Comment: Thrombosis is the endpoint of atherosclerosis and inflammation is linked to the development of atherosclerosis. This study suggests that CD40-CD40L interactions may be one molecular mechanism linking the inflammation and the thrombosis associated with atherosclerosis.

Acute intramural hematoma of the aorta: A mystery in evolution

Evangelista A, Mukherjee D, Mehta RH, and the International Registry of Aortic Dissection (IRAD) Investigators. Circulation 2005;111:1063-70.

Conclusion: There is a 5-7% prevalence of intramural hematoma (IMH) in patients with acute aortic syndromes with 16% of patients evolving to classic aortic dissection (AD) on subsequent imaging studies and a 40% mortality rate of ascending aorta IMH.

Summary: Acute aortic syndromes are characterized by a sudden onset of thoracic pain and consist of both classic AD and intramural aortic hemorrhage. There is an incomplete knowledge of the natural history of IMH. The International Registry of Aortic Dissection (IRAD) involves eighteen referral centers in six countries. Potential patients for inclusion in IRAD are identified prospectively or retrospectively by searching hospital discharge records. Diagnosis of acute aortic syndrome is suspected on history and physical examination and confirmed by imaging study or surgical exploration or post mortem examination.

The current study represents 1,1010 patients enrolled between January 1, 1996 and November 19, 2001. Fifty-eight (5.7%) of patients had IMH. Patients with IMH tended to be older (68.7 years) than those with classic AD (61.7 years, $P < 0.001$). Patients with IMH were also more likely to have distal aortic involvement than patients with classic AD (60.3% versus 35.3%; $P < 0.001$). Patients with IMH described more severe initial pain than those with classic AD. Patients with IMH, however, were less likely to have pulse deficits, ischemic leg pain, or aortic valvular insufficiency. Overall, mortality of IMH was similar to AD (20.7% versus 23.9%; $P = 0.57$). Mortality of patients with IMH of the descending aorta was 8.3% versus 13.1% of patients with AD of the descending aorta ($P = 0.60$). Mortality of patients with IMH of the ascending aorta was 39.1% versus 29.9% of patients with classic AD of the ascending aorta; $P = 0.34$. Sixteen percent of patients with an initial diagnosis of IMH progressed to AD on serial imaging studies.

Comment: The natural history of acute IMH of the aorta as well as its prevalence is difficult to determine. The current study suggests that the prevalence of IMH in patients with non-traumatic acute aortic syndromes is about 6%. This is lower than previously reported. Overall, however, this study, and others suggest, that despite the more limited aortic involvement of IMH and the absence of true dissection flaps at initial presentation, the overall natural history of the disease is similar to that of classic AD. At this point the known natural history of IMH suggests treatment and follow up should be similar to AD.

Engineering of fibrin-based functional and implantable small-diameter blood vessels

Swartz DD, Russell JA, Andreadis ST. Am J Physiol Heart Circ Physiol 2005;288:H1451-60.

Conclusion: Fibrin can serve as an appropriate scaffold for engineering small caliber blood vessels that have both vasoreactivity and considerable mechanical strength.

Summary: Currently, autogenous tissue, such as saphenous vein or radial artery, is the gold standard for an arterial substitute for a small caliber vessel. The authors engineered implantable small diameter blood vessels using a fibrin gel with embedded ovin smooth muscle and endothelial cells. Fibrin gels can achieve high seeding of smooth muscle and endothelial cells with uniform cellular distribution. Fibrin might thus be an alternative to collagen as a scaffold for an engineered small caliber vessel.

The fibrin matrix based tissue engineered vessels developed in this study exhibited considerable reactivity in response to both receptor and non-receptor mediated dilators and vasoconstrictors. Apoprotinin when added to fibrin gel preparation at moderate concentrations increased mechanical strength of the engineered blood vessel but decreased vascular activity. Mechanical strength and reactivity of the blood vessels were comparable to those of native veins. The mechanical strength of the fibrin-based blood vessels was sufficiently strong to withstand implantation into the jugular veins of lambs. Late microscopic analysis indicated tissue engineered vessels integrated well to native tissue while demonstrating similar flow rates and patency as native vessels. At fifteen weeks after implantation the fibrin-based vessels demonstrated matrix remodeling with production of both elastin and collagen fibers and orientation of smooth muscle cells perpendicular to the direction of blood flow.

Comment: One of the "Holy Grails" of vascular surgery is the development of a commercially available, off the shelf, highly effective arterial substitute for a small caliber vessel. This study indicates that use of a fibrin scaffold for development of such an arterial substitute is a potentially fertile line of inquiry. These engineered vessels appear to remain patent when implanted, seamlessly integrate into native vessel, and display vaso-reactivity similar to normal veins. Obviously, development of a commercial product is many years away. Nevertheless, it is good to know that, even after the failure of endothelial seeding of prosthetic grafts, investigators are still pursuing the development of a small caliber arterial substitute.

High rate of early restenosis after carotid eversion endarterectomy in homozygous carriers of the normal mannitose-binding lectin genotype

Rugonfalvi-Kiss S, Dosa E, Madsen HO. Stroke 2005;36:944-8.

Conclusion: Restenosis after carotid endarterectomy is partially genetically determined.

Summary: Mannos-Binding Lectin (MBL) is a serum protein derived from the liver. MBL participates in activating the lectin pathway of compliment. Human MBL is coded on a single gene on Chromosome 10. Mutations associated with this gene can cause low serum levels of MBL. There are three known mutation variants and each reduces the functional MBL subunits in heterozygous individuals by 5 to 10-fold. MBL appears to have both protective and adverse affects in cardiovascular disease. Lack of functional alleles is associated with coronary artery disease and increased carotid plaque formation. However, the Lectin pathway of compliment may also initiate the inflammatory reaction seen with ischemia reperfusion injury. Participation of MBL in this inflammatory reaction suggests a possible mechanism of MBL alleles in restenosis following carotid endarterectomy.

Patients in this study were derived from 123 patients who underwent carotid endarterectomy and were followed by carotid duplex scanning for 14 months. An eversion technique of endarterectomy was employed in this study. The authors then retrospectively examined 17 patients with carotid restenosis following carotid endarterectomy (restenosis defined as greater than 50% stenosis) and 29 patients without carotid restenosis after 29 months. In both groups, MBL genotypes were analyzed by polymerase chain reaction based methods. MBL serum concentrations were also measured.

Compared to values measured six weeks after surgery, the degree of stenosis suggested by carotid duplex scanning 14 months after surgery was significantly higher in patients homozygous for the normal MBL genotype ($P < 0.001$). There was only a slight increase in levels of carotid duplex determined stenosis at 14 months compared to 16 months in patients carrying MBL variant alleles. Differences were more pronounced in females than males. There was a significant increase in the frequency of MBL variant genotypes in patients not experiencing restenosis compared to the patients with restenosis ($P = 0.007$).

Comment: The data indicate that a variant genotype compared to a normal genotype for MBL, may protective with respect to development of carotid restenosis. The pathophysiologic mechanisms underlying the MBL genotype and carotid restenosis are unknown. In addition, the data make it difficult to completely separate the gender effect. Overall, there may be a complicated interplay between genetic and hormonal factors in development of carotid restenosis.

Acute aortic dissection presenting with primarily abdominal pain: A rare manifestation of a deadly disease

Upchurch GR, Nienaber C, Fattori R, et al. Ann Vasc Surg 2005;19:367-3.

Conclusion: There is increased mortality in patients with acute thoracic aortic dissection who present primarily with abdominal pain.

Summary: Classically, thoracic dissection presents with acute, severe tearing back pain. Other presentations of thoracic dissection are, however, possible. Some patients present primarily with abdominal pain. In this study, 992 patients, mean age 62.1 years ± 14.1 years; 68% male, were identified with acute thoracic dissection from 1996 to 2001 from the International Registry of Acute Aortic Dissection. Patients were analyzed for presenting symptoms, demographics, signs of aortic dissection, ultimately determined aortic pathology, and mortality. Patients were divided into two groups: those presenting primarily with abdominal pain (Group 1, 46 patients, 4.6%) and all other presentations (Group 2). The two groups had similar demographics. Sixty-three percent of patients in Group 1 presented with hypertension compared to 47% of patients in Group 2 ($P = 0.04$). Group 1 patients were less likely to present with evidence of end-organ malfunction. Specifically following surgery for Type B dissection, mortality was increased in patients presenting primarily with abdominal pain (28%) versus those not presenting primarily with abdominal pain (10.2%), $P = 0.02$.

Comment: The study indicates a high mortality rate in patients with thoracic aortic dissection who present primarily with abdominal pain. Even in the absence of back pain one should consider thoracic aortic dissection as an etiology for abdominal pain in patients with appropriate risk factors for dissection.