Eur J Vasc Endovasc Surg (2024) 67, 765—774

ORIGINAL ARTICLE

Clinical Impact and Determinants of Fenestration to Target Vessel Misalignment in Fenestrated Endovascular Aortic Repair

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WHAT THIS PAPER ADDS

Fenestrated endovascular aortic repair requires the alignment of fenestrations with the target vessels through the deployment of covered bridging stents. However, imperfect fenestration alignment may be detected on post-operative computed tomography, but its determinants and clinical impact are not well understood. This retrospective study demonstrated that a horizontal misalignment $> 15^{\circ}$ may be considered to be clinically significant, as it is associated with a higher chance of target vessel instability. This may occur as a result of difficult iliac access, excessive pararenal aortic angulation, and a bridging distance $>$ 5 mm. Evolution of endograft materials and profiles may be useful to improve fenestration alignment. Bridging stent reinforcement or closer follow up may be considered for cases with post-implantation horizontal misalignment $> 15^{\circ}$.

Objective: This single centre, retrospective study (2014 — 2022) on juxta-, pararenal, or thoraco-abdominal aortic aneurysms treated by fenestrated endovascular aortic repair (FEVAR) was conducted to investigate the clinical impact and determinants of fenestration to target vessel misalignment in FEVAR.

Methods: Pre-operative supracoeliac, pararenal, and infrarenal aortic angles were measured on three dimensional computed tomography angiography (CTA) reconstructions. Two components of misalignment were measured on the first post-operative CTA: horizontal misalignment (angle between the fenestration and the target vessel ostium on perpendicular CTA cuts) and vertical misalignment (vertical distance between the fenestration and the target vessel at its origin). Endpoints were freedom from target vessel instability (TVI) and alignment change over time.

Results: Of 65 patients treated by FEVAR, 60 (202 target arteries) with juxta-, pararenal (80%), or thoraco-abdominal aortic aneurysm (20%) were included. Mean horizontal misalignment was $9 \pm 12^{\circ}$ (median 5°; IQR 0 — 16) and mean vertical misalignment was 0.7 ± 1 mm (median 0 mm, IQR 0 — 1). Freedom from TVI was 92% (95% CI 88 — 98) at 36 months. Horizontal misalignment $> 15^{\circ}$ was significantly associated with TVI (HR 5.19; 95% CI 1.54 — 17.48; $p = .008$); vertical misalignment did not significantly impact TVI (HR 0.99; 95% CI 0.56 — 1.73; $p = .97$). By multivariable analysis, pararenal aortic angle (OR 1.01 per increased degree of angulation; 95% CI 1.00 — 1.02; $p = .044$), bridging distance $>$ 5 mm (OR 1.07; 95% CI 1.02 — 1.11; $p = .003$), and use of higher profile endografts in tortuous iliac access (OR 7.55; 95% CI 4.55 — 1.11; $p = .003$) were associated with clinically significant misalignment. Bridging distance $>$ 5 mm (OR 2.00; 95% CI 1.02 — 11.29; $p = .044$), degree of baseline misalignment (OR 1.04; 95% CI 1.01 — 1.08; $p = .036$), and persistence of any primary endoleak for $>$ 6 months (OR 5.85; 95% CI 1.23 — 29.1; $p = .023$) were associated with misalignment increase during follow up.

Conclusion: Horizontal misalignment $> 15^{\circ}$ is associated with worsened target vessel outcomes. This may occur as a result of excessive iliac access tortuosity, high pararenal aortic angulation, and bridging distance $>$ 5 mm.

Keywords: Aortic aneurysm, Fenestrated endovascular aortic repair, Computed tomography angiography, Endoleak, Stents

Article history: Received 16 January 2023, Accepted 12 October 2023, Available online 17 October 2023

Presented as best abstract oral presentation at the 2022 ESVS annual meeting (Rome, 20 — 23 September 2022).

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https://doi.org/10.1016/j.ejvs.2023.10.016

INTRODUCTION

Fenestrated endovascular aortic repair (FEVAR) represents a valid treatment for juxta-, pararenal (JRAA/PRAA), and thoraco-abdominal (TAAA) aneurysms.[1–5] A successful FEVAR requires accurate device positioning, with placement of fenestrations at the level of the aortic side branches that are aligned through covered balloon expandable bridging stents. Precise alignment of the fenestrations with each target vessel may be crucial for the outcomes. Fenestration misalignment may be responsible for adjunctive rescue manoeuvres, technical failure, and target vessel related complications.[6–8] However, a mild degree of misalignment may be detected by computed tomography (CT) in many patients after FEVAR,[7,9] but it remains unclear in which situations it may be considered clinically irrelevant or when it should be regarded as a harmful finding, potentially leading to complications such as target vessels endoleak or occlusion.

Factors that may lead to fenestration misalignment are still not well described. It may result from inexact planning, imperfect device positioning, aortic anatomical deformation derived by insertion of stiff devices, or adverse anatomical characteristics causing unintentional movements during deployment.[6,7,9–12] Although these elements may theoretically lead to misalignment, a better understanding of its determinants could be important to improve planning, endovascular materials, and operative techniques used in FEVAR.

This study aimed to investigate the clinical impact of post-implantation fenestration to target vessel misalignment, and to identify the pre-operative and procedural determinants of fenestration misalignment; alignment changes occurring during follow up were also evaluated.

METHODS

Patients

A single centre, retrospective study was conducted on patients treated by FEVAR (January 2014 — June 2022). Only patients with available CT angiography (CTA) within 30 days after FEVAR and a follow up duration of > 30 days were included. Institutional review board requirements were waived for this retrospective study.

Data collection and definitions

Pre-operative, procedural, and post-operative variables were collected. Aneurysm extent was evaluated by CTA.[2] Pre-operative and post-implantation anatomical characteristics were assessed using Aquarius iNtuition software (v4.4.13; TeraRecon, Foster City, CA, USA). Aortic angulation and target vessel orientation were measured using an aortic centreline or three dimensional reconstruction, as previously described.[10,13] Tortuosity of the iliac axis used for the main graft insertion was measured as the ratio of the centreline to straight distance between the origin of the common femoral artery and the aortic bifurcation.[14]

Early post-operative (30 days or within hospital stay if > 30 days) major adverse events included severe acute kidney injury (> 50% decrease in estimated glomerular filtration rate[15]), new onset dialysis, myocardial infarction, respiratory failure requiring prolonged mechanical ventilation or re-intubation, spinal cord injury, stroke, bowel ischaemia requiring surgical resection or intensive medical care, and estimated blood loss > 1 L. Spinal cord ischaemia was classified according to reporting standards.[2]

The bridging distance was measured as the gap between the fenestration and the origin of the target vessel on perpendicular views of the first post-operative CTA.[12] Protrusion length of the bridging stent into the main aortic graft and sealing length into the target artery were evaluated as reported previously.[12] Imaging follow up consisted of CTA or CT and duplex ultrasound of renal and mesenteric arteries at 3, 6, and 12 months, and annually thereafter. In case of aneurysm enlargement, CTA was performed for endoleak characterisation and planning of secondary treatment. Endoleak classification was based on the Society for Vascular Surgery reporting standards.[2] Endoleaks were defined as primary if present at the first post-operative CTA and secondary if occurring during follow up but not present at the first post-operative CTA.[2]

Device design

All patients received patient specific Cook Zenith fenestrated devices (Cook Medical Inc, Brisbane, Australia). No physician modified grafts were included. Planning was made by one vascular surgeon, followed by a technical check and eventual specific queries by the company's planning specialist. A proximal sealing zone > 20 mm was selected in normal suprarenal aortic segments, defined by parallel aortic wall with no thrombus, calcium, or diameter enlargement > 10%. Fenestrations were generally considered for JRAA/PRAA, TAAA with a narrow aortic lumen at the level of the paravisceral aorta, or upward oriented renals (eventually using a mixed branched fenestrated design); directional branches were preferred for cases with a large aortic lumen (> 35 mm) with downward oriented target vessels. Generally large (8 x 8 mm diameter) fenestrations were used to incorporate the coeliac and mesenteric arteries; small fenestrations (6 x6 mm diameter) were used for the renals. A proximal scallop was sometimes used for the superior mesenteric ($n = 6$) or coeliac artery ($n = 2$). A mixed branched fenestrated design was used in five cases. A coeliac artery fenestration was intentionally left unstented in one case. Both standard (20 — 22F) and low profile (18 — 20F) devices were used.[16]

Target vessel stenting

Catheterisation and stenting of target vessels were usually performed by femoral access. No pre-loaded fenestrations were used. Intra-operative fusion imaging was used for ten patients (17%). The Advanta V12/iCAST (Atrium Maquet Getinge, Hudson, NH, USA), Lifestream (BARD Peripheral Vascular, Tempe, AZ, USA), Begraft (Bentley InnoMed,

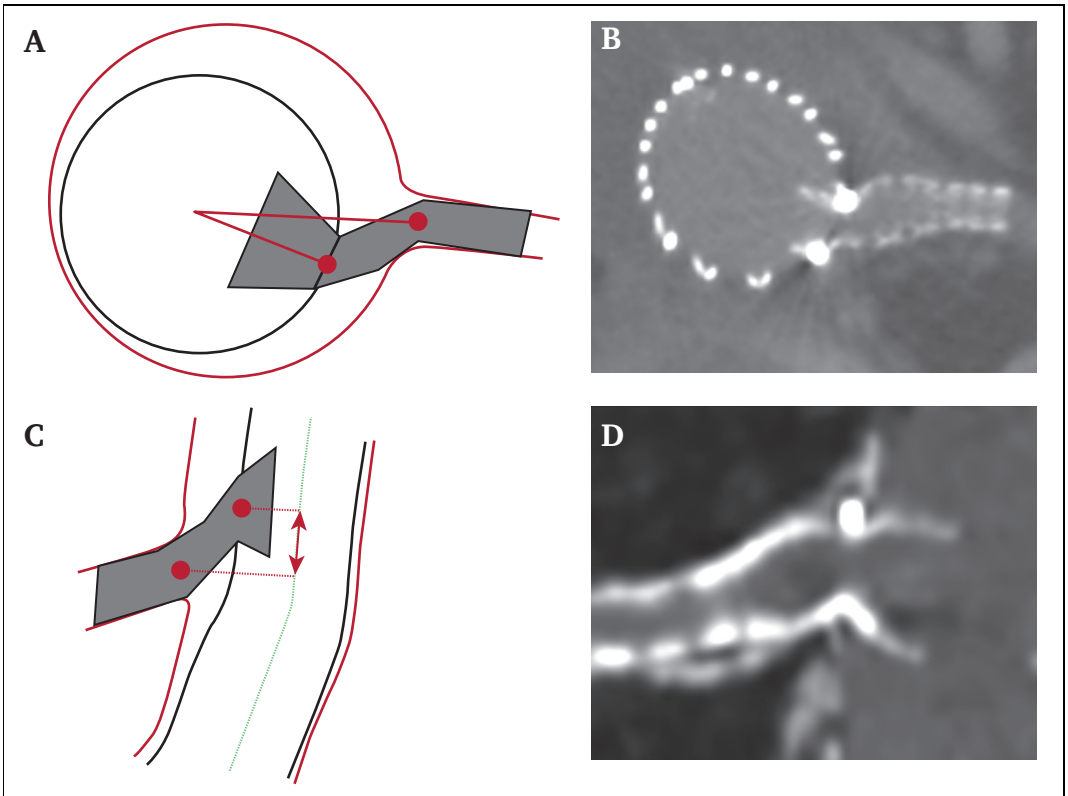

Figure 1. Schematic drawings and post-operative computed tomography angiograms (CTA) showing horizontal and vertical misalignment. (A) Schematic drawing showing the measurement of horizontal misalignment; this was defined as the angle between the midpoint of the fenestration (identified by the radiopaque markers) and the origin of the target vessel on CTA perpendicular views. (B) Post-operative CTA showing the presence of horizontal misalignment. (C) Schematic drawing showing the measurement of vertical misalignment; this was defined as the distance along the aortic centerline between the midpoint of the fenestration (identified by the radiopaque markers) and the origin of the target vessel. (D) Post-operative CTA showing the presence of vertical misalignment.

Hechingen, Germany), Viabahn balloon expandable stent graft (VBX, W.L. Gore & Associates, AZ, USA), or iCover (iVascular, Barcelona, Spain) were used as the main bridging stent. Only the Advanta and Lifestream stents were used until 2018. Starting in 2019, the VBX stent gradually became the first choice, reserving the Begraft or iCover for cases where a lower profile was desirable. Stent diameter was sized on the diameter of the fenestration (usually 6 mm for the renals and 8 mm for the coeliac and mesenteric arteries) and initially inflated at the target artery diameter. Stent length was selected to protrude into the main aortic graft for 3 — 5 mm and achieve a standard length of seal $\geq$ 15 mm into the target artery. After deployment, the proximal edge of the stent was systematically flared using a 12 x 20 mm or 10 x 20 mm semi compliant balloon (Powerflex Pro PTA; Cordis, Santa Clara, CA, USA). An adjunctive stent was sometimes used in cases with intra-operative evidence of a technical defect, such as endoleak, kink, stenosis, or compression. Technical assessment was based on the completion angiogram and first post-operative CTA. Type IC endoleaks or disconnections were considered for post-operative revision. Type III endoleaks were typically observed and revised if persistent $>$ 6 months and or associated with sac enlargement. Post-operative medical therapy was dual antiplatelet therapy (aspirin 100 mg and clopidogrel 75 mg) for 30 days, followed by long term single antiplatelet therapy with aspirin.

Misalignment assessment

Only successfully bridged fenestrations were included in the post-implantation analysis of misalignment; directional branches and scallops were excluded. Measurements were based on the first post-operative CTA (usually performed before discharge). Two components of misalignment were assessed, adapting the methods from Crawford *et al.*[8] Horizontal (rotational) misalignment was measured as the angle between the midpoint of the fenestration and the midpoint of the target vessel ostium on CTA orthogonal views (Fig. 1A and B). Vertical misalignment was measured as the vertical distance along the aortic centreline between the midpoint of the fenestration and the midpoint of the target vessel at its origin (Fig. 1C and D). When a significant misalignment was present in $<$ 50% of the endograft fenestrations, this was referred to as segmental device misalignment. Two blinded and trained physicians independently performed the measurements, and the intra-class correlation coefficient (ICC) was calculated to assess

interobserver agreement. Misalignment changes were measured comparing the last available CTA with the baseline (post-operative) CTA and gauged into three categories: increase (increase in horizontal misalignment $> 5^\circ$ or vertical misalignment > 3 mm), decrease (decrease in horizontal misalignment $> 5^\circ$ or vertical misalignment > 3 mm), or stable.

Endpoints

The primary endpoint was freedom from target vessel instability, defined as any target vessel related complication leading to aneurysm rupture, death, occlusion, component separation, or re-intervention to maintain target vessel patency or treat a target vessel related component separation or endoleak.[2] The secondary endpoint was alignment change over time.

Statistical analysis

The results are reported as number (percentage) for categorical variables and mean ± standard deviation or median (IQR) for continuous variables. Time dependent outcomes were reported using Kaplan—Meier estimates. A penalised splines function without pre-specified knots was used to assess the overall relationship between misalignment (modelled as continuous variable) and the HR for target vessel instability. After assessment of non-linearity, a receiver operating characteristics (ROC) analysis was used to identify a cutoff value for a clinically significant misalignment; this optimal cutoff was defined as the value on the ROC curve maximising the sensitivity + specificity sum, as described by Youden.[17] Uni- and multivariable logistic regression models were used to identify factors associated with clinically significant misalignment, modelled as a dichotomous variable based on the obtained cutoff. A simple Bonferroni correction was used to account for multiple testing. Covariables with univariable significance $p <$ .20 were entered into the multivariable model; a backward stepwise selection was performed and the most parsimonious model with inclusion of significant factors and confounders was selected as the final model. Firth's regression[18] was adopted in case of complete or quasi-complete data separation. The unit of the analysis for target vessel instability was each target vessel. Given the low degree of vertical misalignment in the study cohort, the analysis was focused on rotational misalignment only. A p value $<$ .05 was considered statistically significant. The R 4.0 software (R foundation for statistical computing, Vienna, Austria) was used for the analysis.

RESULTS

Patient cohort

Sixty-five patients were treated by FEVAR and 51 by branched endovascular aortic repair. There were no perioperative deaths among the FEVAR patients. Three patients were excluded because of a total follow up duration $<$ 30 days, and two had no available images from the first post-operative CTA. Sixty patients were included: 48 with JRAA or PRAA (80%), six with Extent I-III (10%; two with a narrow paravisceral aorta, one with upward oriented renals, and three with both), and six with Extent IV (10%) TAAAs; 202 target arteries were incorporated through a fenestration (mean 3.4 ± 0.7 fenestrations per patient). The mean age was 73 ± 9 years and 88% were male. Fifty-nine patients had an atherosclerotic aneurysm (98%) and one (2%) had a type I post-dissection TAAA with the dissection not

Table 1. Demographics, risk factors, and anatomical data of the 60 patients treated by fenestrated endovascular aortic repair

Variable	Patients (n = 60)
Demographics	
Age — years	73.5±8.7
Age > 80 years	10 (16.6)
Male sex	53 (88.3)
Risk factors	
Hypertension	46 (76.6)
Diabetes	7 (11.7)
Hypercholesterolaemia	34 (56.7)
CAD	31 (51.7)
COPD	12 (20.0)
CKD	19 (31.7)
PAD	6 (10.0)
Prior TIA or stroke	5 (8.3)
Prior laparotomy	22 (36.7)
Prior aortic surgery	15 (25.0)
SVS comorbidity score	0.9±0.6
Aneurysm anatomical data	
Aneurysm maximum diameter — mm	56.8±14.2
Anatomic classification	
Pararenal	16 (26.7)
Juxtarenal	32 (53.3)
Thoraco-abdominal	12 (20.0)
Extent I—III	6 (10.0)
Extent IV	6 (10.0)
Chronic dissection	1 (1.7)
Iliac access tortuosity index*	1.4±0.2
Target vessel anatomical data (n = 202)	
Coeliac artery (n = 35)	
Diameter — mm	7.4±1.3
Cranial orientation > 30°	1 (2.8)
Caudal orientation > 30°	22 (62.8)
Superior mesenteric artery (n = 52)	
Diameter — mm	7.9±1.5
Cranial orientation >30°	2 (3.8)
Caudal orientation > 30°	34 (65.4)
Right renal artery (n = 59)	
Diameter — mm	6.29±1.46
Cranial orientation > 30°	2 (3.3)
Caudal orientation > 30°	23 (38.9)
Left renal artery (n = 56)	
Diameter — mm	6.46±1.4
Cranial orientation > 30°	5 (8.9)
Caudal orientation > 30°	22 (39.2)

Data are shown as mean ± standard deviation or n (%). CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; PAD = peripheral arterial disease; TIA = transient ischaemic attack; SVS = Society for Vascular Surgery.
* Intraclass correlation coefficient 0.92.

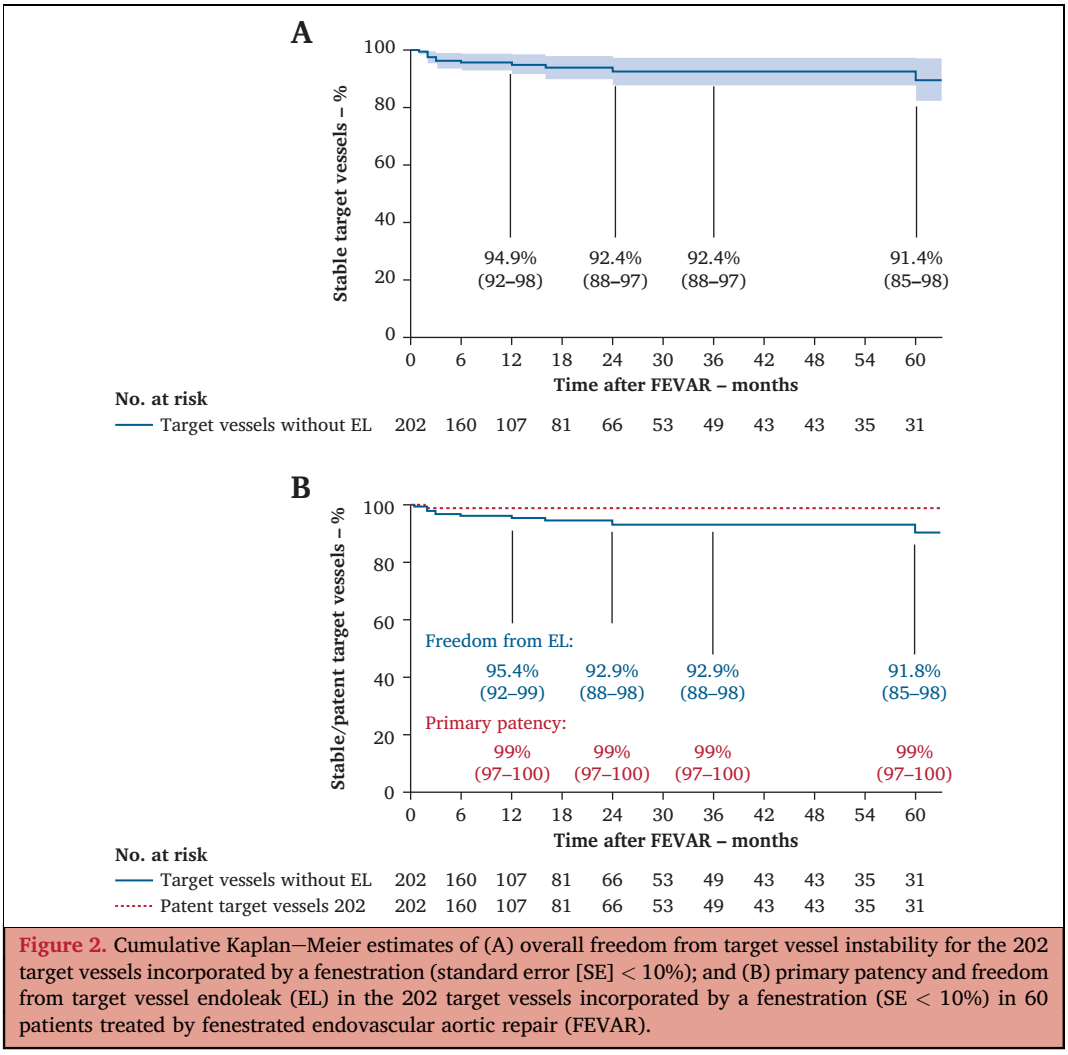

Figure 2. Cumulative Kaplan–Meier estimates of (A) overall freedom from target vessel instability for the 202 target vessels incorporated by a fenestration (standard error [SE] < 10%); and (B) primary patency and freedom from target vessel endoleak (EL) in the 202 target vessels incorporated by a fenestration (SE < 10%) in 60 patients treated by fenestrated endovascular aortic repair (FEVAR).

involving the paravisceral segment (Table 1). The VBX Gore was used as the alignment stent in 135 cases (67%), and 16 target vessels (7.9%) received an adjunctive covered (n = 11, 5.4%) or bare metal (n = 5, 2.4%) stent. The major adverse event rate was 20%; specific procedural data and early complications are described in Supplementary Table S1. A primary target vessel endoleak was detected in 15 patients (25%). Median follow up was 31 months (IQR 6 — 42) and three year survival was 79.5% (95% CI 66 — 91); there were no aneurysm related deaths. During follow up, there were two renal artery stent occlusions and 10 cases of target vessels endoleak needing intervention (eight type III: four primary and four secondary; two type Ic) (Supplementary Table S2). Freedom from target vessel instability was 94.9% (95% CI 92 — 98) at 12 months, 92.4% (95% CI 88 — 98) at 24 months, and 92.4% (95% CI 88 — 98) at 36 months (Fig. 2A). Freedom from target vessel endoleak was 95.4% (95% CI 92 — 99) at 12 months, 92.9% (95% CI 88 — 98) at 24 months, and 92.9% (95% CI 88 — 98) at 36 months. Primary patency was 99% (95% CI 97 — 100) at 12 months, 99% (95% CI 97 — 100) at 24 months, and 99.0% (95% CI 97 — 100) at 36 months (Fig. 2B). Freedom from target vessel instability was 100% (95% CI 99 — 100) in reinforced and 91% (95% CI 81 — 91) in non-reinforced bridging stents (p = .90).

Post-implantation misalignment assessment and clinical impact

Mean horizontal misalignment was 9 ± 12° (median 5°; IQR 0 — 16; ICC 0.90) (Table 2). There was a significant univariable association between higher grade of horizontal misalignment (modelled as continuous variable) and target vessel instability (HR 1.06; 95% CI 1.02 — 1.09; p = .002), with a non-linear relationship (p = .010 for non-linearity) at the splines function (Fig. 3). The ROC analysis identified a 15° horizontal misalignment as the optimal cutoff to predict target vessel complications (0.68 sensitivity, 0.80 specificity, area under the curve 0.75; 95% CI 0.56 — 0.87); therefore, this was considered as clinically significant (HR for misalignment > 15°: 5.19; 95% CI 1.54 — 17.48; p = .008). Horizontal misalignment > 15° was present in 44 target vessels (20% in total, 26% of renal fenestrations and 16% of visceral arteries fenestrations; p = .11) distributed in 26 patients (43% of all patients). Misalignment was segmental in 22 patients (85%) and four (15%) had an entire device

Table 2. General results of the post-implantation analysis of misalignment, stratified by type of target vessel in 60 patients treated by fenestrated endovascular aortic repair

General results	All fenestrations (n = 202)	CT-SMA (n = 87)	Renal (n = 115)	p value
Horizontal misalignment – °				.17
Mean ± SD	9.3±11.7	7.8±9.3	10.3±13.1	
Median (IQR)	5 (0–16)	4 (0–12)	5 (0–17)	
No horizontal misalignment	20 (9.9)	5 (5.7)	15 (13.0)	.099
Horizontal misalignment > 15°	44 (21.7)	14 (16.1)	30 (26.1)	.11
Vertical misalignment – mm				.31
Mean ± SD	0.7±1.1	0.7±1.0	0.6±1.0	
Median (IQR)	0 (0–1)	0 (0–1)	0 (0–1)	
No vertical misalignment	40 (19.8)	16 (18.3)	24 (20.8)	.72
Vertical misalignment > 5 mm	0 (0)	0 (0)	0 (0)	–

CT = coeliac trunk; SMA = superior mesenteric artery; SD = standard deviation; IQR = interquartile range.

misalignment; the mean number of misaligned fenestrations in patients with any misalignment was 1.7 ± 0.7. Mean vertical misalignment was 0.7 ± 1 mm (ICC 0.97); all target vessels had a vertical misalignment < 5 mm and it was not detectable (0 mm) in 40 cases (20%). Univariable Cox proportional hazards showed that there was no association between the severity of vertical misalignment and freedom from target vessel instability (HR 0.99; 95% CI 0.56 – 1.73; p = .97).

Determinants of clinically significant misalignment

After multivariable analysis, pararenal aortic angle (OR 1.01; 95% CI 1.00 – 1.02; p = .044), bridging distance > 5 mm (OR 1.07; 95% CI 1.02 – 1.11; p = .003), and use of higher profile endografts in the context of iliac access tortuosity (OR 7.55; 95% CI 4.55 – 1.11; p = .003) were associated with a clinically significant misalignment > 15° (Table 3). Type of bridging stent (OR 0.54; 95% CI 0.26 – 1.09; p = .076), length of stent coverage (OR 1.01; 95% CI 0.94 – 1.07; p = .72), use of multiple bridging stents (OR 0.45; 95% CI 0.29 – 5.76; p = .61), type of target vessel (renal arteries *vs.* coeliac or mesenteric arteries: OR 1.11; 95% CI 0.97 – 1.27; p = .11), size of fenestration (OR 0.97; 95% CI 0.70 – 1.31; p = .85), and intra-operative fusion imaging (OR 0.76; 95% CI 0.32 – 5.67; p = .34) were not significantly associated.

Alignment changes over time

The fate of misalignment during follow up is detailed in Figure 4. Fenestration alignment remained stable in 151 (74.7%) target vessels, increased in 20 (9.9%), and decreased in six (2.9%). Target vessels with a clinically significant baseline misalignment more frequently developed a misalignment increase during follow up (20% *vs.* 7%; p = .017). Alignment changes were not different when comparing the use of supracoeliac *vs.* infracoeliac proximal landing zones (OR 2.11; 95% CI 0.69 – 6.34; p = .18). After multivariable analysis, a bridging distance > 5 mm (OR 2.00; 95% CI 1.02 – 11.29; p = .044), degree of baseline misalignment on the post-operative CTA (OR 1.04 per increased degree of angulation; 95% CI 1.01 – 1.08; p = .036), and presence of any primary endoleak persisting for > 6 months (OR 5.85; 95% CI 1.23 – 29.1; p = .023) were

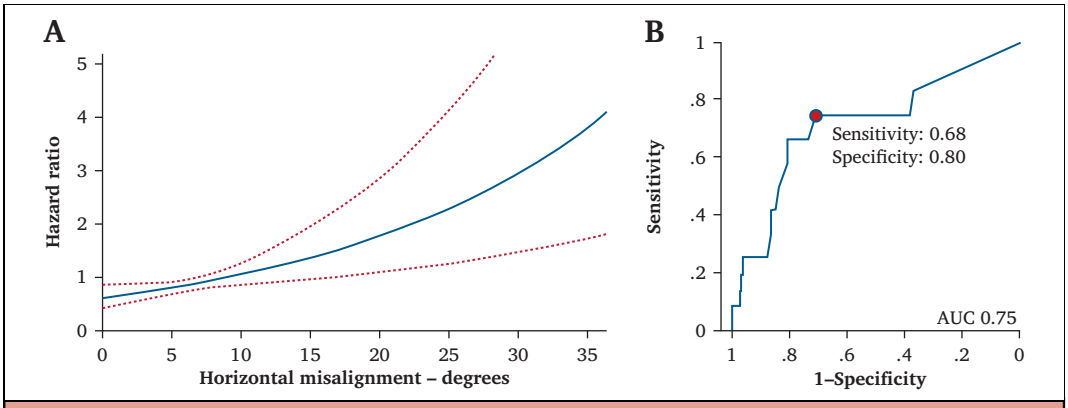

Figure 3. Clinical impact of horizontal misalignment on target vessel instability. (A) Penalised smooth splines representing the hazard ratio (HR) for target vessel instability *vs.* horizontal misalignment (note the substantial increase in the HR for target vessel instability for horizontal misalignment > 15°); and (B) receiver operating characteristic (ROC) curve of horizontal misalignment in the prediction of target vessel instability after fenestrated endovascular aneurysm repair in 60 patients. The dashed line indicates 95% confidence interval and the red dot indicates a 15° cutoff.

Table 3. Univariable and final multivariable logistic regression models for clinically significant post-implantation misalignment, defined as horizontal misalignment > 15° in 60 patients treated by fenestrated endovascular aortic repair

Variable	Univariable		Multivariable	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age – years	1.00 (0.95–1.06)	.89	–	–
Male sex	0.75 (0.25–2.51)	.62	–	–
TAAA	1.43 (1.22–1.66)	<.001	–	–
Aneurysm maximum diameter – mm	1.00 (0.99–1.01)	.87	–	–
Number of target vessels	0.79 (0.49–1.27)	.33	–	–
Target vessel				
Coeliac–mesenteric artery	Reference	–	–	–
Renal artery	1.11 (0.97–1.27)	.11	–	–
Fenestration size – mm	0.97 (0.70–1.31)	.85	–	–
Proximal landing zone				
Supracoeliac	Reference	–	–	–
Infracoeliac	1.23 (0.62–2.46)	.55	–	–
Supracoeliac aortic angle – °	1.01 (0.99–1.03)	.27	–	–
Pararenal aortic angle – °	1.04 (1.00–1.03)	.024	1.01 (1.00–1.02)	.044
Infrarenal aortic angle – °	0.99 (0.72–1.03)	.72	–	–
Iliac access tortuosity index	1.73 (1.10–2.70)	.017	1.55 (1.01–2.61)	.047
Minimum iliac access diameter – mm	0.94 (0.89–0.99)	.043		
Type of stent – VBX	0.54 (0.26–1.09)	.076	–	–
Use of multiple bridging stents	0.45 (0.29–5.76)	.61	–	–
Total length of stent coverage – mm	1.01 (0.94–1.07)	.72	–	–
Protrusion length – mm	1.06 (0.89–1.25)	.50	–	–
Sealing length – mm	0.98 (0.92–1.04)	.65	–	–
Bridging distance > 5 mm	1.59 (1.14–2.12)	.006	1.07 (1.02–1.11)	.003
Endograft profile – Fr	1.79 (1.01–3.17)	.046	1.57 (0.95–3.67)	.12
Endograft profile*iliac access tortuosity	6.35 (4.28–9.41)	.022	7.55 (4.55–10.11)	.016
Intra-operative fusion imaging	0.76 (0.32–5.67)	.34	–	–

TAAA = thoraco-abdominal aortic aneurysm; VBX = Viabahn balloon expandable; OR = odds ratio; CI = confidence interval.

significantly associated with an increase in follow up misalignment (Table 4).

DISCUSSION

This study sought to investigate the clinical impact and determinants of fenestration to target vessel misalignment after FEVAR. A post-implantation horizontal misalignment > 15° was identified as clinically significant, as it was associated with substantially increased target vessel instability during follow up (HR 5.19; 95% CI 1.54 – 17.48; $p = .008$). An interesting finding was that horizontal misalignment was more frequent (22% *vs.* 0%) and had a greater clinical impact than vertical misalignment. A possible explanation is that during the procedure, the main graft is typically deployed under an antero–posterior projection, and this bidimensional fluoroscopic view is more accurate in identifying the height of the target vessel's origin rather than the clock position. Also, if intra-operative misalignment occurs, this is usually sufficient to detect vertical misalignment and drive an eventual adjustment manoeuvre. Horizontal misalignment is often not obvious under fluoroscopy, while it is more easily identified on CT. Crawford *et al.*[7,8] studied misalignment of renal fenestrations during FEVAR, describing horizontal misalignment in 40% of cases and vertical misalignment in 30%. Their measurements were based on fluoroscopy alone and were assessed after unsheathing of the main body device, without accounting for target vessel bridging or eventual adjustments. Conversely, the current study focused analysis only on post-implantation misalignment, assuming that the final FEVAR conformation had a greater impact on clinical outcomes. Furthermore, it aimed to examine the fairly common clinical concern that may arise whenever some sort of misalignment is noticed on post-operative imaging.

Device malrotation may result from multiple contributing factors acting during the pre-, intra-, and post-operative phases of FEVAR. These factors do not necessarily influence the whole device orientation; segmental device misalignment affecting just one or two fenestrations may also occur (85% of cases in this cohort), probably as a result of segmental endograft misalignment from the beginning or intra-operative adjusting manoeuvres on a initially malrotated device. Pre-operative planning is of vital importance for improved fenestration alignment. The bridging distance has recently emerged as being associated with a higher risk of endoleaks,[12,19] especially when > 5 mm, as reported by two independent studies.[12,19] The current results are concordant in showing that a short bridging distance may be useful to reduce post-implantation horizontal misalignment. This is probably linked to a decreased parallax under fluoroscopy, and a reduction in the physiological displacement of the target vessel ostium produced by the introduction of stiff endovascular devices. However, total stent

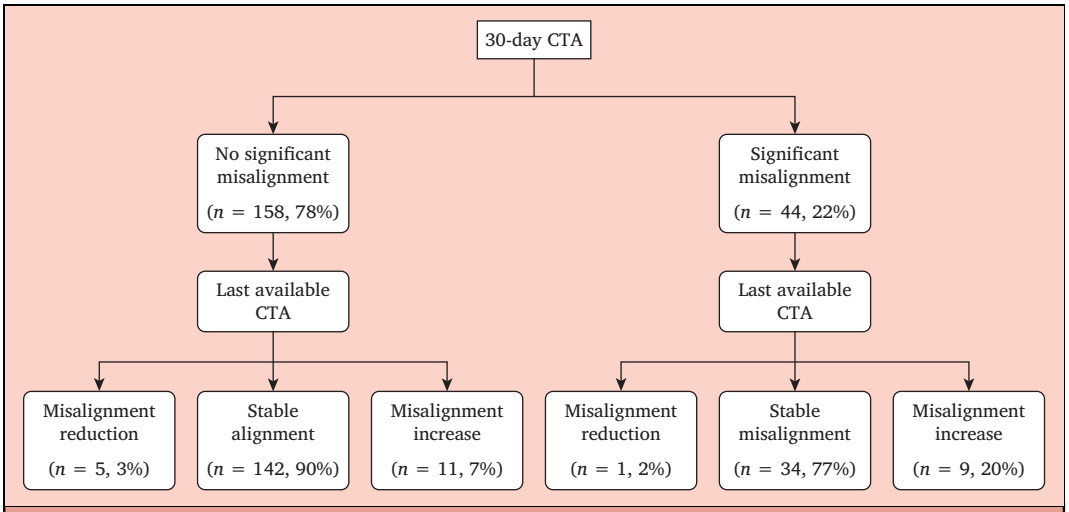

Figure 4. Flow chart representing the fate of fenestration alignment during follow up, after a median observation period of 31 months in 60 patients treated by fenestrated endovascular aortic repair. CTA = computed tomography angiography.

length was not associated with misalignment, as this also includes the length of stent protruding into the aorta and the length of sealing into the target vessel, which may act as fixation points.[12] Fenestration alignment may be maximised using larger endografts and placing the fenestrations above the tapered part of the device, when possible, in order to maintain the bridging distance as short as possible.

Several factors may cause endograft malrotation during FEVAR. Small size or excessive tortuosity of the iliac access may increase the friction between the shaft and iliac artery, interfering with correct device orientation and intentional adjustment movements that may be required during deployment.[7] Moreover, in the presence of significant friction, rotational energy accumulates in the stent graft while it is introduced and advanced, and is then released when the graft is unsheathed. The use of lower profile endografts or pre-placement of a large introducer sheath may be considered in these cases to reduce the friction during advancement and deployment, facilitating intentional alignment adjustments.

Aortic angulation represents a great challenge in complex endovascular aortic repair, and has been implicated in target vessel endoleaks and occlusions.[10] Aortic angulation leads to more difficult fenestration alignment (OR 1.01; 95% CI 1.00 — 1.02; $p = .043$), and may be responsible for displacement forces that cause inadvertent device movements both during deployment and after implantation (OR 1.03; 95% CI 1.00 — 1.07; $p = .048$). The introduction of stiff guidewires and devices into a severely angulated aorta also produces significant anatomical modifications, possibly resulting in a final imperfect position. Some intra-operative tips may be adopted to deal with this issue. After insertion of the stiff guidewire, the level of origin of each target vessel can be marked using intravascular ultrasound,[20] enabling more precise identification of the desired position of the fenestrations. Also, deployment of the device using a femoral—brachial through and through guidewire system may improve alignment in these cases. Intra-operative fusion imaging may theoretically improve endograft alignment, although this was not significant in the current series ($p = .34$). However, its accuracy may be hindered by angulations and tortuosity, but also by other external factors such as the quality of the pre-operative CTA, and skills and experience of the radiology technician. Accurate setting and eventual adjustment based on ancillary techniques (i.e., IVUS) are important in improving accuracy of deployment in current practice.

There is no current consensus regarding the specific bridging stent to be used in FEVAR. More rigid stents may theoretically improve fenestration alignment, but the flaring of the proximal part may be suboptimal. Conversely, a more conformable stent may be more prone to stent compression in a misaligned endograft, but it may be easier to correctly flare the proximal edge. Where VBX stents were used in most fenestrations in the current study, the type of stent and also bridging stent reinforcement did not have a significant impact on post-implantation misalignment. However, use of multiple stents was adopted in a small number of cases and only if there was an intra-operative finding of suboptimal conformation, and this might have biased the results. Further studies are required to investigate this aspect and to clarify which stent performs better in cases with fenestration misalignment.

Alignment modifications may occur during follow up. These may be the result of two opposite forces acting after endograft complete deployment: displacement forces that tend to increase the misalignment, and alignment forces that tend maintain the endograft in position. The use of supracoeliac landing may improve the stability of the implant. The level of the proximal landing zone and the number of fenestrations in the current cohort were not associated with alignment changes during follow up, but this finding might be biased by the choice of a four-fenestration design in more complex aneurysms involving the paravisceral aorta. The presence of aortic angulation,

Table 4. Univariable and final multivariable logistic regression models for misalignment increase during follow up in 60 patients treated by fenestrated endovascular aortic repair

Variable	Univariable		Multivariable	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
TAAA	1.66 (0.40–5.89)	.44	–	–
Aneurysm maximum diameter – mm	1.04 (0.99–1.07)	.055	–	–
Number of target vessels	0.74 (0.36–1.52)	.42	–	–
Proximal landing zone			–	–
Supracoeliac	Reference			
Infracoeliac	2.11 (0.69–6.34)	.18	–	–
Target vessel				
Coeliac-mesenteric artery	Reference	–	–	–
Renal artery	1.52 (0.89–2.75)	.13	–	–
Supracoeliac aortic angle – °	1.02 (0.98–1.06)	.18	–	–
Pararenal aortic angle – °	1.03 (1.00–1.07)	.048	1.01 (1.00–1.02)	.082
Infrarenal aortic angle – °	0.95 (0.88–1.01)	.14	–	–
Type of stent – VBX	0.27 (0.08–0.81)	.022	0.34 (0.09–1.21)	.095
Use of multiple bridging stents	0.73 (0.03–5.01)	.79	–	–
Total length of stent coverage – mm	1.03 (0.93–1.15)	.48	–	–
Protrusion length – mm	1.18 (0.91–1.55)	.19	–	–
Sealing length – mm	1.08 (0.98–1.20)	.79	–	–
Low-profile endograft	2.07 (0.64–7.39)	.23	–	–
Bridging distance > 5 mm	2.02 (1.03–5.22)	.042	2.00 (1.02–11.29)	.044
Baseline misalignment – °	1.78 (1.05–5.24)	.027	1.04 (1.01–1.08)	.036
Primary endoleak > 6 months*	9.53 (1.68–74.27)	.014	5.85 (1.23–29.1)	.023

TAAA = thoraco-abdominal aortic aneurysm; VBX = Viabahn balloon expandable; OR = odds ratio; CI = confidence interval.
* Target vessel endoleak present on the first post-operative computed tomography angiogram and persisting for > 6 months.

bridging distance > 5 mm, and a baseline misalignment on the first post-operative CTA may be associated with greater displacement forces and higher rate of misalignment increase. Persistent primary endoleaks lasting > 6 months were a determinant of misalignment growth during follow up (OR 5.85; 95% CI 1.23 – 29.1; $p = .023$). Target vessel endoleaks are the most frequent type of primary endoleak after FEVAR, occurring in approximately 10% of patients.[21] Unlike secondary endoleaks, primary target vessel endoleaks are usually considered benign and do not necessarily lead to target vessel instability; however, their persistence may produce structural instability of the endovascular system and exacerbate a previously present misalignment. Although this represents an interesting observation, the long term clinical implications need to be further investigated.

This study carries some direct clinical implications. During both planning and intervention, key anatomical aspects of iliac access size and tortuosity, aortic pararenal angulation, and anticipated bridging distance should be evaluated carefully, and device profile, design, and surgical strategy should be adapted accordingly.[20] If a horizontal misalignment > 15° is detected on the cone beam CT or post-operative CTA (depending on each centre's protocol for technical assessment), strict follow up may be appropriate; it is the authors' opinion that bridging stent reinforcement may be considered if a concomitant primary target vessel endoleak or significant kink is also present.

This study had some notable limitations. It was a single centre retrospective study, with a limited number of patients and follow up. The small number of events may have limited the power of the statistical analysis, potentially leading to type II error. The vertical component of misalignment was not observed in this cohort, preventing an in depth analysis on vertical or oblique (combination of vertical and horizontal) misalignment.

Conclusion

A post-implantation fenestration to target vessel horizontal misalignment > 15° may be considered clinically significant, as it is associated with worsened target vessel outcomes. This may occur as a result of excessive iliac access tortuosity, high pararenal aortic angulation, and a bridging distance > 5 mm, which may act both during planning and the endovascular procedure. Careful planning and evolution of endograft materials and profiles may be useful in improving fenestration alignment. Further studies are needed to investigate how to improve the outcomes in case of post-implantation horizontal misalignment > 15°, eventually with bridging stent reinforcement or a closer follow up.

CONFLICT OF INTEREST STATEMENT AND FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2023.10.016.

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