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A Comparison of Distal Endoluminal Graft Fixation Methods: Healing Characteristics of Metallic Stents and the Endoluminal Suture Technique

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Rationale: Endoluminal grafts (EG) are a promising alternative to conventional open surgical approaches in the treatment of aneurysmal and occlusive arterial diseases. These devices generally employ metallic stents to secure the proximal and distal EG extents. However, the problem of intimal hyperplasia at the distal EG anastomotic ends similarly affect long-term outcomes as in conventional interposition grafting methods. A technique of distal EG anastomosis using hand-sewn endoluminal sutures is described and its effects on subsequent development of intimal hyperplasia compared with that of metallic endoluminal stents.

Methods: Ten adult mongrel dogs underwent bilateral common iliac artery endoluminal grafting procedures. On one side, the distal EG anastomosis was anchored with metallic stents while on the contralateral side the distal EG was secured with endoluminal sutures. The grafts were harvested after one month and the intimal characteristics were observed using histopathological methods.

Results: Distal EG metallic stents and endoluminal sutures resulted in similar patency rates of 90%. The average time to deploy distal EG metallic stents was 56 seconds, while the average time to secure the distal EG anastomosis using endoluminal sutures was 3 minutes 42 seconds. Metallic stents induced the development of intimal hyperplasia to a degree greater than endoluminal sutures (316 ± 12 µm vs. 245 ± 30 µm, $p<0.05$), but did not affect patency.

Conclusion: Hand sewn endoluminal suture technique results in a lesser degree of intimal hyperplasia compared with that produced by endoluminal metallic stents, while the patency rates are comparable.

Keywords: hyperplasia, stents, suture techniques, arterial occlusive disease

The use of endoluminal stent grafts is a promising new modality for the treatment of aneurysmal[1,2] and occlusive artery disease.[3-7] The key technical principle involves the delivery and deployment of an endovascular graft (EG) from a point distal from the affected area and utilizing metallic stents to secure the EG at its proximal and distal anastomoses[5] (Figure 1) Initial reports of its technical success and short-term patency are encouraging, but its long- term efficacy is still to be demonstrated.[4,6] Early studies suggest that late failures of these grafts appear to be due to the development of restenosis particularly at the distal anastomotic ends.[2,3,5-11]

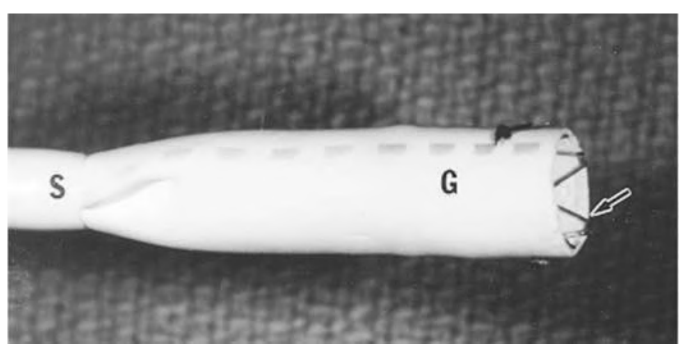

Figure 1.The endovascular graft (EG) system. The polytetrafluoroethylene (PTFE) graft (G) is stented intraluminally (arrow) with a Palmaz metal stent. The EG is crimped onto a balloon angioplasty catheter and inserted inside a French 9 hemostatic sheath (S).

The different ways in which the distal end of the EG is managed have been described.[12] There are reports on the effects of metallic stents on vessel healing characteristics, and comparisons have been made of the histological characteristics at the anastomotic regions of metallic stents versus those of conventional end-to-end or end-to-side suture anastomoses.[12-16] However, these comparisons may not really be appropriate inasmuch as metallic stents secure the ends of *endoluminal* grafts, while conventional graft anastomoses are only possible with *non-endoluminal* interpositions.

A technique of endoluminal distal EG fixation, the hand sewn endoluminal suture anastomosis, is the main method of distal graft fixation employed for aortounifemoral endovascular treatment of aortoiliac occlusive and abdominal aneurysmal disease in one center, and has anecdotally produced a lower rate of hemodynamically significant anastomotic intimal hyperplasia.[17] This study was designed to compare the effects of this technique of endoluminal fixation with that of metallic stents on graft patency and intimal healing characteristics.

Methods

Subjects

Ten adult female mixed-breed dogs weighing 20-25kg were used in this study. Dogs were selected because their vascular response to EG has been previously described and well studied.[17] All animal care was performed in accordance with the "Principles of Laboratory Animal Care" and the "Guidelines for the Care and Use of Laboratory Animals" (NIH Publication No. 80-23, revised 1985).

Materials

Thin-walled 5mm x 40mm polytetrafluoroethylene (PTFE) grafts (Gore-Tex, W. L. Gore, Arizona, USA) were prepared by securing with CV-6 PTFE sutures a 10mm length of a metal stent (Palmaz stent, Johnson and Johnson Interventional Systems, New Jersey, USA) at the intraluminal proximal end. The grafts were then crimped and folded onto a 6mm x 20mm angioplasty balloon (Meditech, Boston Scientific, USA) and inserted into French 9 hemostatic sheath.

Procedure

The subjects were pretreated with acepromazine (0.1mg/kg) and atropine HCl (0.04mg/kg) administered intramuscularly. Anesthesia induction proceeded via intravenous administration of thiopental sodium (10-20mg/kg), followed by endotracheal intubation and anesthesia maintenance with 1 to 2.5 per cent isoflurane. Prophylactic cephalosporin (10mg/kg) was given intravenously prior to skin incision. After abdominal skin antisepsis and draping procedures, a midline laparotomy incision was performed to expose the abdominal aorta and the iliac arteries. The lower lumbar arteries were ligated and divided. Systemic heparin (100u/kgBW) was given intravenously prior to aortic clamping. Proximal control was obtained by dissecting out the aorta and placing an infrarenal clamp. Clamping the iliac arteries distal to and including their internal iliac branches achieved distal control. Endoluminal access was achieved through a 1cm anterior aortotomy.

The sheath containing the EG was then inserted and advanced into the iliac artery. Once positioned, the sheath was withdrawn and the balloon inflated to 4 ATM pressure in order to expand the graft and anchor the metal stent at the proximal end. Deployment was followed by withdrawal of the sheath and balloon catheter. The endoluminal grafts were then visualized through the wall of the vessel. On one side determined randomly, a 10mm length metal stent was loaded onto the balloon catheter, advanced in a sheath for positioning onto the distal anastomosis, and deployed. On the contralateral side, upon visualization of the distal EG, an iliac arteriotomy was done, through which the distal end of the graft was then secured endoluminally using prolene 6-0 sutures applied in six circumferential U-stitches. The arteriotomy was then closed with prolene sutures, and the flow reestablished by removal of the clamps. The time to perform either technique was recorded. Immediate patency was ensured by visualization and palpation of the distal outflow vessels.

After adequate hemostasis, the abdominal incision was closed in layers with interrupted full thickness non-absorbable sutures for the musculofascial layers and continuous absorbable sutures for the skin. Completion angiography was then performed by injection of 5 mL intravenous contrast material (50% diatrizoate meglumine and diatrizoate sodium, Renograffin-50, Squibb) through a graticulated pigtail catheter inserted through a carotid artery access sheath. Fluoroscopic images of both grafts were taken and stored on C-arm fluoroscope disk (Philips BV 313) and recorded on a videocassette recorder (National Panasonic, Japan).

The subjects were allowed to recover from anesthesia and were given intramuscular injections of buprenorphene (0.02 mg/kg) twice a day for 5 days. Postoperative diet was supplemented by a daily dose of 325 mg of aspirin. Patency was evaluated by daily pulse examinations.

At the 8th post-operative week, the subjects were again anesthetised. Carotid artery access was achieved and the patencies of the grafts were confirmed under fluoroscopy using contrast dye delivered through a graticulated pigtail catheter and recorded on videocassette for offline analysis. After a repeat angiography, the subjects were sacrificed by lethal injection of intravascular pentothal (120 mg/kg BW), KCL (800 meq) and introduction of bilateral pneumothoraces. The specimen including the distal aorta and bilateral iliac arteries were then harvested and perfusion-fixed in 10% formaldehyde solution. Angiographic measurements of intraluminal diameters were taken offline on video playback.

Specimen Preparation and Analysis

Specimens were sectioned longitudinally and the endoluminal surfaces observed. Histomorphologic examination of the distal graft anastomosis was accomplished by doing cross sections at 5 mm intervals starting 10 mm proximal and distal to the metal struts or endoluminal suture anastomosis. The sections were then embedded in paraffin, the metal stent struts gently removed, and the specimens subsequently postfixed in osmium tetroxide and dehydrated in increasing concentrations of ethyl alcohol. Tissue samples were then infiltrated with propylene oxide and flat-embedded in Epon 812. After polymerization, 1m sections of the specimens were cut and stained with Elastica von Gieson and Hematoxylin-eosin .

Graft wall and intimal thickness were measured in the 1 m sections and analyzed with a computer-digitized morphometric system (Bioscan Optimas, WA).

Statistical Analysis

The grafts where the distal anastomosis was secured with metal stents were compared to those where hand sewn endoluminal suturing was done with respect to 1) procedure time, 2) patency rates, 3) angiographic intraluminal diameter, and 4) histomorphometry and mean thickness of intimal growth at the site of the anastomoses. Statistical analysis was performed using the paired Student's t test (two-tailed). Values were reported as the mean SEM, and results were considered significant if $p<0.05$.

Results

Procedure Time

The average time it took to secure the distal anastomosis using the metal stent was 56 ± 13 seconds, while the average time required to secure the distal anastomosis using hand suturing of the endoluminal stitches was 222 ± 42 seconds (Figure 2). The first timed procedure which showed outlying data was not included in the computations to remove the influence of the learning curve skewing the average times.

Vessel Patency

Daily clinical examination of the distal outflow vessels during the postoperative period showed that 90% of the grafts in the stented and in the sutured group remained patent during the study period. This was confirmed at harvest time 8 weeks after the procedure angiographically and intraoperatively. Upon gross examination, the occluded grafts in both groups were seen to contain organized thrombi (Figure 3). Both grafts were also seen to have folds and wrinkles, indicating improper deployment not observed or detected by visualization or completion angiography.

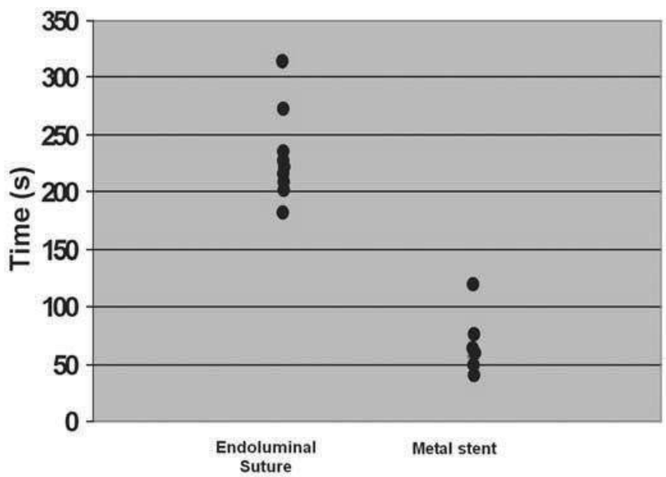

Figure 2. Scatterplot graph showing comparison of procedure times for endoluminal suture anastomosis (ES) vs metal stent anastomosis (MS). Each point represents one timed procedure. (n=10; average time for ES is 222 ± 42 seconds, MS is 56 ± 13 seconds.) The time for the first procedure was not included in the analysis in order to remove the influence of the learning curve skewing the average times.

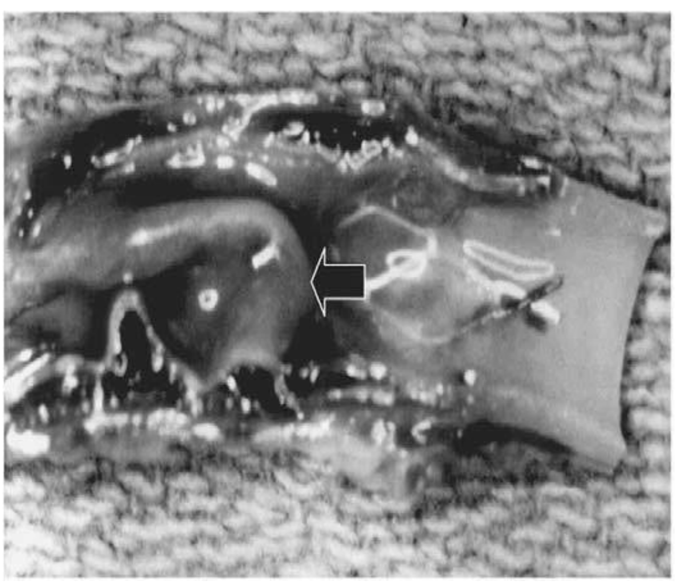

Figure 3. Gross appearance of an occluded graft. Note the graft wrinkles (arrow) that predisposed to thrombus formation leading to occlusion.

Angiographic Intraluminal Diameter

There was no angiographic evidence of proximal or distal leakage in the patent grafts of both groups. Offline analysis of intraluminal diameters taken of the patent grafts at the end of 8 weeks showed no significant differences between the stented and the hand sutured groups (5.9 ± 0.2 mm and 5.8 ± 0.7 mm, p>0.05) nor between these and the baseline completion angiograms (stented, 6.1 ± 0.2 mm; hand sutured, 5.9 ± 0.5 mm) (Figure 4).

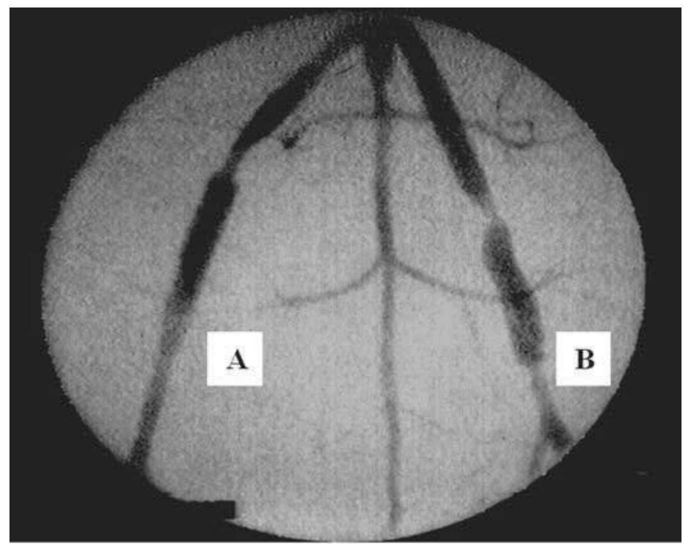

Figure 4. Fluoroscopic image of bilaterally stented iliac arteries. The distal end of the right iliac artery graft (A) was anastomosed with the handsewn endoluminal suture, while the distal end of the left iliac artery graft (B) was fixed with a metal stent. Luminal diameters were comparable in all animals.

Gross and Histomorphometric Analysis

Gross examination of the specimens showed complete intimal covering of the distal anastomoses in both groups. Histopathological examination of the arterial segments showed a normal 3-layered wall structure distal to the EG. Radial pressure by the expanded EG caused a distinct compression of the arterial wall, but with discontinuities of the internal elastic lamina. Photomicrographs show the development of neointima consisting of a collagenous matrix containing myofibroblasts and histiocytes and bordered by accumulated fibrin covering the distal anastomoses. The average neointimal thickening was 316 ± 12 µm for the metal stent group and 245 ± 30 µm ($p<0.05$) for the endoluminal suture group. (Figure 5).

Discussion

The concept of endoluminal placement of an arterial bypass graft is an exciting development in the management of aneurysmal and occlusive arterial disease.

A

B

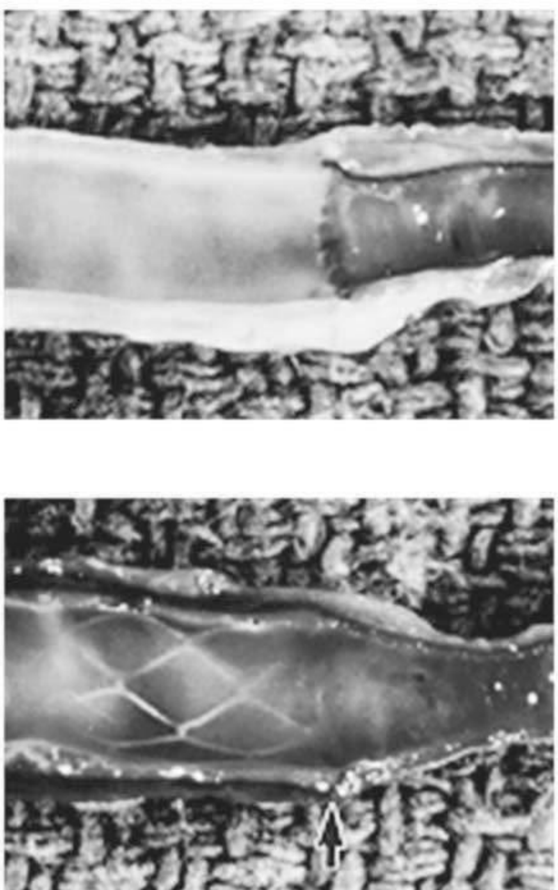

Figure 5. Longitudinal section of distal EG anastomosis. A. Hand sewn endoluminal suture, and B. metal stent. The distal anastomoses in both techniques may be seen to be covered completely with a thin intimal layer. Note how the metal stent in B. has been fully covered (arrow).

The attraction lies in the procedure's minimally invasive nature and remote access capability, thus potentially decreasing the level of risk in performing vascular interventions as compared to direct arterial exposure and bypass.

From the very first investigations carried out by Dotter[18] using a laboratory designed device, to the first clinical application performed by Parodi,[19] up to the present commercially available devices approved for use and under investigation, a basic principle underlying endoluminal grafting involves securing the proximal and distal anastomoses endoluminally in order to prevent perigraft leak, graft dislodgement and migration. This has traditionally been accomplished by way of the radial force supplied by balloon-expanded or self-expanding metal stents either along the whole length of the EG in the so-called fully supported grafts or at the proximal and distal ends in the partially supported grafts.

Metal stents, however, exhibit thrombogenic properties that may limit its long-term efficacy.[15,20,21] This may be due to the inherent thrombogenicity of the materials used, the hemodynamic changes associated with stent-induced turbulence or the compliance mismatch of the rigid stent and the compliant arterial wall, or both, leading to early thrombotic occlusion or late stenosis resulting from the development of intimal hyperplasia. These problems are of significant concern particularly at the distal anastomotic ends of the fully or partially supported EG.

Various methods of addressing this problem at the distal anastomosis of the EG have been proposed.[15,16] (Figure 6). On one extreme is the unsecured endoluminal distal end, and on the other extreme is the technique of vessel ligation and/or transection to allow for conventional end-to-end or end-to side suture anastomosis. In between is the method of fixation using metallic stents and the hand-sewn endoluminal suture technique.

The technique of the hand sewn endoluminal suture (Figure 7) evolved from the investigative use of endovascular aortounifemoral grafts and femorofemoral bypass initially employed for aortoiliac occlusive disease[17] but now applicable also to a wide variety of abdominal aortic aneurysm configurations.[22] Securing the distal EG by way of endoluminal U-stitches was believed to result in greater long term patency rates seen in fixed

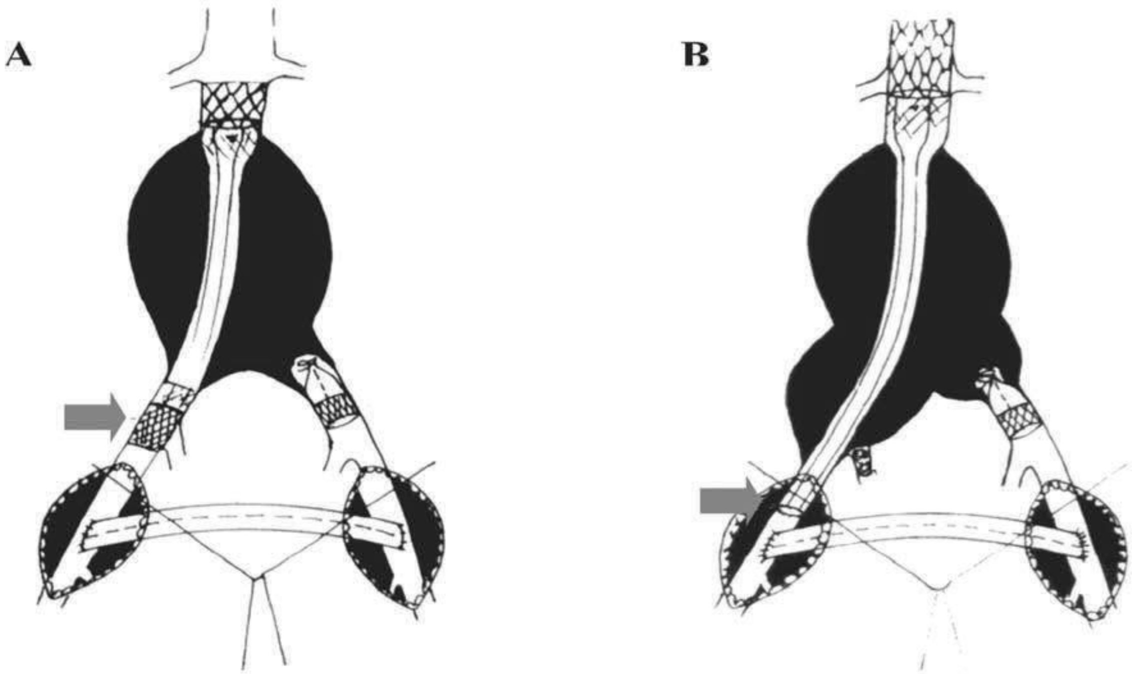

Figure 6. Techniques of distal endovascular graft fixation. A. Metal stent fixation. The distal end of the graft ends more proximally remote from the skin incision and arteriotomy. B. Endoluminal suture anastomosis. The distal end of the graft ends at the arteriotomy site. (*illustration used with permission from Ohki T, Veith FJ, Sanchez LA, Marin ML Cynamon J and Parodi J. Varying strategies and devices for endovascular repair of abdominal aortic aneurysms. Semin Vasc Surg 1997; 10:242-56.*)

distal anastomoses while benefiting from the absence of thrombogenic endoluminal stents which may induce in a greater degree the development of intimal hyperplasia.

The data of the present study show that the hand sewn endoluminal method of distal EG fixation results in similar short term patency rates as the stented distal anastomosis. Graft occlusions occurred in both groups in equal frequencies, and upon gross examination, the occluded grafts in both groups exhibited folds and wrinkles, indicating improper deployment or inadequate graft expansion or both. These wrinkles and folds are exclusive complications of the partially supported EG; the fully supported or stented EG will not exhibit this kind of complication. The wrinkles and folds resulted in turbulent flow that led to accelerated deposition of fibrin and platelets and thus proceeded to thrombotic occlusion. It was interesting to note that the wrinkles and folds were not detected angiographically, thus accentuating the limitations of this modality in the evaluation of endoluminal device placement and position. Post-deployment evaluation of the EG is probably best obtained with the use of the intravascular ultrasound (IVUS) as an adjunct to the standard completion fluoroscopic or angiographic evaluation. IVUS will demonstrate graft luminal irregularities as well as the adequacy of stent deployment. In any case, the wrinkles and folds are best avoided by using fully supported EG, or ensuring adequate deployment by re-expanding the appropriately sized angioplasty balloon to seat the EG firmly against the vessel wall.

Deployment of the metal stents was technically easy as evidenced by the shorter amount of time required as compared with the hand-sewn technique. The latter technique demanded more time and technical skill in that the U-stitches must be carefully placed in a manner that will lay the EG ends flat against the endothelium, all the

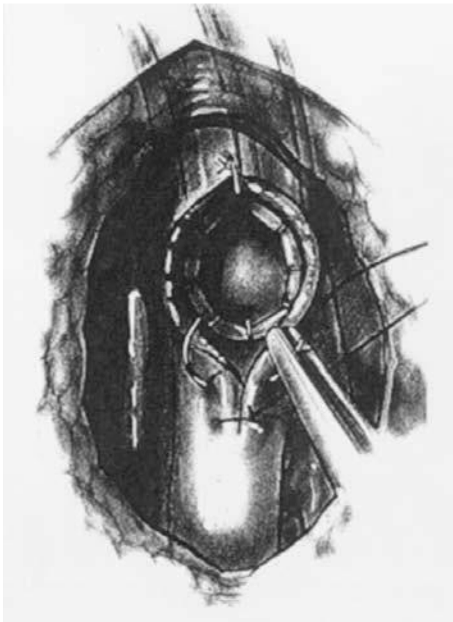

Figure 7. Technique of the hand sewn endoluminal suture. The distal end of the endoluminal graft is seen through the arteriotomy. A series of U-stitches fix the distal end to the arterial lumen. The arteriotomy may then be sutured closed or a sequential graft may be anastomosed over the arteriotomy. (*illustration used with permission from Ohki T, Veith FJ, Sanchez LA, Marin ML Cynamon J and Parodi J. Varying strategies and devices for endovascular repair of abdominal aortic aneurysms. Semin Vasc Surg 1997; 10:242-56.*)

while trying to avoid twisting and folding the EG. As with all new techniques, the learning curve was eventually surmounted, though it must be said that it was quite steep.

There may be certain situations where the use of the endoluminal suture technique may be preferable or even the method of choice for distal EG fixation. The endoluminal suture technique may be applicable only in selected cases where the distal EG is immediately accessible, as in the femoral artery in groin incisions or the iliac arteries in abdominal incisions, while metallic stents may be utilized best in remote access conditions where the distal end of the EG is located in an inaccessible location. Moreover, the endoluminal suture may be the appropriate option in cases where the pattern of distribution of the lesion requires a sequential graft to the contralateral side or more distal vessel segment.

In this study, intimal hyperplasia was significantly greater with the stented than with the hand sewn distal EG. At first glance, it would appear incongruous for it to be so, inasmuch as in performing the hand sewn endoluminal suture technique, the necessary arteriotomy, vessel handling and suture placement are added injuries to the vessel and endothelium that contribute to the development of intimal hyperplasia. On the other hand, the radial expansion force of metallic stents produces continuous injury over a greater surface area of endothelium, which, in addition to the adverse intimal effects of compliance mismatch between the stent and vessel, may all conspire to induce a greater degree of intimal hyperplasia.

In spite of this, angiography did not demonstrate appreciable differences in luminal diameter between the two techniques and across time. The greater degree of intimal hyperplasia of the stented grafts at eight weeks apparently was not sufficient to cause angiographically significant luminal stenosis. This indicates an encouragingly high short-term patency rate for either technique; it remains to be seen though, whether these promising trends will be carried over to the mid- and long term. The histologic picture of the disjointed internal elastic lamina suggests an ongoing process of smooth muscle cell migration into the intima, which in turn points to continued intimal layer growth.[23] Nonetheless, continued smooth muscle cell proliferation and migration does not immediately translate to a thicker intimal layer since the eventual thickness of the intima is dependent on the equilibrium attained with the opposing processes of apoptosis and remodeling. The question of whether intimal hyperplasia will continue to develop and eventually lead to graft stenosis and occlusion or whether the process shall equilibrate at a steady state must be addressed in further studies.

Conclusion

Hand sewn endoluminal suture technique and metallic endovascular stent graft fixation at the distal end result in similar acceptable patency rates. Although intimal hyperplasia is greater with metallic stents compared with endoluminal sutures, the angiographic luminal diameters did not vary significantly. The decision on which method of endoluminal graft fixation at the distal end may rest more on the location and accessibility of the distal end of the endoluminal graft, the necessity of a sequential graft, and the surgeon's technical facility with either procedure.

References

1. Razavi MK, Dake MD, Semba CP, Nyman UR, Liddell RP. Percutaneous endoluminal placement of stent-grafts for the treatment of isolated iliac artery aneurysms. Radiology 1995; 197(3): 801-4.
2. Cardon JM, Joyeaux A, Vidal V, Noblet D. Endovascular repair of iliac artery aneurysm with endoprosystem I: a multicentric French study. J Cardiovasc Surg 1996; 37(S1 - S3): 45-50.
3. Pernes, JM, Auguste MA, Hovasse D, Gignier P, Lasry B, Lasry JL. Long iliac stenosis: initial clinical experience with the Cragg Endoluminal Graft. Radiology 1995; 196(1): 67-71.
4. Marin ML, Veith FJ, Cynamon J, Sanchez L, Wengerter KR, et al. Transfemoral endovascular stented graft treatment of aortoiliac and femoropopliteal occlusive disease for limb salvage. Am J Surg 1994; 168: 156-62.
5. Henry M, Amor A, Cragg,A, Porte J, Henry I, Amicable C, Tricoche O. Occlusive and aneurysmal peripheral arterial disease: Assessment of a stent-graft system. Radiology 1996; 301(3): 717-24.
6. Marin ML, Veith FJ, Sanchez LA, Cynamon J, Lyon RT, Suggs WD, Bakal CW, Parsons RE. Endovascular repair of aortoiliac occlusive disease. World J Surg 1996; 20: 679.
7. Wilkinson JM, Beard JD, Gaines PA. Aortoiliac occlusion treated by a combination of aortoiliac stent and femorofemoral crossover grafting. Eur J Vasc Endovasc Surg 1996; 12: 372-4.
8. Demasi RJ, Snyder SO, Wheeler JR, Gregory RT, Gayle RG, Parent FN, Gandhi RH. Intraoperative iliac artery stents: combination with infra-inguinal revascularization procedures. Am Surg 1994; 60: 854-9.
9. Cikrit DF, Gustafson PA, Dalsing MC, Harris VJ, et al. Long term follow up of the Palmaz stent for iliac occlusive disease. Surgery 1995; 118(4):608-14.
10. Van Beusekom HM, van der Giessen WJ, van Suylen RJ, Bos E, Bosman FT, Serruys PW. Histology after stenting of human saphenous vein bypass grafts: observations from surgically excised grafts 3 to 320 days after stent implantation. JACC 1995; 21(1): 45-54.
11. Schurmann K, Vorwerk D, Uppenkamp R, Klosterhalfen B, Bucker A, Gunther RW. Iliac arteries: Plain and heparin-coated Dacron covered stent grafts compared with non-covered metal stents-an experimental study. Radiology 1997; 203: 55-63.
12. Marin ML, Veith FJ, Sanchez LA, et al. Endovascular aortoiliac grafts in combination with standard infrainguinal arterial bypasses in the management of limb-threatening ischemia: preliminary report. J Vasc Surg 1995; 22(3): 316-25.
13. Chalmers RT, Hoballah JJ, Sharp WJ, Kresowik TF, Corson JD. Effect of an endovascular stent on healing of an end-to-end polytetrafluoroethylene-artery anastomosis in a canine model. Br J Surg 1994; 81: 1443-7.
14. Chalmers RT, Hoballah JJ, Sharp WJ, Kresowik TF, Corson JD. The effect of an intraluminal stent on neointimal hyperplasia at an end-to side polytetrafluoroethylene graft arterial anastomosis. Am J Surg 1994; 168: 85-90.
15. Ombrellaro MP, Stevens SL, Kerstetter K, Freeman MB, Goldman MH. Healing characteristics of intraarterial stented grafts: Effect of intraluminal position on prosthetic graft healing. Surgery 1996; 120(1): 60-70.
16. Ohki T, Marin ML, Veith FJ, Lyon RT, Sanchez LA, Suggs WD, et.al. Endovascular aortounifemoral grafts and femorofemoral bypass for bilateral limb-threatening ischemia. J Vasc Surg 1996; 24: 984-97.
17. Ohki T, Marin ML, Veith FJ, Yuan JG, et al. Anastomotic intimal hyperplasia: a comparison between conventional and endovascular stent-graft technique. J Surg Res 1997; 69: 255-67.
18. Dotter CT. Transluminally placed coilspring endarterial tube grafts: long term patency in canine popliteal artery. Radiol 1969; 4: 329-32.
19. Parodi JC, Palmaz JC, and Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg 1991; 5: 491-9.
20. Worsey MJ, Laborde AL, Miller BV, Bower TR, Landas S, Kresowik T, et al. Endovascular canine anastomotic stenting. J Surg Res 1993; 54: 29-33.
21. Eton D, Warner DL, Owens C, Cava R, Borhani M, Farolan MJ, et al. Histological response to stent graft therapy. Circulation 1996; 94:II-182-7.
22. Ohki T, Veith FJ, Sanchez LA, Marin ML Cynamon J and Parodi J. Varying strategies and devices for endovascular repair of abdominal aortic aneurysms. Semin Vasc Surg 1997; 10: 242-56.
23. Garrat KN, Edwards WD, Kaufmann UP, et al. Differential histopathology of primary atherosclerotic and restenotic lesions in coronary arteries and saphenous vein bypass grafts: analysis of tissue obtained from 73 patients by directional atherectomy. J Am Coll Cardiol 1991; 17:442-9.