surgical group were associated with incompetence of the below knee GSV. Perhaps length of GSV stripping should more reflect the length of the refluxing vein and not concerns about injuring the saphenous nerve? Another interesting point is that neovasculariztion, thought to be the leading cause of recurrence of varicosities in patients with traditional open surgical treatment of GSV varicosities, appears rare after EVLA. The reason for this is unclear, but may be due to decreased inflammation following EVLA. Interestingly, all patients with recanalization after EVLA in this trial, were treated with an energy density of 60 J/cm. No recanaliztion was seen when energy densities were above 115 J/cm.

Comparative Predictors of Mortality for Endovascular and Open Repair of Ruptured Infrarenal Abdominal Aortic Aneurysms

Sarac TP, Bannazadeh M, Rowan AF, et al. Ann Vasc Surg 2011;25:461-8.

Conclusion: Mortality rates for EVAR treatment and open treatment of ruptured aortic aneurysm are equal with regard to 30 day and long term mortality.

Summary: Many patients with ruptured abdominal aortic aneurysm (rAAA) die before reaching surgery (Acosta S. J Vasc Surg 2006;44:237-43). In-hospital mortality rates range between 30 and 70%. A large meta analysis found an overall 48% mortality (Brown MJ Br J Surg 2002;89:714-30). EVAR for rAAA was first described in 1994 (Marin ML et al. Ann Surg 1995;222:449-65) and is gaining in popularity. The authors sought to evaluate their results of treatment of rAAA with a particular focus in comparing endovascular repair of rAAA versus open surgery repair. Between January of 1990 and May of 2008 there were 160 patients who underwent repair of rAAA. Twenty percent (n = 32) underwent EVAR for rAAA. 112 were felt to have free rupture (70%) and 48 a contained rupture (30%). Average acute physiology and chronic health evaluation II score was 13.3 ± 6.7. Survival at 30 days, 6 months, 1 year and 5 years was 69%, 57%, 50% and 25%. There were no differences seen in the EVAR group compared to the open surgical group ($P = .24$). There was 5.6 % intraoperative mortality. No patient undergoing EVAR suffered intraoperative death ($P = .03$). Thirty-day mortality for EVAR was 31.2% and was 32% for open surgery ($P = .93$). Renal insufficiency (OR, 2.4; 1.1-5.3; $P = .04$), hypotension (OR, 2.4; 1.1-5.3; $P = .02$) and cardiac arrest (OR, 3.8; 1.1-11.6; $P = .03$) were all associated with increased mortality. The only independent predictor of decreased long term survival was preoperative renal insufficiency (OR, 2.32; 1.55-3.47; $P < .001$).

Comment: There is clearly a trend towards increasing use of EVAR for treatment of rAAA and most clinician's clinical impression is that outcomes are better. This study however showed equal morality with open and endovascular repair of rAAA. The series is retrospective with different surgeons over time. We don't know the precise selection criteria for the two procedures and there may be unmeasured confounding variables. What we can really say from this paper is that despite the use of EVAR for repair for rAAA, mortality remains high. EVAR is clearly a viable option for treatment of rAAA. Despite many surgeon's clinical impression, whether EVAR, when applicable, truly reduces mortality of rAAA in equal patients, compared to open repair, has not been conclusively proven to everyone's satisfaction.

Effect of Hypoxia-Inducible Factor-1α Gene Therapy on Walking Performance in Patients With Intermittent Claudication

Creager MA, Olin JW, Belch JJ, et al. Circulation 2011;124:1765-73.

Conclusion: Gene therapy with intramuscular administration of Ad2/HIF-1α/VP16 is not effective treatment for intermittent claudication.

Summary: Induction of angiogenesis of lower extremity arteries via protein, gene based, or cellular therapy may result in new blood vessel formation and improved blood flow in patients with intermittent claudication. Hypoxia- inducible factor 1α (HIF-1α) is a transcriptional regulatory factor with important roles in cellular response to changes in oxygen tension (Semenza GL. Science 2007; 318:62-4). HIF-1α exerts control on multiple genes providing adaptive responses to hypoxia at the cellular level. HIF-1α/V16 is hybrid transcription factor comprised of a truncated HIF-1α sequence fused to a herpes simplex virus (VP16) transactivator. A previous phase 1 trial of patients with critical limb ischemia indicated that Ad2/HIF-1α/VP16, an engineered recombinant type 2 adenovirus vector encoding active HIF-1α, provided resolution of rest pain and ulcer healing (Rajagopalan S et al. Circulation 2007;115:1234-43). The authors postulated intramuscular administration of Ad2/HIF-1α/VP16 could improve peak walking time (PWT) in patients with intermittent claudication. This was a randomized double blind prospective study where 289 patients with claudition were randomized to one of three doses of Ad2/HIF-1α/VP16 ($2x10^9$, 2×10^{10}, or 2×10^{11} viral particles) or placebo. Medications were administered with 20 intramuscular injections to each leg. Graded treadmill exercise tests were performed at baseline, and at 3, 6 and 12 months after treatment. The primary endpoint was a change in PWT from baseline to 6 months, and the secondary endpoint was a change in claudition onset time. Tertiary endpoints included changes in ankle-brachial index and quality of life assessments.

Median PWT increase by 0.82 minutes (interquartile range, −0.05-1.93 minutes) in the placebo group and increased by 0.82 minutes (interquartile range, −0.07-2.12 minutes), 0.28 minutes (interquartile range, −0.37-1.7 minutes), and 0.78 minutes(interquartile range, −0.02-2.10 minutes) in the HIF-1α 2×10^9, 2×10^{10} 2×10^{11} viral particle groups respectively (P = NS for all comparisons). There were no significant differences in claudication onset time, ankle-brachial index or quality of life measurements between the placebo group and each of the HIF-1α groups. There were no dramatic safety differences between the placebo groups and the HIF-1α groups.

Comment: HIF-1α may be ineffective inducing angiogenesis. However, there are other possible reasons the study failed to prove efficacy of HIF-1α for treatment of intermittent claudication. There may differences in biologic activity of HIF-1α in patients with claudication compared to critical limb ischemia. Adenovirus transfection may not be efficient in skeletal muscle. Duration of gene expression may be to short for development and maintenance of collateral vessels. The distance between injection sites may have been too great to enable efficient collateral development. Finally, despite attempts to mitigate the placebo response, patients randomized to placebo increased peak walking distance by approximately 30%. This study should be regarded as negative under the conditions employed in the study. Cellular and gene based therapies still remain intriguing possibilities in the treatment of PAD. However, it is going to be time consuming and expensive to prove they are not just intriguing but also effective.

Systematic Review and Meta-Analysis of Growth Rates of Small Abdominal Aortic Aneurysms

Powell JT, Sweeting MJ, Brown LC et al. Br J Surg 2011;98:609-18.

Conclusion: In studies reporting growth rates of small abdominal aortic aneurysms (AAA) there is considerable variation in growth rate, beyond that which can be explained by aneurysm diameter alone.

Summary: Many institutions and countries have adopted policies for screening for AAA in older men. However, there is relatively little information on optimal surveillance protocols in patients where an AAA has been identified but does not currently meet criteria for repair. Observational studies have also reported growth rates of small AAAs with disparate recommendations for follow up examinations of AAAs that do not meet threshold criteria for repair. Other clinically relevant questions include whether AAA growth rate is faster in smokers, slower in patients with diabetes, and whether there are any gender differences in growth rates. Based on these considerations, the authors thought to synthesize the published data on growth rates of small AAA in a systematic review to provide an evidence basis for surveillance intervals.

The review consisted of literature published prior to January 2010. There were 61 potentially eligible reports identified. Review of these reports yielded 15 studies providing growth rates for aneurysms between 3.0-5.5 centimeters in diameter. These 15 studies included 7630 individuals (predominately men) who were enrolled between 1976 and 2005. The review indicated the pooled growth rate for AAA was 2.32 mm per year (95% CI, 1.95 to 2.7 mm/year). There was high heterogeneity between studies with growth rates ranging from −0.33 mm/year to 3.95 mm/year. There was a trend for growth rates to increase with aneurysm diameter. A 10 mm increase in aneurysm diameter was associated with a mean (s.e.m.) 1.62 (0.20) mm/year increase in growth rate. Percentage of women in studies and mean age did not have a significant effect on growth rate. Medical therapies, smoking, and co-morbidities were inconsistently reported in the 15 studies and their influence on growth rates could not be evaluated. On average, the data indicate a 3.5 cm aneurysm will take 6.2 years to reach 5.5 cm. A 4.5-cm aneurysm will reach 5.5 cm in about 2.3 years.

Comment: This study provides evidence growth rates of AAAs increase with aneurysm diameter. However, it did not completely satisfy the primary goal to determine optimal surveillance intervals because of the marked heterogeneity of growth rates in individual studies. Whereas the data would indicate that larger aneurysms grow faster than smaller aneurysms, something most of us already suspected, it does not provide useful information on the influence of patient characteristics, including age, sex smoking, diabetes and other relevant factors on AAA growth rates that would help optimize recommendations for surveillance intervals.

The von Willebrand Inhibitor ARC1779 Reduces Cerebral Embolization After Carotid Endarterectomy a Randomized Trial

Markus HS, McCollum C, Imray C, et al. Stroke 2011;42:2149-53.

Conclusion: von Willebrand factor inhibition reduces thromboembolism and may play a role in treatment of stroke and myocardial ischemia.

Summary: Minor stroke and transient ischemic attacks are followed by a high early risk of recurrent stroke. Risk is highest in patients with larger artery disease. Aspirin can reduce recurrent stroke, but actually fails to prevent 80% of stroke recurrences (Antithrombotic Trialists' Collaboratio. BMJ 2002;324:71-86). There are now novel antiplatelet therapies that may be considered. It appears inhibition of platelet receptor glycoprotein (GPIb)