Stent Graft for Nephrologists: Concerns and Consensus

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The role of the stent graft is emerging in the management of arteriovenous dialysis access. Physicians are incorporating this device in the management of three distinct problems—vein-graft anastomotic stenosis, pseudoaneurysm formation, and cephalic arch stenosis—with varying degrees of success. Indeed, a recent randomized, controlled trial to evaluate the role of angioplasty plus stent graft versus angioplasty alone for the management of stenosis at the vein-graft anastomosis led to the approval of the stent graft by the Food and Drug Administration; however, several elements of the management of stenosis at the vein-graft anastomosis/cephalic arch as well as the repair of pseudoaneurysms by stent graft remain controversial. The situation is further complicated and warrants a cost-to-benefit ratio analysis when the added cost of the device is appended to the procedure. In contrast to the controversies, angioplasty-induced complete vascular rupture is one situation in which a stent graft is indicated beyond any doubt. With recent conditional Food and Drug Administration approval, it is anticipated that the use of stent grafts might increase in our patients. In this context, it is critically important that nephrologists be familiar with the current controversies and consensus that surround the use of stent grafts for dialysis access. Just as therapeutic interventions are analyzed in other disciplines within nephrology, these experts must appraise the use of this device for dialysis access. This report presents an up-to-date synopsis on the use of the stent graft that would assist renal physicians in requesting or rejecting the device for the optimal management of their patient’s vascular access dysfunction.


Stent Graft for Stenosis at VGA

VGA is a predominant location for VGA stenosis and has been a major site for the application of therapeutic interventions (1,8–12). Because of its safety, success, and ease of performance, percutaneous transluminal balloon angioplasty (PTA) is becoming a standard technique for the management of VGA stenosis (8). It has been a general perception that PTA offers >50% primary patency rates at 6 months for venous stenosis related to an arteriovenous graft (8). Traditionally, the value of PTA in treating venous stenosis was also strengthened by the fact that randomized, controlled trials had failed to show any benefit of bare metal stents over simple PTA (11,12). Recently, a large (n = 190), multicenter, randomized, controlled trial by Haskal et al. (1) found better patency rates for stent graft versus simple PTA for the treatment of stenosis at the VGA. The target lesion primary patency at 6 months for stent graft (51%) was superior to that for PTA (23%; P < 0.001). Similarly, the 6-month primary patency of the access circuit was superior for the device (sten graft 38%, angioplasty 20%; P = 0.008). It is important to mention that the 6-month access circuit assisted primary patency (sten graft 65.5%, angioplasty 73.8%; P = 0.25) as well as access circuit cumulative patency (sten graft 81.3%, angioplasty 85.8%; P = 0.5) for this study were superior for simple PTA compared with the stent graft (2); however, the difference did not reach statistical significance.

Although study by Haskal et al. (1) is the largest clinical trial conducted to evaluate the role of the stent graft for the treatment of venous stenosis, several issues regarding the study are worth exploring. A simple comparison with the PTA group of a previous randomized, controlled trial by Vesely and Siegel...
(10) demonstrated unexpectedly low patency rates for simple PTA in the study by Haskal et al. (1). The 6-month primary patency of the target lesion (46.9%) as well as the access circuit (40.9%) were far superior to the 23 and 20% obtained by Haskal et al. (1) for their target lesion and access circuit, respectively (Table 1). The exact reasons for this discrepancy are unclear. Both studies were randomized with comparable sample size, used the same technique for angioplasty and patency definitions, and conducted analysis on an intention-to-treat basis (1,2,10); however, one point regarding the protocols of the two studies helps to explain the patency discrepancy to some degree. In clinical trial by Vesely and Siegel (10), no routine follow-up diagnostic studies were performed. In other words, subsequent PTA was done only on the basis of clinical indications. In contrast, in the study by Haskal et al. (1), all patients had scheduled protocol angiograms at 2 and 6 month. Most of those patients might not have been referred for an angiogram on clinical grounds. This difference might have accounted for the lower primary patency in the PTA group in the study by Haskal et al (1).

Form a nephrology standpoint, the delivery of dialysis therapy depends on the blood flow within the access circuit. It is not uncommon for the dialysis access circuit to harbor multiple coexisting lesions (13). A significant lesion anywhere within the access circuit would have the capability to restrict flow and minimize patency rates. In this context, isolated superior patency of the target lesion might be irrelevant in the presence of a coexisting lesion elsewhere within the circuit. Indeed, the exact location of secondary lesions was not described in the study by Haskal et al. (1). It is conceivable that a discrepancy in the number of patients with central venous stenosis (lower patency for these lesions) between the two groups confounded the results.

It is important to mention that one of the theoretical goals of preemptive PTA of graft stenosis is to prevent graft thrombosis; however, a great majority of randomized, controlled trials that evaluated stenosis surveillance with preemptive angioplasty did not reveal a reduction in thrombosis in the interventional group (14,15). Likewise, in the study by Haskal et al. (1), despite a lower primary patency in the PTA group, there was no difference in graft thrombosis between PTA (21%) and the stent graft (33%; $P = 0.10$).

The cost for placing a stent graft is significant and must be balanced against the cost of an angioplasty alone or the alternative of surgery. This cost is often looked at only from the viewpoint of a single patient; however, we should consider the total costs for each patient who is benefited. It is easy to calculate this figure. The cost of the procedure is derived from a combination of the procedure reimbursement rate plus the price of the device. In this instance, that is as follows for place of service 11 (POS 11):

- **Code 37205** = 114.02 Relative Value Unit (RVU)
- **Code 75960** = 7.43 RVU
- Total RVU = 121.45 = $4380.29
- Average cost of device = $2500.00
- Procedure = $4380.29
- Total cost per patient = $6880.29 to increase 6-month primary patency by 18%

- Cohort of 100 patients cost $688,029.00
- Only 18 (18%) patients actually benefited (38% – 20%)
- Cost per patient benefited = $38,223.83

This does not include that 24.7% of the patients required more than one device. When this number is included, the cost is increased to $47,665.12. We suggest that this is actually the pertinent cost number and is rather high.

Finally, a stenosis at the VGA provides an excellent opportunity for a surgical intervention (creation of a secondary arteriovenous fistula [AVF]). Both the Fistula First and the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) vascular access guidelines support this concept (8,16). The concept is based on the fact that the outflow vein of a graft has already undergone arterialization as a result of flow and pressure and can be readily available for conversion to an AVF (17–19). Whereas a tunneled dialysis catheter might be needed in the postoperative period for short-term use, a substantial number of patients can use the new secondary AVF immediately with primary patency of 87% at 6 months (19). A stent graft placed at the VGA may jeopardize future conversion to a secondary AVF, especially when these devices are placed above the elbow joint.

In the presence of increased costs, similar access circuit-assisted and cumulative patency rates documented by the stent-graft study (2), and the availability of superior primary patency rates for PTA from a separate trial (10), it is difficult to conclusively endorse the use of a stent graft over PTA for the treatment of stenosis at the VGA. In the presence of these confounding factors, the debate regarding the role of stent-grafts versus PTA continues and demands studies with appropriate design and sample size and longer follow-up.

### Table 1. Comparison of two multicenter, randomized clinical trials

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Haskal et al., 2010 (1) (Elective PTA&lt;sup&gt;a&lt;/sup&gt;)</th>
<th>Vesely and Siegel, 1995 (10) (Elective PTA&lt;sup&gt;a&lt;/sup&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>93</td>
<td>94</td>
</tr>
<tr>
<td>Target area patency at 6 months (%)</td>
<td>23.0</td>
<td>46.9</td>
</tr>
<tr>
<td>Access circuit patency at 6 months (%)</td>
<td>20.0</td>
<td>40.9</td>
</tr>
<tr>
<td>Graft thrombosis at 6 months (%)</td>
<td>21.0</td>
<td>NA</td>
</tr>
</tbody>
</table>

<sup>a</sup>PTA was performed for stenotic grafts and not thrombosed accesses.
Stent Graft for Cephalic Arch Stenosis

The cephalic arch is the term given to the final arch of the cephalic vein at the shoulder before it joins the axillary vein to form the subclavian vein (20). It passes beneath the clavicle, turns sharply to pierce the clavicular fascia, and terminates in the axillary vein. In patients with brachiocephalic fistulas, the cephalic arch is particularly vulnerable to the development of stenosis (20–22). Indeed, the prevalence of cephalic arch stenosis (CAS) has been estimated to be approximately 40% in patients with brachiocephalic fistulas (21). Several potential factors might be responsible for the high prevalence. The portion of the cephalic arch that is situated underneath the clavicular head of the pectoralis major muscle and the portion that pierces the clavicular fascia might be under extrinsic compression and halt remodeling of this segment of the vein. The presence of valves in this portion of the vein might interfere with dilation of the cephalic arch after fistula creation. In addition, hemodynamic forces might make this segment prone to injury (23).

Major impediments in the management of these lesions have included the resistant nature of the stenoses, the development of early restenosis, and poor patency and high vein rupture rates (20–22).

Recently, stent grafts have been used for the management of CAS. In this context, a randomized study to evaluate the role of the stent graft versus bare stent provided interesting observations (3). 25 patients with recurrent CAS (within 3 months of successful balloon angioplasty) were randomly assigned to receive angioplasty plus deployment of either stent graft or bare-metal stent. Only patients with brachiocephalic fistulas were included, and demographic characteristic of the study groups showed no difference. Twelve patients received bare stents, and 13 had stent grafts. The average follow-up for this study was 13.7 months (range 1.7 to 21.6 months). At 3 months, angiography was performed to assess the degree of stenosis. At that point, two patients in the bare stent and one in the stent-graft group had died. One patient in the stent-graft group had received a renal transplant. Of the 21 patients, significant stenosis (≥50%) was found in seven (70%) of 10 bare stents and two (18%) of 11 stent grafts (95% confidence interval 1.03 to 14.38; P = 0.024). During the follow-up period, nine patients died (bare stent = 4; stent graft = 5), three patients in the stent-graft group received a transplant, and one patient in the bare stent group thrombosed. Six-month primary patency for stent graft and bare stent was 81.8 and 39.1%, respectively. One-year primary patency for stent graft and bare stent was 31.8 and 0.0%, respectively (P = 0.002). The authors concluded that restenosis rates in recurrent cephalic arch restenosis were significantly better for stent grafts compared with bare stents. The investigators further suggested that in patients in whom intimal hyperplasia is a possibility, stenting should be limited to the use of stents that are completely covered with PTFE material.

Although the aforementioned study demonstrated the use of stent grafts in the management of CAS in a randomized manner, a very small sample size was a severe limitation. Although the number of multiple stent grafts was not reported specifically, the study mentions that multiple stents were indeed used in the study. The stent graft used in this study was reported to be Fluency (Bard Peripheral, Phoenix, AZ). The cost of each stent graft ranges from $2095.00 to 2195.00. The cost-to-benefits ratio must be balanced especially when multiple stent grafts are used in one patient. Finally, primary patency analysis included protocol angiograms and duplex ultrasound rather than clinical indications for a repeat angiogram. Although important, from a practical standpoint, these parameters might not be considered clinically meaningful end points.

Surgical intervention could also be considered. A relatively recent surgical study of patients with recurrent CAS provides a good comparison with the above-cited stent-graft study (22). Thirteen patients with frequently recurring CAS were referred for surgical intervention. The surgical procedure entailed transecting the healthy portion of the cephalic vein distal to the stenotic segment in the shoulder area, moving and connecting it to the veins in the inner part of the upper arm (basilic/axillary vein). After surgical revision, development of access dysfunction was treated with percutaneous balloon angioplasty. Patency rates for angioplasty before and after the surgical revision were evaluated. Primary patency rates for angioplasty before the surgical revision were 23, 8, and 0% at 3, 6, and 12 months, respectively. After surgical revision, all patients needed an angioplasty procedure; however, primary patency increased to 92, 69, and 39% at 3, 6, and 12 months, respectively (P = 0.0001). Secondary patency before the surgical revision at 3, 6, and 12 months was 100, 39, and 8%, respectively, compared with 92% at 3, 6, and 12 months after surgical revision (P = 0.0003). The results of this study demonstrated that surgical transposition of the cephalic vein in frequently recurring CAS was a viable option and yielded better patency rates for future angioplasty procedures. No stent grafts or bare stents were used in this study. Nevertheless, the 1-year primary patency (39%) for conventional angioplasty (without stents) after surgical revision of recurrent CAS compared favorably with that obtained by the stent graft (1-year primary patency 31.8%). Finally, a stent deployed in the CAS can migrate into the axillary-subclavian area and jeopardize any future chance of creating an arteriovenous access in the entire ipsilateral extremity (Figure 1). Constant movement of the shoulder girdle especially before the stent is endothelialized might be a reason for this migration. Although the two types of stents were evaluated, no randomized study has yet evaluated the role of conventional balloon angioplasty versus stent placement in management of CAS.

It is important to mention that the largest study that reported on CAS actually used conventional balloon angioplasty for the management of this lesion (21). A total of 177 failing fistulas were retrospectively investigated. A total of 116 (66%) were in the forearm and 61 (34%) were in the upper arm. A total of 39% of brachiocephalic fistulas had a CAS compared with 2% of radiocephalic fistulas. Primary patency was 42% at 6 months and 23% at 1 year. Primary assisted patency was 83% at 6 months and 75% at 1 year. An average of only 1.6 procedures a year was required per fistula to maintain primary assisted patency.

On the basis of the available information, there is not enough evidence to conclusively endorse the use of a stent graft for the treatment of recurrent CAS. Surgical intervention seems to yield better subsequent patency rates for simple angioplasty.
and bypasses the risk for axillary-subclavian occlusion (as a result of stent migration). Conventional balloon angioplasty without stent placement (stent graft or bare stent) remains the first-line treatment for CAS.

**Stent Grafts for Pseudoaneurysms**

Investigators have reported on the role of these stents in the percutaneous treatment of pseudoaneurysms (4–7). In a one study, 11 patients had undergone endoluminal insertion of covered stents to repair pseudoaneurysms (7). All 11 procedures were technically successful. The primary access patency rate reported in this study was 71% at 3 months and 20% at 6 months. Although these studies demonstrated the exclusion of pseudoaneurysm, problems such as recurrence of the pseudoaneurysm and stent-graft damage as a result of repeated cannulation remains a major predicament (7). The broken stent struts can potentially protrude through the skin and pose a threat of injury to the staff placing the patient on dialysis (Figure 1). Such a scenario was recently observed (Figure 2). The patient was successfully treated with surgical intervention. Dialysis staff responsible for cannulating the access through the stent might require a specific order by the nephrologist. The issue

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**Figure 1.** (Left) A stent in the cephalic arch is seen protruding into the axillary-subclavian junction. Stent fracture is also seen (arrow). (Right) A separate patient demonstrating migration of a stent with kinking (arrow) in the cephalic arch.

**Figure 2.** (Left) A stent strut protruding through the skin surface (arrow). (Right) A hemostat holding on to the end of a stent strut protruding through the skin is seen on fluoroscopy.
gains more importance because the exclusion of a pseudoaneurysm using a stent graft represents an “off-label” use of the device. It is critically important that the nephrologists be familiar with the site of stent graft deployed in a patient with access dysfunction and whether the device is being used for cannulation.

Stent-graft infection is another important consideration when cannulation is performed through these devices. A report highlighted two cases in which cannulation through the stent graft resulted in infection of the device and required surgical removal of the entire access to combat infection (24). Indeed, the safety of cannulation through stent grafts that are used to treat pseudoaneurysm has not been conclusively established in a prospective manner. Similarly, the role of surgical intervention in the treatment of pseudoaneurysms has not been directly compared with the stent graft. Such a comparison would helpful in clarifying the optimal management of this complication.

Perhaps the ability of the stent graft to provide rescue therapy in the event of angioplasty-induced vascular rupture is the most important role of these devices. Complete rupture is one situation in which the stent graft is indicated beyond any doubt. Using a stent graft, an operator easily excludes the rupture by placement of a stent graft that opposes the walls of the vessel at the site of rupture. Alternatives to this form of therapy include surgical revision or ligation of the access. An interesting case was reported in which an endovascular stent was used to repair an iatrogenic superior vena cava injury that occurred in the setting of a catheter placement (25). The perforation in the vena cava occurred at the confluence of the brachiocephalic veins when left subclavian catheter was being inserted. The covered stent was delivered through a femoral approach while the catheter was simultaneously removed to attenuate hemorrhage. The stent-graft insertion clearly avoided what would have required emergent surgical intervention.

Conclusions

Although stent grafts are used in dialysis access, at present, their use cannot be conclusively endorsed for the treatment of stenosis at the VGA. The use of these devices for CAS must take into account the alternative surgical approach especially considering the risk for axillary-subclavian vein occlusion as a result of possible migration and loss of the venous capital of the entire upper extremity. Stent graft in pseudoaneurysms poses multiple risks, including the recurrence, damage as a result of cannulation, and infection. Further studies with appropriate design, sample size, and follow-up are desperately needed for proper evaluation of the role of stent grafts in dialysis access. A multidisciplinary approach that consists nephrologists, surgeons, and radiologists must convene to accomplish this task.

Disclosures

None.

References


