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


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 vascularulce 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 polyethyleneimine (PEI) with pyridylidithio 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(PVT)/HL-treated stent surfaces demonstrated in vitro sustained release for 30 days. They also demonstrated localized green fluorescent protein expression in rat arterial smooth muscle cells. This expression was not sensitive to inhibition by neutralizing antianadovirus antibodies or inactivation after storage at 37°C. In rat carotid studies, stent stents configured with PABT/PEI(PVT)/HL-tethered adenoviral vectors demonstrated site-specific arterial adenovirus green fluorescent protein expression and adenovirus-hucarboxylic 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 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 10² 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 Interposition Vein Grafting at 2 Years Minimum Follow-Up


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 vein grafts, no known collaterals vascular disease, coagulopathy, or peripheral vascular disease, and a minimum follow-up of 24 months. There were 13 patients (13 hands) identified and ATE, estimated glomerular filtration rate, sex, age, hypertension, diabetes mellitus, and smoking all predicted ATE (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. Estimated 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.

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


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 208 consecutive patients (95% men) with nephrotic syndrome. Their mean age was 42 ± 18 years. Mean follow-up was 10 ± 9 years. Proteinuria >5.5 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. Estimated 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 Ultrasoundography in Occlusive Diseases of the Brachiocephalic and Proximal Subclavian Arteries


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 of 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 angiography 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
second group, 80 up to endarterectomies were examined with color DU imaging and digital subtraction angiography; of these, 95% of the brachiocephalic arteries and 72% of the subclavian arteries were normal. One brachiocephalic artery had stenosis and one had occlusion, and 15 subclavian arteries were occluded and six were stenosed. 48 normal sides (90%) correctly, and 14 of 16 cases (88%) of stenosis and 16 of 16 cases (100%) of occlusion were correctly diagnosed. Eight of nine lesions on the right (90%) and 23 of 24 lesions on the left (96%) were correctly diagnosed. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 88%, 94%, 78%, 97%, and 94%, respectively, for detecting stenosis. There was a high level of agreement between DU imaging and digital subtraction angiography for detecting stenosis (κ = 0.78) and for detecting occlusion (κ = 0.96).

Comment: The authors describe excellent results in identifying occlusive lesions of the origin of the subclavian and brachiocephalic arteries. This was despite the fact that the equipment they used in this study was a bit dated. A newer machine with smaller footprint probes using the sternal notch as a window likely would be even more accurate in assessing the great vessels of the aortic arch. Criteria for stenosis are slightly different than that used elsewhere. Whereas a peak systolic velocity ratio of ≥2 indicated stenosis, stenosis also was also implied by monophasic flow without actual visualization of a high velocity jet and by reverse flow in a vertebral artery. These additional criteria are necessary to assess the brachiocephalic vessels. If only peak systolic velocity ratios are used, the numbers of both false-positive and false-negative results will be higher.

Functional Assessment at the Buttok Level of the Effect of Aortobifemoral Bypass Surgery


Conclusion: Proximal (hip, buttok, lower back) claudication after aortobifemoral bypass grafting (AFBG) affects almost one-third of patients with treadmill walking. Prevalence is higher in patients with end-to-end vs end-to-side bypass.

Summary: Surprisingly little is known about proximal claudication after AFBG. In this study, 48 patients performed a treadmill test before and ≤6 months after AFBG. Exercise-induced proximal claudication and regional pelvic blood flow impairment were studied using the San Diego Claudication Questionnaire and chest-corrected decrease from rest of transcutaneous oxygen pressure measurements on the buttocks. A decrease from rest of transcutaneous oxygen pressure values of less than –15 mm Hg was used to indicate regional blood flow impairment.

Nine women and 39 men were studied. The mean age was 60 ± 9 years. The lowest ankle-brachial index (ABI) was 0.55 ± 0.18, and maximal walking distance was 188 ± 192 m in an inclusion of the study. After surgery, ABI and maximal walking distance were improved (0.83 ± 0.19 and 5.18 ± 359 m respectively, P < .0001). Regional blood flow impairment at the buttok level was present in 39 patients preoperatively and in 29 patients after AFBG. Proximal claudication with underlying regional blood flow impairment in one or both sides was observed in 29 patients before AFBG and in none of 26 (41%) vs six of 22 patients (23%) with end-to-end vs end-to-side proximal aortic graft anastomoses (P < .05).

Comment: Overall, it appears that there is not a large step up from AFBG to the end-to-end bypass. AFBG may not uniformly improve thigh and buttock claudication, and the patients should understand this before undergoing the operation. The hypogastric arteries uniformly improve thigh and buttock claudication, and the patients should understand this before undergoing the operation. The hypogastric arteries were treated in 18 cases and vein graft stenoses in two. Three redo atherectomy were attempted from 2883 adults aged >20 years after an 8-hour fast (weighted to a US population of 128.5 million) from a National Health and Nutrition Examination Survey 2003-2004, a nationally representative cross-sectional survey. The number of adults in the National Cholesterol Education Program at recommended levels for LDL-C, non-HDL-C, HDL-C, triglycerides, and combined lipids, stratified by ethnicity, age, sex, and the presence of cardiovascular morbidities was determined.

Of persons without cardiovascular disease or related comorbidities, 85% to 88% were at recommended levels for LDL-C, non-HDL-C, HDL-C, and triglycerides. However, only 36% to 37% of those with cardiovascular disease or comorbidities for cardiovascular disease were at recommended levels for LDL-C and non-HDL-C, and only 17% achieved recommended levels for all lipids. The treated patients compared with those untreated had better (ie, lower) LDL-C (112.3 vs 156.7 mg/dL, P < .001) and non-HDL-C levels (145.9 vs 188.7 mg/dL, P < .001). Levels of HDL-C and triglycerides were similar in treated and untreated patients (52.0 vs 50.1 mg/dL, P = .09; and 160.1 vs 148.7 mg/dL, P = .20, respectively).

Conclusion: The National Cholesterol Education Program promotes guidelines for goal lipid levels. Treatments that are recommended from management of LDL-C. This emphasis has resulted in improvements in LDL-C levels in the United States. The data here, however, point out that those patients perhaps in most need of control of their lipid levels (ie, those with cardiovascular disease or related comorbidities) had really quite poor overall control of their lipid levels. In patients with cardiovascular disease, diabetes, or chronic kidney disease, only one-third were at goal LDL-C and non-HDL-C levels. Only 26% were at recommended levels for all lipids. That lipid levels are not being achieved in this population may reflect a lack of awareness, not being treated despite awareness, or inadequate treatment. It appears that even greater use of efficacious dosages of lipid-lowering agents is needed, and likely greater use of combination therapy, to address patients with multiple lipid disorders, especially if such patients have cardiovascular disease or significant comorbidities for cardiovascular disease.

Midterm Patency Following Atherectomy for Infragingual Occlusive Disease: A Word of Caution


Conclusions: At 1 year there is poor patency of excisional atherectomy using the SilverHawk device (FortHollow Technologies, Redwood City, Calif).

Summary: The authors sought to evaluate their experience with peripheral atherectomy using the SilverHawk device. From March 2005 to May 2006, 379 separate atherectomy procedures were done in 53 patients (34 TASC A, 17 B, and 13 C in eight, with a mean number of two treated lesions per limb (range, 1-4). The most distal native stenosis was a superficial femoral artery in 12 cases, the popliteal artery in six, and a tibial artery in two. Eighteen primary procedures were successful, and all three repeat atherectomy procedures were successful. Additional balloon dilatation was used in five procedures. The ankle-brachial index was 0.51 ± 0.6 and at 1 month improved to 0.80 ± 0.16 (P < .001). At 12 months, only two vessels remained patent, with recurrence developing in 16 of the successful primary procedures and all three repeat atherectomy procedures. Recurrence was treated in 14 instances in a total of 35 lesions. Major limb amputations were required in five patients. Primary patency rates per treated limb at 3, 6 and 12 months were 38%, 10%, and 10%, respectively, and the corresponding assisted primary patency rates were 22%, 14%, and 11%, respectively.

Comment: The primary surgeon had previously performed six cases at another hospital. Most were in conjunction with an industry representative, though the surgeon himself did not participate, and the surgeon both wrote the final draft anatomic and surgical technique of the atherectomy. Therefore, regardless of whether one is or is not enthusiastic about peripheral atherectomy, the results here may very well be what an individual surgeon can expect in similar types of patients. The authors are recommending that the atherectomy be done using a 20-gauge catheter as the microcatheter to be used elsewhere. Whereas a peak systolic velocity ratio of ≥2 indicated stenosis, stenosis also implied by monophasic flow without actual visualization of a high velocity jet and by reverse flow in a vertebral artery. This was despite the fact that the equipment they used in this study was a bit dated. A newer machine with smaller footprint probes using the sternal notch as a window likely would be even more accurate in assessing the great vessels of the aortic arch. Criteria for stenosis are slightly different than that used elsewhere. Whereas a peak systolic velocity ratio of ≥2 indicated stenosis, stenosis also was also implied by monophasic flow without actual visualization of a high velocity jet and by reverse flow in a vertebral artery. These additional criteria are necessary to assess the brachiocephalic vessels. If only peak systolic velocity ratios are used, the numbers of both false-positive and false-negative results will be higher.