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Incidence and predictive factors for endograft limb patency of the fenestrated Anaconda endograft used for complex endovascular aneurysm repair

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ABSTRACT

Objective: In the present study, we have described the incidence, risk factors, and outcomes of treatment of limb occlusion for patients who had undergone treatment of complex thoracoabdominal aortic aneurysms with the fenestrated Anaconda endograft (Terumo Aortic, Inchinnan, UK).

Methods: Between June 2010 and May 2018, 335 patients had undergone elective fenestrated aortic aneurysm repair at 11 participating centers using the fenestrated Anaconda endograft with a median follow-up of 14.3 months (interquartile range, 27.4 months). The primary outcome measure was freedom from limb occlusion. The secondary outcome measures were freedom from limb-related reintervention, secondary patency, and the risk factors associated with limb occlusion.

Results: Of the 335 patients, 30 (9.0%) had presented with limb occlusion during follow-up with a freedom from limb occlusion rate of 98.5%, 91.2%, and 81.7% at 30 days and 1 and 5 years, respectively. In 87% of the cases, no obvious cause for limb occlusion was documented. Primary occlusion had occurred within 30 days in 36.7% and within 1 year in 80.0%. Of the 30 patients, 23 (77%) had undergone an occlusion-related reintervention and 7 (23.3%) had been treated conservatively. The freedom from limb occlusion-related reintervention at 30 days and 1 and 5 years was 97.8%, 93.2%, and 88.6%, respectively. Secondary patency was 91.3% after 1 month and 86.2% after 1 and 5 years. Female sex (odds ratio [OR], 3.27; 95% confidence interval [CI], 1.28-8.34; $P = .01$) was a statistically significant predictor for limb occlusion. A greater proportion of thrombus in the aneurysm sac appeared to be protective for limb occlusion (0% vs <25%: OR, 0.22; 95% CI, 0.07-0.63; $P = .01$; 0% vs 25%-50%: OR, 0.20; 95% CI, 0.07-0.57; $P = .00$; and 0% vs >50%: OR, 0.08; 95% CI, 0.02-0.38; $P = .00$), as did iliac angulation (OR, 0.99; 95% CI, 0.98-1.00; $P = .04$).

Conclusions: Limb occlusion remains a significant impediment of endograft durability for patients treated with the fenestrated Anaconda endograft, especially for female patients. In contrast, a high aneurysmal thrombus load and a high degree of iliac angulation appeared to be protective for limb occlusion, for which no obvious cause could be identified. (J Vasc Surg 2022;75:1512-20.)

Keywords: Fenestrated endovascular repair; Limb occlusion; Thoracoabdominal aortic aneurysm

Endovascular aneurysm repair (EVAR) has evolved into the preferred treatment modality for most patients with an abdominal aortic aneurysm (AAA) requiring treatment, provided the anatomy is suitable and a reasonable life expectancy is present.[1,2] A hostile neck anatomy is a known risk factor endangering endograft durability and has been related to proximal endoleaks, greater AAA-related mortality, and the requirement for more secondary interventions compared with standard EVAR.[3] The introduction of fenestrated EVAR (FEVAR) has advanced endovascular repair to include the treatment of increasingly complex AAAs.[1,2] FEVAR has been shown to have comparable outcomes in terms of early and overall mortality, lower morbidity, and shorter lengths of stay compared with open surgical repair and is now considered the recommended treatment of

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complex juxtarenal AAAs, when feasible.[1,2,4] However, the long-term durability has remained a particular concern with FEVAR, with freedom from secondary intervention of 90% at 1, 86% at 2, and 70% at 3 years postoperatively.[1] With an incidence of 0% to 7%, endograft limb occlusion accounts for one third of all reinterventions after EVAR and has remained a significant cause of rehospitalization.[5-8] The custom-made fenestrated Anaconda endograft (Terumo Aortic, Inchinnan, UK) was designed to overcome the anatomic difficulties resulting from angulated and short-necked infrarenal and complex juxtarenal AAAs.[9-12] Despite the good overall performance, relatively high rates of limb occlusion have been seen with both the infrarenal and the fenestrated Anaconda at ≤14% and ≤23%, respectively.[9,11,13-25] The aim of the present study was to describe the incidence, risk factors, and outcomes of treatment for limb occlusion for patients who had undergone treatment of complex AAAs with the fenestrated Anaconda.

ARTICLE HIGHLIGHTS

- **Type of Research:** A multicenter retrospective analysis of prospectively collected registry data
- **Key Findings:** Fenestrated endovascular repair of complex thoracoabdominal aneurysms in 335 patients treated with the fenestrated Anaconda endograft (Terumo Aortic, Inchinnan, UK), resulted in limb occlusion in 9.0% of patients. Female sex was a risk factor. In contrast, a high aneurysmal thrombus load and a high degree of iliac angulation were protective for limb occlusion.
- **Take Home Message:** Limb occlusion remains a significant impediment of endograft durability for patients treated with the fenestrated Anaconda endograft, especially for female patients.

METHODS

Study design and data collection. The present study is a continuation of previous work by our group. The complete study protocol and participant details of the fenestrated Anaconda study and technical specifications have been previously reported.[12] In brief, between June 2010 and May 2018, consecutive patients who had undergone elective FEVAR for a complex AAA or type IV thoracoabdominal aneurysm using the fenestrated Anaconda endograft at 11 participating centers were eligible for enrollment in the present study. The institutional review board in each participating country had exempted the present study from the requirement for approval because the data were collected anonymously and the analysis was performed retrospectively (institutional medical ethical board reference nos. M16.203416 for the Netherlands, 18-268 for Germany, IRAS 225488 for the United Kingdom, and REB17-0510 for Canada).

Variable definitions and study endpoints. Complex AAAs were defined as juxtarenal or suprarenal AAAs or infrarenal AAAs with a hostile neck anatomy (neck length <15 mm, neck width >28 mm, and neck angulation >60° and/or a reversed conical-shaped neck).[3] Type IV thoracoabdominal aneurysms were also included. Limb occlusion was defined as complete obstruction of flow in the iliac limb graft, irrespective of symptoms, diagnosed using computed tomography angiography and/or duplex ultrasound in accordance with the reporting standards for FEVAR.[26] The morphologic parameters such as aortic angle, aortic tortuosity index, iliac angle, and iliac tortuosity index were measured, as described by Chaikof et al.[27] Since the introduction of the third-generation device (ONE-LOK) in mid-2011 (Anaconda, ONE-LOK, Terumo Aortic, Inchinnan, UK), standardized intraoperative ballooning of the graft limbs has been included in the instructions for use (IFUs). Nevertheless, worldwide communication of this advice occurred around mid-2014. Therefore, the timing of limb graft ballooning was included. Data on whether the patient had been symptomatic were not consistently available and were, therefore, not included in the present study.

The primary outcome was freedom from limb occlusion. Limb occlusion was assessed separately for the left and right limbs and was further analyzed as a whole. Main graft body occlusion was regarded as bilateral limb occlusion. Target vessel patency has been discussed in brief; however, it had been described previously in more detail by our group.[12] The secondary outcomes were freedom from limb-related reintervention, secondary patency, and the risk factors associated with limb occlusion.

Statistical analysis. Nominal and categorical variables are presented as frequencies and proportions. Continuous variables were analyzed for a normal distribution using quartile–quartile plots and the Kolmogorov-Smirnov test and are presented as the mean ± standard deviation. Continuous variables with a skewed distribution are presented as the median and interquartile range (IQR). Occlusion and reintervention-free survival rates were calculated using Kaplan-Meier survival analysis. To identify the potential predictors for limb occlusion, a univariate generalized estimating equations model was calculated (corrected for limb side), using a cutoff value for statistical significance of $P \leq .10$. Statistically significant variables on univariate analysis were subsequently entered into a multivariate generalized estimating equations model (backward elimination method using the likelihood ratio), together with the anatomic and design characteristics with a potential correlation determined from previously reported data (corrected for limb side). Predictive variables with $P \leq .05$

Table I. Anatomic features

Variable	No. (%)
Aneurysm location	335 (100)
Infrarenal with hostile neck anatomy[a]	98 (29.3)
Juxtarenal	191 (57.0)
Suprarenal	27 (8.1)
Type IV thoracoabdominal	19 (5.7)
Aneurysm type	335 (100)
Fusiform	315 (94.0)
Saccular	20 (6.0)
Previous surgery	10 (3.0)
Open repair (para-anastomotic)	5 (1.5)
Endovascular repair	5 (1.5)
Aortic neck[a]	271 (80.9)
Length, 4.63 ± 8.0 mm	329 (98.2)
Diameter, 27.6 ± 7.1 mm	330 (98.5)
Angulation, 157.0° ± 15.8°	328 (97.9)
Calcification/thrombus	258 (77.0)
<25%	221 (85.7)
25%-50%	35 (13.6)
>50%	2 (0.8)
Aortic aneurysm[a]	
Maximum diameter, 61.5 ± 9.9 mm	335 (100)
Aortic tortuosity index, 1.10 ± 0.1	249 (74.3)
Aortic angulation, 154° ± 17.4°	255 (76.1)
Thrombus	329 (98.2)
0%	32 (9.6)
<25%	97 (29.0)
25%-50%	124 (37.0)
>50%	76 (22.7)
Iliac artery[b]	
Calcification (% of vessel length)	
Left	329 (98.2)
Right	329 (98.2)
None	
Left	87 (26.4)
Right	92 (28.0)
<25%	
Left	172 (53.5)
Right	169 (51.4)
25%-50%	
Left	45 (13.7)
Right	42 (12.8)
>50%	
Left	25 (7.6)
Right	26 (7.9)
Diameter/occlusive disease[c]	
Left	329 (98.2)
Right	327 (97.6)
0	
Left	186 (56.5)
Right	188 (57.1)
1	
Left	98 (29.8)
Right	96 (29.2)
2	
Left	32 (9.7)
Right	33 (10.0)
3	
Left	13 (4.0)
Right	10 (3.0)
Iliac artery tortuosity index	
Left, 1.50 ± 2.9	300 (89.6)
Right, 1.30 ± 0.26	301 (89.9)
Iliac artery angulation	
Left, 113° ± 42.2°	310 (92.5)
Right, 109° ± 42.8°	310 (92.5)
Iliac artery aneurysm	34 (10.7)

(Continued)

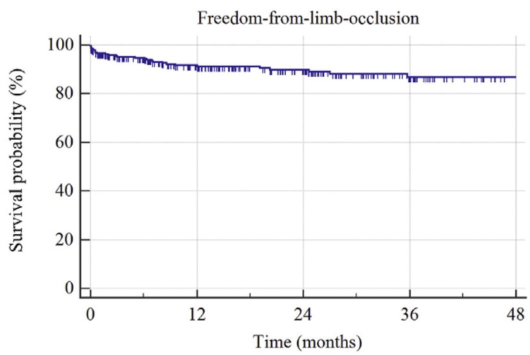
Table I. Continued.

[a]Hostile neck anatomy was defined as a neck length <15 mm, neck width >28 mm, neck angulation >60°, and/or a reversed conical shaped neck.[4]
[b]Categorization of morphology according to the Society for Vascular Surgery/American Association for Vascular Surgery grading system by Chaikof et al.[27]
[c]Classification of diameter/occlusive disease: 0, diameter ≥10 mm with no occlusive disease; 1, diameter ≥8 but <10 mm with no stenosis <7 mm in diameter or >3 cm long; 2, diameter ≥7 but <8 mm or any diameter with focal stenosis <7 mm in diameter and <3 cm in length; 3, any one of the following: diameter <7 mm plus stenosis <7 mm in diameter and ≥3 cm in length or more than one focal stenosis <7 mm in diameter.[27]

were deemed statistically significant for inclusion in the definitive model. The predictive risk of these variables for developing limb occlusion is presented as the odds ratios (OR) with the 95% confidence interval (CI). Variables not eligible for the univariate generalized estimating equations model were analyzed separately using the Pearson χ^2 test. The data were analyzed using IBM SPSS Statistics, version 21.0 (IBM Corp, Armonk, NY).

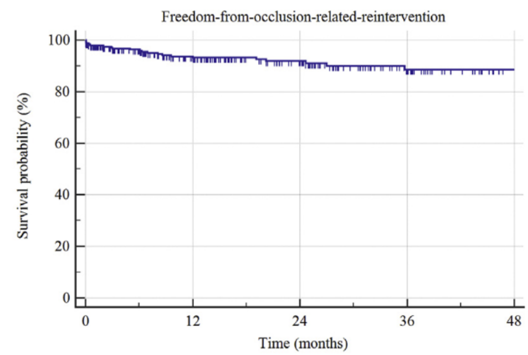
RESULTS

Patient demographics and endograft features. A total of 335 patients had undergone treatment with the fenestrated Anaconda endograft (Terumo Aortic) during the study period. The median follow-up was 14.3 months (IQR, 27.4 months). In brief, the patients were aged 73 ± 6.9 years, and 292 patients (87.2%) were male. The risk factors included active (31.0%) or previous (32.5%) smoking, hypertension (79.1%), hypercholesterolemia (64.8%), diabetes mellitus (19.7%), cerebrovascular disease (13.4%), cardiac disease (46.2%), pulmonary disease (31.1%), renal disease (29.9%), and peripheral artery disease (20.9%). In most patients, a bifurcated endograft had been placed



Number at risk	333	185	118	63	32
Survival (%)	99.1	93.2	91.8	88.6	88.6
Standard error (SE)	0.02	0.02	0.02	0.03	0.03

Fig 1. Estimated cumulative survival with standard error (*SE*) for freedom from limb occlusion.



Number at risk	334	186	118	63	32
Survival (%)	99.7	91.2	89.9	86.8	86.8
Standard error (SE)	0.00	0.02	0.02	0.03	0.03

Fig 2. Estimated cumulative survival with standard error (*SE*) for freedom from limb occlusion-related reintervention.

(96.1%) with a straight (43.0%), flared (50.4%), or tapered (3.3%) limb configuration. The fenestrated target vessels included the celiac (22.7%), superior mesenteric (58.2%), left renal (96.1%), and right renal (95.8%) artery, with a total of one (3.6%), two (39.4), three (36.7%), four (19.4%), or five (0.9%) fenestrations. The main device was routinely introduced through a right-sided femoral access. The anatomic features are summarized in Table I.

Incidence of limb occlusion and target vessel patency. A total of 30 patients (9.0%) had presented with 31 limb occlusions during the follow-up period (4.6% of all limbs). Of the 30 patients, 15 (50.0%) had developed occlusion on the right side and 8 (26.7%) on the left side. Three patients had developed bilateral and simultaneous occlusions (10.0%), and three had developed graft body occlusions (10.0%; scored as bilateral limb occlusion). Although right-sided limb occlusion was more prevalent, the difference was not statistically significant ($P = .31$). In one patient (3.3%), both the left and right limbs had become occluded, although not simultaneously. The freedom from limb occlusion at 30 days and 1 and 5 years was 98.5%, 91.2%, and 81.7%, respectively (Fig 1). The median interval to the first occlusion was 4.0 months (IQR, 9.7 months). Primary occlusion had occurred within 30 days for 11 patients (36.7%). For 24 patients (80.0%), primary occlusion had occurred within the first year. The annual occlusion rate was 0% to 25.0%, without an apparent change over time (Supplementary Table, online only). For the participating centers, the incidence of occlusion had ranged from 0% to 22.4%. The rate of intraoperative limb ballooning was 100%, except for two centers that had reported a rate of 87.0% and 60.3% (92.5% of all patients). The center with the highest occlusion rate also reported the lowest rate of intraoperative limb ballooning (60.3% of patients). In all centers, intraoperative limb ballooning was the standard of care. A total of 37 target vessel adverse events had occurred in 32 patients (9.6%), which included stenosis (48.6% of all events), occlusion (35.1%), kinking (8.1%), and stent fracture (8.1%). In patients with limb occlusion, target vessel-related adverse events had occurred in three patients (10.0%). This included stenosis of a renal artery fenestration and occlusion of a celiac and renal artery fenestration, both of which were treated conservatively. Although target vessel patency was lower for patients with limb occlusion than for patients without limb occlusion (10.0% vs 3.6%), this difference did not reach statistical significance ($P = .38$).

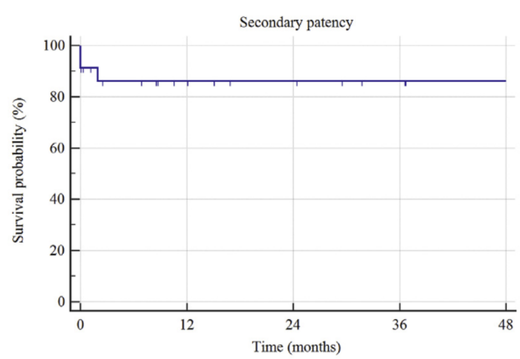
Treatment of limb occlusion. Overall, 69 endograft-related reinterventions had been performed in 64 of the 335 patients (19.1%) during the study period, of which 23 reinterventions (of 335 patients) were related to limb occlusion (6.9%). A total of 30 patients had limb occlusion, of which 23 (76.7%) required an intervention. The remaining 7 (23.3%) patients were treated conservatively (Fig 2). Of the 23 patients, 7 had required limb occlusion-related reintervention within 30 days postoperatively and 16 patients during further follow-up. All graft body and bilateral occlusions required intervention; however, 6 of 27 unilateral limb occlusions (22.2%) had been treated conservatively. Further details on occlusion-related treatment are presented in Table II. In 3 of the 23 treated patients (13.0%), reocclusion had occurred after initial successful revascularization, resulting in a secondary patency rate of 91.3% at 30 days and 86.2% after 1 and 5 years, respectively (Fig 3). The details on reocclusion are presented in Table III. During the study period, no major or minor amputations were performed.

Uni- and multivariate analysis of factors related to limb occlusion. Of the 30 patients, 4 (13.3%) had required device explanation for limb occlusion. The causes included limb kinking owing to aneurysm sac shrinkage, dissection of the common iliac artery, device migration

Table II. Treatment for limb occlusion

Type of treatment	Graft body	Unilateral limb	Bilateral limb	Reocclusion
Intervention	3 (100)	18 (75.0)	2 (66.6)	3 (100)
Endovascular	1 (33.3)	13 (54.2)	1 (33.3)	0 (0)
Thrombectomy	1 (33.3)	4 (22.2)	–	–
Thrombectomy with relining	–	8 (44.4)	1 (33.3)	–
Endoluminal bypass	–	1 (4.2)[a]	–	–
Extra-anatomic bypass	0 (0)	4 (16.7)	1 (33.3)	1 (33.3)
Axillofemoral	1 (33.3)	1 (4.2)	–	–
Femorofemoral	–	3 (12.5)	–	1 (33.3)
Ilioprofunda	–	–	1 (33.3)[b]	–
Femoropopliteal	–	1 (4.2)[c]	–	–
Graft explantation with open reconstruction	1 (33.3)	0 (0)	0 (0)	2 (66.6)
Conservative	0 (0)	6 (25.0)	1 (33.3)	0 (0)
Total	3 (100)	24 (100)	3 (100)	3 (100)

Data presented as number (%).
[a]Open endarterectomy of the common femoral artery followed by endoluminal bypass with crural thrombectomy.
[b]Left-sided open endarterectomy of the common femoral artery, followed by right-sided ilioprofunda bypass.
[c]Open endarterectomy of the common femoral artery combined with femoropopliteal bypass to improve outflow.



Number at risk	21	12	9	6	4
Survival (%)	91.3	86.2	86.2	86.2	86.2
Standard error (SE)	0.06	0.07	0.07	0.07	0.07

Fig 3. Estimated cumulative survival with standard error (*SE*) for secondary patency.

after earlier intervention for limb occlusion, and stent compression. Univariate analysis identified several factors related to limb occlusion ($P \leq .10$). These included sex ($P = .07$), aortic neck length ($P = .00$), aortic neck diameter ($P = .03$), aortic neck angulation ($P = .00$), proportion of thrombus in the aneurysm sac ($P = .00$), aortic diameter at the level of the renal arteries ($P = .06$), aortic tortuosity index ($P = .00$), aortic angulation ($P = .00$), iliac angulation ($P = .00$), the presence of endoleak on the completion angiogram ($P = .03$), and intraoperative limb ballooning ($P = .07$). Which center participated was also associated with the development of limb occlusion ($P = .02$). However, owing to the relatively high number of participating centers, this variable was ineligible for multivariate analysis. The variables associated with iliac anatomy that were not significantly related to occlusion were iliac calcification ($P = .14$), iliac diameter ($P = .33$), iliac tortuosity index ($P = .83$), the length ($P = .68$) and diameter of the iliac sealing zone ($P = .67$), and graft extension into the external iliac artery (EIA; $P = .66$). Endograft type (uni-iliac or bifurcated) was not predictive for limb occlusion ($P = .61$) nor was type of femoral access (percutaneous vs open; $P = .18$), proportion of oversizing of the endograft ($P = .60$), graft oversizing beyond the IFUs (>20%; $P = .85$), or the presence of an endoleak during follow-up ($P = .17$). Graft limb oversizing was not documented. In 181 patients (54.0%), the aneurysm had decreased in size during follow-up. This did not seem to increase the risk of occlusion ($P = .55$) nor did the maximum aneurysm size ($P = .88$), the presence of peripheral ($P = .42$) or aortic ($P = .99$) occlusive disease, or smoking ($P = .33$).

Multivariate analysis identified female sex (OR, 3.27; 95% CI, 1.28-8.34; $P = .01$) as a predictor for limb occlusion. A greater proportion of thrombus in the aneurysm sac was found to be protective for limb occlusion (0% vs <25%: OR, 0.22; 95% CI, 0.07-0.63; $P = .01$; 0% vs 25%-50%: OR, 0.20; 95% CI, 0.07-0.57; $P = .00$; 0% vs >50%: OR, 0.08; 95% CI, 0.02-0.38; $P = .00$), as was iliac angulation (OR, 0.99; 95% CI, 0.98-1.00; $P = .04$).

DISCUSSION

The results from the present study have demonstrated that the freedom from limb occlusion for the fenestrated Anaconda endograft is 98.5%, 91.2%, and 81.7% at 30 days and 1 and 5 years respectively, with female sex predictive of limb occlusion. However, a high aneurysmal thrombus load and a high degree of iliac angulation were found to be protective for limb occlusion. The average rate of limb occlusion was 9.0%, which was greater than that reported by most earlier studies of the fenestrated

Table III. Treatment of limb reocclusion

Case No.	Initial treatment	Cause of secondary occlusion	Secondary treatment
1	Stent relining	Endograft migration 2 months later	Endograft explantation with open aortobifemoral reconstruction
2	Thrombectomy with angioplasty of common iliac artery	Unknown	Femorofemoral crossover bypass; common iliac artery occlusion with threatened bypass 2 months later, treated with thrombolysis and iliac angioplasty
3	Bilateral occlusion; kissing self-expanding covered stents	Unknown	Endograft explantation with open aortobifemoral reconstruction

Anaconda (occlusion rate, 0%-7.0%).[9,11,18-21,28] Only Shahverdyan et al[22] found an exceptionally high occlusion rate of 23%, with a plausible explanation for fewer than one half of the cases and no significant differences in limb oversizing, EIA kinking, or the distal landing zone. In the present study, we found different occlusion rates between the participating centers (0%-22.4%). The center with the greatest occlusion rate also reported the lowest rate of intraoperative limb ballooning. In 9 of 11 participating centers (81.8%), intraoperative limb ballooning was implemented after the change in IFUs in 2011; the 2 remaining centers had implemented these changes in 2014. Nonetheless, it was not a significant predictor of limb occlusion on multivariate analysis. This result suggests that occlusion is not only related to endograft design and anatomy but is also clinician dependent, despite a minimum threshold of 15 treated patients before inclusion in the present study for each participating center and warrants further attention.

Multivariate analysis revealed a higher occlusion rate for women. EVAR for women has been associated with higher mortality and morbidity rates compared with men, in both the acute and the elective setting.[29,30] Women have generally been older at surgery and have had smaller vessel diameters with more challenging aortoiliac anatomy, including a short and angulated aneurysm neck.[29,31,32] Smaller vessel diameters can lead to access problems, with associated dissection, rupture, and subsequent limb complications, including occlusion.[31-33] In addition, the 30-day mortality rate has been higher for women, with mesenteric ischemia more frequently observed.[29] Furthermore, women can experience more rapid aneurysm sac shrinkage at 24 months owing to greater aortic wall compliance and better adaptation of the endograft.[29]

Surprisingly, the aneurysmal thrombus load was found to be protective for limb occlusion. This finding contradicts that from earlier studies, which had found that a higher aneurysmal thrombus load was a risk factor for limb occlusion, potentially related to the more narrow distal aneurysmal lumen and extrinsic compression of the proximal limb, which had increased the risk of limb kinking or stenosis.[5,34,35] Possibly, this effect was minimized by intraoperative ballooning of the limbs. Finally, a high degree of iliac angulation showed a mild protective effect for limb occlusion, which also contradicted earlier findings. A complex iliac anatomy, including increased iliac angulation, tortuosity, and calcification, has previously been linked to increased access and procedural complexity, intraoperative adjunctive maneuvers, endoleak, and occlusion.[36-40] Counterintuitively, the tortuosity index was not a significant predictor of occlusion in the present study. The tortuosity index is considered to be more representative of aortoiliac anatomy, as it also takes curvature and the asymmetrical nature of aortoiliac morphology into account, rather than angulation alone.[40] These controversial findings may reflect the multifactorial nature of limb occlusion in endovascular surgery, rather than a specific cause in individual patients.

The fenestrated Anaconda endograft is a modular, bifurcated woven polyester endograft, with an unsupported main body and two separate limbs, reinforced with ringed nitinol stents embedded in the woven polyester fabric. In contrast, most of the other fenestrated grafts contain Z-shaped stents throughout the endograft. A ringed design makes the endograft less susceptible to fabric abrasion; however, the area of unsupported fabric is greater.[41,42] Although this vacuum cleaner design of the Anaconda limbs offers enhanced flexibility and kink resistance in those with a tortuous and angulated aortoiliac anatomy, a possibility exists of graft material infolding between the nitinol rings.[43] A possible explanation could be the "accordion" effect, which is characterized by reexpansion of the endograft to its original length over time.[5] Simmering et al[43] showed an increase in curvature, limb shortening, and reduced inter-ring distance during 2 years after implantation of an infrarenal Anaconda endograft in 15 patients. If these resulting plications reduce the wall shear stress and blood flow, thrombus formation could be promoted.[43] Possibly related to this, the second-generation

infrarenal Anaconda endograft was prone to the development of limb occlusion, which had been thought to be related to compression of the limbs owing to a mismatch between the smaller main body and relatively large limb diameters.[17,44] To allow for easier limb size selection, the third-generation graft (ONE-LOCK) was launched in 2011, with a standardized proximal docking zone and different types of distal limb configurations (straight, flared, or tapered).[17] Most of the reported experience with the Anaconda endograft has come from second-generation devices.[15,16,24,25] Only one reported study had included only third-generation devices,[23] with a few studies including mixed populations.[7,13,14,17] Rödel et al[17] had included both second- and third-generation grafts and had reported an overall occlusion rate of 9.8% during a mean follow-up of 47 months, with no difference in occlusion between the second- and third-generation grafts. They did, however, find a higher occlusion rate in the patients with small distal limb diameters.[17] Recently, Midy et al[23] reported an occlusion rate of 7.9% for third-generation Anaconda endografts during a median follow-up of 59 months, with 10.7% of patients treated outside the IFUs. This was associated with an increased risk of late failure, including migration, probably owing to a lack of adequate sealing.[23] They did not relate treatment outside the IFUs to the development of limb occlusion. The limb occlusion-related reintervention rate was 9.0% (16 of 177), which was slightly greater than the 6.9% found in the present study. In contrast to earlier studies, no increased risk of limb occlusion in patients with graft extension to the EIA was found.[8,34,45-49] Bogdanovic et al[8] identified extension into the EIA and a narrow EIA (<10 mm) as risk factors for limb occlusion for several commonly used infrarenal devices. In addition, they found a higher than average occlusion rate for the Zenith Alpha device (Cook Medical Inc, Bloomington, Ind). The manufacturer suggested that excessive overlap of the flared limbs can lead to lumen restriction, in addition to limb misalignment, which led to a change in the IFUs to include that deployment of short, flared limbs should not exceed the minimal overlap. Nonetheless, this could not be validated statistically, and Bogdanovic et al[8] concluded that these risk factors were not distinctly prevalent in the patients with occlusion in their cohort. In the present study, multivariate analysis did not identify graft oversizing beyond the IFUs (>20%), iliac diameter, or graft extension into EIA as significant predictors of limb occlusion.

Generally, endograft kinking has been regarded as the main cause of endograft occlusion,[35] causing 42.8% to 56% of occlusions.[5,50] Early kinking can result from severe iliac angulation[5,36,39] or tortuosity.[5,38,39] In contrast, late kinking can be caused by aneurysm sac shrinkage,[5,38,43] proximal or distal graft migration,[5,48] or artificial endograft straightening of elongated, tortuous sections of the native artery.[5] Although the fenestrated Anaconda endograft is less susceptible to kinking than Z-shaped endografts, it is not immune to it. In one patient, aneurysm remodeling after sac shrinkage led to limb kinking and subsequent occlusion. Nonetheless, the aneurysm size and aneurysm shrinkage were not significantly related to the occurrence of limb occlusion. In addition, 36.7% of the occlusions had occurred within 30 days postoperatively, suggesting a user-related error, possibly owing to early kinking. Early kinking can be missed if the intraoperative completion angiogram has been performed with the stiff wire still in place and could be reduced by intraoperative ballooning of the graft limbs.[50] In addition, primary adjunctive stenting of vessels at risk has the potential to reduce the incidence of limb occlusion.[36,45,51,52] All four investigative groups had eliminated limb occlusion in their cohorts after implementing an aggressive preventive stenting strategy.[36,45,51,52] Furthermore, Isernia et al[7] found that routine intraoperative kissing balloon dilatation of the limbs significantly reduced limb occlusion (freedom from limb occlusion, 98.0% vs 88.4%; $P = .03$). This was not routinely performed in our patients. Although these findings require validation in larger cohorts, standardized adjunctive stenting and/or intraoperative kissing balloon dilatation of the limbs have shown the potential for reducing the incidence of limb occlusion, especially in unsupported grafts that are more susceptible to limb kinking.

The European Society for Vascular Surgery guidelines regarding surveillance after EVAR have advised patient stratification according to the risk of late complications.[1] With an increasingly greater number of patients treated outside the IFUs, increased surveillance might identify some patients at risk of limb occlusion. Increased vigilance is warranted in the first postoperative year, because 80% of patients had developed occlusion within this period, with similar findings in a recent study of infrarenal devices (70% occlusion within the first year).[8] However, more might be achieved by identifying patients at risk at an early stage and applying an aggressive adjunctive stenting protocol.[36,45,51,52] Although speculative, women and patients with less angulated iliac anatomy might benefit most from the results of the present study. Future research on adjunctive stenting in larger FEVAR cohorts might aid in optimizing surveillance and treatment strategies, which will also benefit advancements in future generation endografts. In addition, future studies linking clinical outcomes to changes in geometric parameters after FEVAR, including curvature, tortuosity, endograft shortening, and reduced inter-ring distances in larger cohorts of patients, could also lead to a better understanding of the pathophysiology of limb occlusion.[43] Furthermore, it would be interesting to determine whether the length variations in the main body and limbs have an effect on flow hemodynamics and limb angulation. One of the strengths of the present study

was the relatively large number of patients, long follow-up period, and the international, multicenter approach. Nonetheless, the limitations included the retrospective design, which contributed to not all datasets being complete. Also, antiplatelet therapy was not routinely documented. Postoperative intragraft formation of mural thrombus was not routinely measured, although it was frequently observed after EVAR; however, the clinical relevance of this finding with respect to limb occlusion has remained unclear. Finally, the consistent use of standardized terminology and outcome measures is essential for the objective comparisons of patient outcomes and different endograft designs. Recently, Oderich et al[26] reported updated standards for FEVAR. Although most definitions used in the present study were based on the Society for Vascular Surgery reporting standards for EVAR, investigators should adhere to these updated reporting standards to maximize the quality, replicability, and unambiguous interpretation of future research findings.[27]

CONCLUSIONS

The fenestrated Anaconda endograft is safe and effective in the treatment of complex AAAs. Nonetheless, limb occlusion remains a particular concern, especially for female patients and has been associated with a significant rate of secondary interventions. In contrast, a high aneurysmal thrombus load and high degree of iliac angulation appeared to be protective for limb occlusion, for which no obvious cause could be identified. Further research is warranted to compare our results to those for other fenestrated endografts and to reduce this complication after FEVAR.

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Supplementary Table (online only). Annual occlusion rates for the fenestrated Anaconda endograft from 2010 to 2018[a]

Variable	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
Occlusion rate, %	0.0	14.3	3.5	14.9	6.4	10.0	13.0	0.0	25.0	9.0
Occlusion										
Yes	0	2	1	7	4	6	7	0	3	30
No	2	14	29	47	63	60	54	24	12	305
Total	2	16	30	54	67	66	61	24	15	335

[a]Data inclusion from June 2010 to May 2018.