in the injured patient or critically ill surgical patient.

Randomized Clinical Trial of Mesh versus Sutured Wound Closure After Open Abdominal Aortic Aneurysm Surgery

Bevis PM, Windhaber RAJ, Lear PA, et al. Br J Surg 2010;97:1497-502.

Conclusion: Routine mesh placement reduces the rate of postoperative incisional hernia after open abdominal aortic aneurysm (AAA) repair and is not associated with increased complications.

Summary: There appears to be an increased risk of incisional hernia in patients undergoing aortic surgery for an aneurysm compared with those undergoing aortic surgery for occlusive disease (Takagi H, Eur J Vasc Endovasc Surg 2007;33:177-81). Rates of incisional hernia after AAA repair may be as high as 38% (Holland AJ, Eur J Vasc Endovasc Surg 1996;12:196-200), and patients with AAA are postulated to have a connective tissue disorder that increases susceptibility to incisional hernia (Adey B, Luna G, Am J Surg 1998;175:400-2). Prophylactic placement of prosthetic mesh in the preperitoneal space during wound closure after open AAA repair may result in lower rates of incisional hernia (O'Hare JL, Eur J Vasc Endovasc Surg 2007;33;412-3).

The authors performed a randomized trial to see if mesh closure after AAA repair would result in fewer incisional hernias. Patients undergoing open AAA repair were randomized to routine abdominal mass closure or to prophylactic placement of polypropylene mesh with abdominal wall closure. The study included 85 patients (91% men) with a mean age of 73 years (range, 59-89 years). There were five perioperative deaths; none related to mesh. Hernia was determined by clinic examination or by ultrasound study. During follow-up, incisional hernia developed in 16 patients in the control group and in 5 in the mesh group (hazard ratio, 4.1; 95% confidence interval, 1.7.2-9.82; $P = .002$). Hernia development occurred between 170 and 585 days in the control group and between 336 and 1122 days in the mesh group. A minority of the hernias were repaired: four in the control group and one in the mesh group ($P = .375$). There were no mesh infections, but mesh was removed in one patient after seroma formation.

Comment: There are significant concerns regarding placement of prophylactic polypropylene mesh. Certainly, mesh has been associated with infection and adhesion to underlying bowel. Although these complications were not noted in this series, the number of patients is small. The study does confirm a high rate of hernia formation in patients undergoing midline incisions for AAA repair and suggests hernia formation can be reduced by prophylactic mesh replacement. The clinical significance of this is unclear because the number of actual incisional hernia repairs was not statistically different in the patients undergoing routine mass closure vs those undergoing prophylactic mass closure, implying many of the hernias perhaps were small or did not trouble the patient.

Diabetes Mellitus, Fasting Blood Glucose Concentration, and Risk of Vascular Disease: A Collaborative Meta-Analysis of 102 Prospective Studies

The Emerging Risk Factors Coalition. Lancet 2010;375:2215-22.

Conclusion: Diabetes confers a twofold excess risk for a wide range of vascular diseases. This is independent from other conventional risk factors. Fasting blood glucose concentration in people without diabetes is also modestly, but not linearly, associated with risk of vascular disease.

Summary: The authors used data from 121 prospective studies of vascular risk factors involving individual records of 1.27 million adults. All studies had accrued >1 year of follow-up. They used these data to produce estimates of the association of diabetes and fasting blood glucose concentrations with fatal or first ever nonfatal incident vascular disease (and deaths from other vascular disorders) under a wide range of conditions.

Analyses included data for 698,782 people. There were 52,765 nonfatal or fatal vascular outcomes over 8.49 million person-years at risk. Adjusted hazard ratios (HRs) for diabetes were 2.00 (95% confidence interval [CI],