Limb Patency Outcomes in Contemporary Data

A review of peer-reviewed publications on real-world limb patency rates.

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During the last decade, endovascular aneurysm repair (EVAR) has gained wide acceptance as the preferred method of treating suitable patients with abdominal aortic aneurysms.[1] EVAR is associated with lower 30-day mortality and morbidity rates, faster discharge, and fewer complications than with surgery, but seems to be associated with higher secondary intervention rates.[2] Graft limb stenosis or thrombosis are important causes of secondary interventions after EVAR.

Graft limb patency in the major randomized controlled EVAR trials has not been extensively reported. In the OVER and ACE trials, no separate data on outcomes of graft limbs are available.[3,4] The DREAM study reported a 6.9% rate of thromboembolic events, but did not provide detailed data on these graft limb complications.[5] In the EVAR 1 trial, limb graft stenosis and thrombosis were found in 0.6% and 3.2% of patients, respectively, during a mean follow-up of 6 years.[6] In the EUROSTAR registry, the limb occlusion rate was 5% at 2 years, but first-generation stent grafts were mainly used.[7] Mehta et al retrospectively evaluated 1,768 EVAR patients and reported a 1.4% limb occlusion rate during a mean follow-up of 34 months. Furthermore, 7.4% of the secondary procedures were performed for graft limb occlusion.[8]

GRAFT-SPECIFIC REPORTS

Modern commercially available stent grafts each have important variations, both in graft material (polyester or polytetrafluoroethylene [PTFE]), stent material (stainless steel or nitinol), and stent configuration ("Z-M" or helical shaped). These variations may result in different adaptations of the graft limb to the iliac artery anatomy, especially in cases of severe angulation or nonuniform-diameter landing zones.

Anaconda

The Anaconda graft limbs (Vascutek, a Terumo Company) are made of independent nitinol circular stents with no interconnection struts, which are combined with woven polyester graft material. This configuration is specifically designed for tortuous iliac anatomy; however, the lack of columnar support may result in a higher risk of proximal limb retraction.[9] In the largest single-center clinical experience using this stent graft, Freyrie et al reported a 5.1% secondary intervention rate for limb thrombosis/stenosis in 177 patients during a mean follow-up period of 33 months.[10] Similar results have also been described in a smaller recent study, which reported a 1.4% graft limb occlusion rate during a 29-month period.[9]

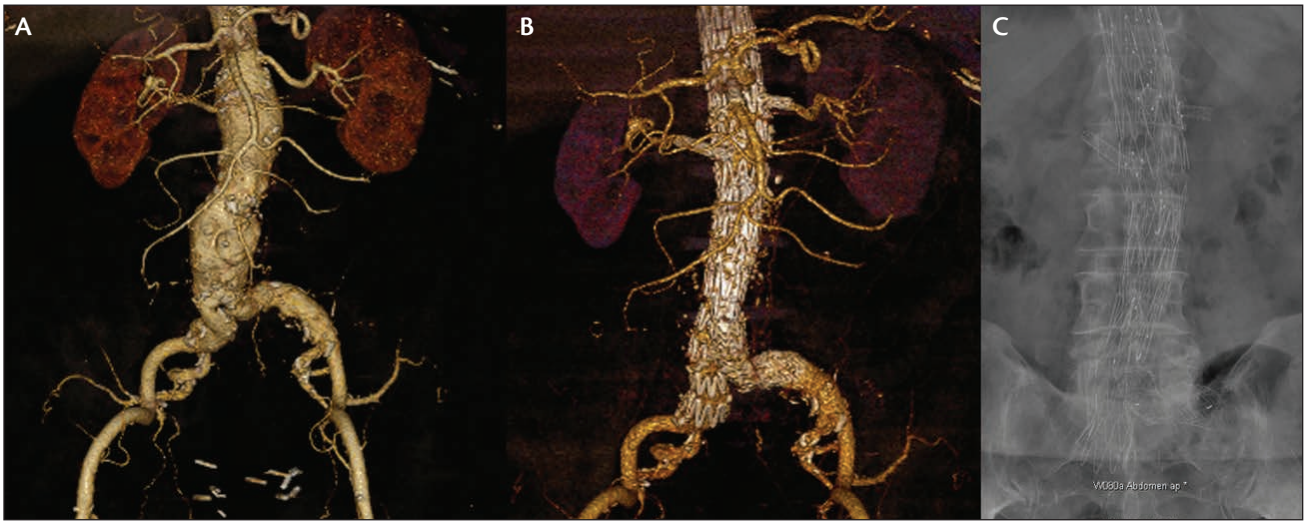

Figure 1. Three-dimensional volume-rendered CT reconstruction of a patient with severe left iliac angulation treated with a combination of a Zenith stent graft body (Cook Medical) and an Excluder (Gore & Associates) iliac limb (A). CTA (B) and x-ray (C) 2 years postoperatively, showing good patency of the graft limb.

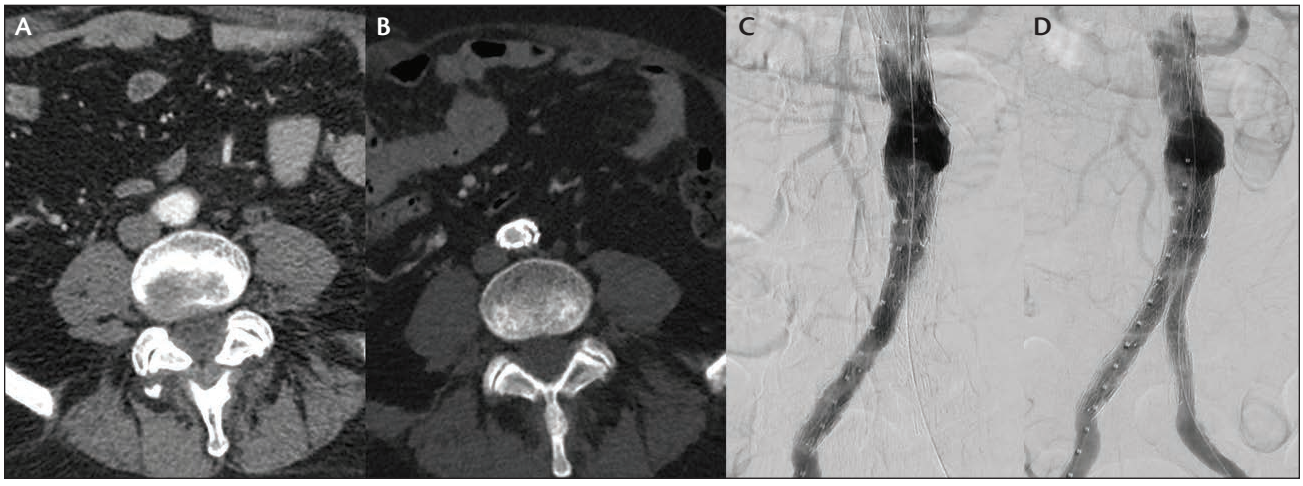

Figure 2. Preoperative CTA showing a narrow (18 mm) aortic bifurcation (A). CTA 4 hours postoperatively depicting acute thrombosis of a Zenith (Cook Medical) left limb due to collapse (B). Intraoperative digital subtraction angiography showing left limb thrombosis (C). Completion angiography after thrombectomy and relining of an Express left limb (Boston Scientific Corporation) (D).

Aorfix

The Aorfix limbs (Lombard Medical, Inc.) are made of woven polyester material and a continuous nitinol wire following a ring stent configuration that allows the device to be flexed axially without kinking.[11] The initial results were promising, as no iliac thromboses occurred in 30 patients with angulated proximal necks and/or tortuous iliac arteries during a mean follow-up of 27 months.[11] In a retrospective 12-year study, Weale et al reported great results when using Aorfix in complex iliac anatomy. After 2007, patients with highly angulated iliac anatomy were treated with the Aorfix stent graft, or when a Zenith main body (Cook Medical) was chosen, the Aorfix iliac limbs were used. A substantial reduction in limb thrombosis rates was noted after the adoption of this policy, and Aorfix iliac limbs were implanted in highly angulated iliac anatomy (6.2% vs 0%).[12]

Endurant

The Endurant graft limb (Medtronic) is made of M-shaped nitinol stents surrounded by polyester material. The ENGAGE registry prospectively included 1,143 patients treated with bifurcated devices who were followed for up to 2 years.[13] The rate of graft limb occlusion was 3.4%. Out of the 42 diagnosed occlusions, 13 (31%) were observed within 30 days, and 30 (71%) were seen within 6 months.[13] Bisdas et al reported a graft limb occlusion rate of 3.7% during a mean follow-up period of 42 months in a total of 273 patients who were treated with the Endurant stent graft.[14]

Excluder

The Excluder limbs (Gore & Associates) are fabricated from ePTFE with an outer self-expanding nitinol support structure. These limbs are thin and very flexible, adapting well to complex iliac anatomy. Clinical reports have demonstrated promising results in clinical performance. ITER (Italian Excluder Registry) included 872 patients and reported nine (1.1%) graft limb thromboses at a mean follow-up of 20.6 months. Interestingly, five of these occurred in the first 12 months.[15] In the GREAT registry, reintervention for graft limb occlusion was low (2%) during a mean follow-up period of 16 months, confirming the excellent performance of Excluder graft limbs.[16]

Ovation

The Ovation iX™ Iliac Stent Graft Limbs (TriVascular, Inc.) consist of highly flexible nitinol stents encapsulated in a low-permeability PTFE and are delivered through a 10- to 13-F integrated sheath, reducing the risk of iatrogenic vessel injury. The overall device characteristics allow access in iliac arteries as small as 4.7 mm. The iliac limbs feature one continuous piece of nitinol wire that resists kinking and twisting, even in hostile iliac anatomy. This wire is precisely manufactured to lie on the PTFE to reduce kinking of the material between the stents. The stents are embedded between layers of PTFE and are not sutured onto the graft material, creating a smooth luminal surface. Clinical reports confirm low limb occlusion rates. In a prospective multicenter study of 161 patients treated with the Ovation Iliac Stent Graft (TriVascular, Inc.), Mehta et al reported three (1.8%) reinterventions for graft limb stenoses or occlusions during the first year.[17] In a smaller multicenter study of 36 patients treated with the Ovation iliac stent graft, no limb occlusions were reported during a 2-year follow-up period.[18] The Ovation iliac stent graft seems to behave well in challenging iliac access anatomies, as no iliac occlusions occurred in a report of 42 patients with hostile iliac configuration, irrespective of iliac diameter or angulation.[19]

Zenith

The Zenith stent graft is constructed with individual Gianturco Z-stents surrounded by polyester material.

Greenberg et al reported the 5-year results of the Zenith United States multicenter trial in 2008 and found a cumulative risk of 2.6% for graft limb occlusion.[20] Furthermore, Mertens et al reported a graft limb stenosis in 2.1% and occlusion in 5.6%.[21] Most graft limb occlusions occurred during the first 3 months after the procedure. Initially, the interrupted stent design of the first-generation Zenith stent graft was considered to be associated with a higher risk of iliac limb kinking and occlusion. The manufacturer therefore increased the spacing between the Z-stents to enhance compatibility with hostile iliac anatomy. Recently, Cook released a new graft limb that is constructed of two self-expanding stainless steel Z-stents at the ends and a continuous nitinol spiral stent in between. The initial results for this device are promising, as no limb occlusions and only one graft limb stenosis out of 100 graft limbs were reported during a 6-month period.[22]

COMPARATIVE STUDIES

Large, prospective, randomized studies comparing limb patency rates among different endografts are lacking. In a device-specific analysis of the effect of three different first-generation endografts (Zenith, Excluder, and AneuRx [Medtronic]) on EVAR outcomes, Excluder had the lowest graft limb thrombosis rate, despite being implanted more frequently in women and outside the indications for use.[23] In contrast, Mantas et al found no significant differences in the incidence of graft limb thrombosis between the different types of second- and third-generation endografts, although the small sample size should be acknowledged.[24] Nevertheless, it seems that some graft limbs are behaving better in hostile iliac anatomies, although this does not seem to play an important role toward an overall clinical benefit. Although, perhaps, it has not been studied enough.

In an experimental study, Demanget et al investigated the mechanical performance of eight different graft limbs. The authors concluded that spiral and circular stents may provide greater flexibility, as well as lower stress values, compared to Z-stents. They further associated this with potentially better durability.[25] These findings have been confirmed in the clinical setting in a retrospective study investigating the impact of stent grafting on aortoiliac tortuosity. The reduction of the iliac tortuosity index was greatest with Zenith compared with Endurant, and the least change was seen after Excluder implantation, probably as a result of better adaptation to the iliac anatomy.[26] Interestingly, no significant differences in graft limb complication rates between the three stent grafts were found.[26] Bos et al showed that there is a preferential strategy in using flexible graft limbs (e.g., Excluder) in complex iliac artery anatomy and even used them in combination with a stent graft body of a different type (e.g., Zenith with a suprarenal fixation) (Figure 1). This hybrid endograft solution proved feasible, with no adverse events at the midterm follow-up.[27]

We reviewed the contemporary limb patency data, including data from all commercially approved, investigational device exemption (IDE) studies (Table 1), as well as peer-reviewed publication studies with at least 100 patients and 1-year follow-up published since 2012 (Table 2). Overall, loss of limb patency ranged from 0.4% to 7.7%, with the lowest rates reported for the Excluder and Ovation systems (Table 1). Considering that > 90% of limb complications required secondary intervention in these studies, selection of a suitable stent graft and identification of patient-related risk factors for limb occlusion are crucial to reduce limb-related morbidity.

FACTORS POTENTIALLY AFFECTING ILIAC OUTCOMES

Graft-related factors providing resistance to limb occlusion have not been adequately studied. Although a reduced inflammatory response after implantation of an ePTFE stent graft compared to those of polyester is known, there is no evidence depicting the effect of graft material on limb thrombosis.[28] Several anatomical risk factors that predispose to graft limb thrombosis have been reported. Faure et al investigated the patients of the ENGAGE registry and found that the strongest independent predictors for graft limb thrombosis were (1) distal landing zone on the external iliac artery, (2) an external iliac diameter < 10 mm, and (3) kinking.[19]

TABLE 1. COMPARISON OF 1-YEAR LIMB OCCLUSION RATES FROM IDE STUDIES*

	Ovation IDE (TriVascular, Inc.)	Zenith Flex IDE† (Cook Medical)	PowerLink IDE (Endologix, Inc.)	Excluder Combined IDE (Gore & Associates)	Aorfix IDE (Lombard Medical, Inc.)	Endurant IDE (Medtronic)
Number of patients enrolled	161	200/100	192	565	218	150
Limb occlusions‡	1.2%	0.5%/3%	3.1%	0.4%	3.7%	2.7%

**Data adapted from instructions for use and annual clinical updates.*
†Values are for Zenith standard-risk/high-risk patient cohorts, respectively.
‡Based on investigator-reported events. Includes reinterventions on day 0, defined as reintervention to treat a limb occlusion.

TABLE 2. LOSS OF LIMB PATENCY RATES FROM LITERATURE*

Peer-Reviewed Articles	Stent Graft	Limb Occlusion		Secondary Intervention for Limb Occlusion	
		n/N	%	n/N	%
Kalteis et al,[29] 2012	Various†	[5/106]	[4.7%]	[5/106]	[4.7%]
Conway et al,[30] 2012	Various‡	31/661	4.7%	31/661	4.7%
van Zeggeren et al,[31] 2013	Endurant	20/496	4%	20/496	4%
Verhoeven et al,[16] 2014	Excluder	8/400	2%	8/400	2%
Mehta et al,[32] 2014	Aptus (Aptus Endosystems, Inc.)	12/155	7.7%	12/155	7.7%
Bisdas et al,[14] 2014	Endurant	[10/273]	[3.7%]	[10/273]	[3.7%]
Taudorf et al,[33] 2014	Zenith	18/504	3.6%	18/504	3%
Freyrie et al,[10] 2014	Anaconda	9/177	5.1%	9/177	5.1%
Ishibashi et al,[34] 2014	Various‡	5/175	2.9%	3/175	1.7%
Mantas et al,[24] 2014	Various§	18/439	4.1%	18/439	4.1%
Pratesi et al,[15] 2014	Excluder	9/872	1.1%	9/872	1.1%
Donas et al,[35] 2015	Endurant	15/712	2.1%	15/712	2.1%
Böckler et al,[36] 2015	Endurant	8/171	4.7%	5/171	2.9%
Faure et al,[13] 2015	Endurant	42/1143	3.4%	[42/1143]	[3.4%]

**All studies were published in the last 3 years, include at least 100 patients, and have reported at least 1-year follow-up data. Brackets represent estimates, assuming that all limb occlusions were treated with secondary intervention.*
†Primarily the Zenith device.
‡Primarily the Zenith and Excluder devices.
§Primarily the Zenith, Excluder, and Anaconda devices.

These findings have recently been partially confirmed in a case-control–designed study reporting the presence of significant angulation and calcification of the iliac arteries, as well as excessive limb oversizing as important predisposing factors.[24] Carroccio et al also suggested that graft limb occlusion is associated with a limb diameter < 14 mm, whereas Abbruzzese et al reported a higher incidence of graft limb stenosis when deployment was performed at least outside one instruction for use.[37,38] The wide range of anatomic factors associated with graft limb occlusion demonstrates the importance of meticulous preoperative sizing and planning for assessing the thrombosis risk. In the ENGAGE registry, almost all occlusions (90.5%) occurred in high-risk iliac arteries.[9] Recognizing high-risk patients may help define specific strategies to prevent graft limb occlusion and improve overall outcomes.

LIMB STENOSIS: NEED FOR RELINING

Angioplasty of iliac stenosis after stent graft deployment seems to potentially reduce the risk of extrinsic compression or kinking (Figure 2). Selective preoperatively planned relining of the graft limbs with a bare-metal stent may offer supplementary radial force to amplify limb diameter and prevent thrombosis or to prevent kinking in between two Z-stents. Whereas the first reason may apply to all types of graft limbs, the second may be redundant when choosing a graft limb that is less prone to kinking. Oshin et al found a significantly lower limb occlusion rate in EVAR patients treated with a more liberal use of adjunctive stenting based on preoperative imaging.[39] Meticulous focus on the preoperative CT angiography (CTA) followed by scrutinization of the completion angiogram to identify limbs at risk is of importance.

In our practice, we tend to liberally reline iliac limbs that seem to be at a higher risk for kinking and occlusion based on the preoperative CT. In our opinion, a completion angiogram that looks good should not be the reason to change one's mind about relining, when the preoperative CTA showed severe kinking. Indeed, in the beginning, the graft limb will win over the artery, but with time, the artery will force the graft limb to go back into the original angulated path. We advocate the use of self-expandable stents to avoid kinking in a graft limb and the use of kissing-balloon–expandable stents in case of a small distal aortic diameter (< 20 mm) to keep the lumen open.

CONCLUSION

Graft limb patency clearly affects the long-term durability of EVAR. Different stent grafts provide different graft limb properties, which may eventually affect the clinical outcome. It seems that spiral and circular stents provide better flexibility and less risk of kinking, especially in hostile iliac anatomy. It needs to be taken into account, however, that the amount of available evidence is low. Prophylactic relining of high-risk limbs should be considered in order to reduce graft limb–related complications and secondary interventions. ■

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