Abstracts

Gregory L. Moneta, MD, Abstracts Section Editor

Local Delivery of Gene Vectors From Bare-Metal Stents by Use of a Biodegradable Synthetic Complex Inhibits In-Stent Restenosis in Rat Carotid Arteries

Fishbein I, Alferiev I, Bakay M, et al. Circulation 2008;117:2096-103.

Conclusion: Sustained release of gene vectors is possible through reversible immobilization of adenovirus vectors on bare-metal surfaces of vascular stents.

Summary: Polymer-coated stents facilitate local drug delivery to the vasculature and have proven efficacious in preventing in-stent restenosis. There are, however, concerns about the inflammatory effects of polymer coatings and late outcomes of drug-eluting stents. The authors investigated whether adenoviral vectors could be delivered from bare metal surfaces of stents using a synthetic complex for reversible vector binding. Three components of a gene vector-binding complex were synthesized: (1) a polyallylamine bisphosphonate with latent thiol groups (PABT), (2) a polyethylenimine (PEI) with pyridyldithio groups for amplification of attachments sites [PEI (PVT)], and (3) a bifunctional amine-reactive and thiol-reactive cross-linker with labile ester bond (HL).

The HL-modified adenovirus attached to PABT/PEI(PDT)-treated steel surfaces and demonstrated in vitro sustained release for 30 days. They also demonstrated localized green fluorescent protein expression in rat arterial smooth muscle cell cultures. This expression was not sensitive to inhibition by neutralizing antiadenovirus antibodies or inactivation after storage at 37°C. In rat carotid studies, steel stents configured with PABT/PEI(PDT)/HL-tethered adenoviral vectors demonstrated site-specific arterial adenovirus green fluorescent protein expression and adenovirus-luciferase transgene activity by optical imaging. Adenovirus encoding inducible nitric oxide synthase delivered by a carotid stent resulted in significant inhibition of restenosis.

Comment: This study investigated local delivery of gene therapy from bare-metal stent surfaces using reversible chemical attachment of vectors to the bare-metal stents. Adenovirus vectors on the surfaces of the stents demonstrated >1-month release kinetics and site-specific transduction of target cell types in vitro and in vivo in this rat model. Deployment of stents configured with 10^9 adenovirus vectors encoded for inducible nitric oxide synthase resulted in significant reduction of in-stent restenosis. It appears that the concept of gene-eluting stents is valid and may provide a mechanism of local and systemic delivery of gene products by the vasculature.

Post-Traumatic Ulnar Artery Thrombosis: Outcome of Arterial Reconstruction Using Reverse Interpositional Vein Grafting at 2 Years Minimum Follow-Up

Chloros GD, Lucas RM, Li Z, et al. J Hand Surg [Am] 2008;33:932-40.

Conclusion: Successful arterial reconstruction of patients with symptomatic post-traumatic ulnar artery thrombosis (UAT) improves function in microvascular physiology, decreases symptoms, and positively affects quality of life.

Summary: The authors report follow-up of use of interposition vein grafts to treat symptomatic patients with UAT. Patients included in this retrospective study had to have arteriographically proven UAT treated with excision and reversed interposition veins grafts, no known collagen vascular disease, coagulopathy, or peripheral vascular disease, and a minimum follow-up of 24 months. There were 13 patients (13 hands) identified and evaluated before surgery and at final follow-up using health-related quality of life outcome instruments. These included the McCabe cold sensitivity scale, the McGill visual analog pain scale, the Levine symptom and function scale, and the Wake Forest University symptoms scale incorporating pain, numbness, and cold intolerance. Microvascular perfusion testing was done using laser Doppler perfusion imaging. Cold stress tests were also performed. Results of cold testing were compared with 28 healthy controls. Graft patency was assessed by Allen testing or Doppler ultrasound imaging, or both.

At the final follow-up, 10 of 13 grafts (77%) were patent. In patients with patent grafts, the Levine symptom scale, the McGill visual analog pain scale, and the McCabe cold sensitivity severity score all uniformly improved postoperatively. Cold testing responses also improved at final follow-up and were not different from those of normal controls. Changes in Levine function scale, Wake Forest University scale, and laser Doppler perfusion were not significant. In the three patients with nonpatent grafts, two complained of pain, numbness, and cold sensitivity, whereas the other had minimal symptoms.

Comments: Although the number of patients is small, this is actually a relatively large series with prolonged follow-up of an unusual condition infrequently treated by operation. Of particular interest is improvement in quality of life noted in these patients and the normalization of their physiologic response to cold testing. Interposition vein grafting of the distal ulnar artery is relatively straightforward if the thrombosed segment does not involve the digital vessels. In such cases the saphenous vein at the ankle is an appropriate conduit. The operation, of course, is considerably more technically demanding when digital arteries must be reimplanted into the saphenous vein graft. This may be done through individual anastomoses of the digital arteries to the saphenous vein graft, or more commonly in our experience, incorporation as a patch graft of the portion of the thrombosed ulnar artery from which the digital arteries originate onto a longitudinally oriented venotomy in the saphenous vein graft.

High Absolute Risk and Predictors of Venous and Arterial Thromboembolic Events in Patients With Nephrotic Syndrome: Results from a Large Retrospective Cohort Study

Mahmoodi BK, ten Kate MK, Waanders F, et al. Circulation 2008;117:224-30.

Conclusion: The ratio of proteinuria to serum albumin predicts venous thromboembolism (VTE) in patients with nephrotic syndrome. Estimated glomerular filtration rate and classic risk factors for atherosclerosis predict arterial thromboembolism (ATE).

Summary: An increased risk of VTE and ATE has been observed for >50 years in patients with nephrotic syndrome. Such data are based on small studies with short-term follow-up. Absolute risks of either VTE or ATE are not available. In this single-center retrospective study, the authors sought to assess the absolute risk of symptomatic VTE and ATE and to identify predictive factors in a large cohort of patients with nephrotic syndrome. The study enrolled 298 consecutive patients (59% men) with nephrotic syndrome. Their mean age was 42 ± 18 years. Mean follow-up was 10 ± 9 years. Proteinuria >3.5 g/d was used to identify nephrotic syndrome. Patients were classified according to underlying histologic lesions accounting for their nephrotic syndrome. Symptomatic venous or arterial thromboembolic events were the primary outcome events recorded.

Annual incidences were 1.48% (95% confidence interval [CI], 1.07-1.99) for ATE and 1.02% (95% CI, 0.68-1.46) for VTE. During the first 6 months, these rates were 5.52% for ATE and 9.85% for VTE. Whereas proteinuria and serum albumin levels tended to be related to VTE, only the predictive value of the ratio of protein to serum albumin was significant (hazard ratio, 5.6; 95% CI, 1.2-26.2; $P = .03$). Neither, serum albumin levels or the degree of proteinuria were significantly related to ATE. Prior ATE, estimated glomerular filtration rate, sex, age, hypertension, diabetes mellitus, and smoking all predicted ATE ($P < .02$).

Comment: This study provides the first assessment of absolute risk of symptomatic VTE and ATE in patients with nephrotic syndrome. Estimates of VTE are significantly higher than the estimated age- and sex-weighted absolute risk of the general population. The risk of VTE was excessively high in the first 6 months of observation, and factors influencing the risk of VTE and ATE in patients with nephrotic syndrome are not the same. Patients with nephrotic syndrome may benefit from VTE prophylaxis during this first 6 months of their illness.

Color Doppler Ultrasonography in Occlusive Diseases of the Brachiocephalic and Proximal Subclavian Arteries

Yurdakul M, Tola M, Uslu OS. J Ultrasound Med 2008;27:1065-70.

Conclusion: Color duplex ultrasound (DU) imaging is highly accurate for diagnosing stenoses and occlusions of the brachiocephalic and proximal subclavian arteries.

Summary: Little information is available regarding the accuracy of color DU imaging in diagnosing stenoses and occlusions of the brachiocephalic and proximal subclavian arteries. In addition, it is widely perceived that examinations of the brachiocephalic and proximal subclavian arteries are technically difficult and frequently provide inadequate diagnostic information. The authors of this study sought to investigate the capability of color DU imaging for examining the brachiocephalic and proximal subclavian arteries and to determine accuracy in diagnosis of occlusive disease of those arteries. Two groups of patients were studied. The first group was a feasibility group and was used to determine whether brachiocephalic and subclavian origins could be seen. The second group included patients with occlusive disease who underwent both color DU imaging and digital subtraction angiography, and the two modalities were compared.

In the feasibility study, the origins of 42 of 50 brachiocephalic arteries (84%) and 48 of 50 right subclavian arteries (96%) and 25 of 50 left subclavian arteries (50%) could be visualized by color DU imaging. In the