

Original Article

## Predictive factors of extremity graft occlusion after endovascular repair of abdominal aortic aneurysm: A 13-year single center experience

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### Abstract

**Aim:** Graft leg thrombosis (GLT) after Endovascular Aortic Repair (EVAR) is an important problem affecting morbidity/mortality. In addition to anatomical factors such as aortic neck angle and diameter in graft leg thrombosis; we aimed to convey the roles of graft extension to the external iliac artery and the effect of graft type selection on the results.

**Material and Methods:** Analysis of 512 patients who underwent EVAR between 2010 and 2023 was performed. The effects of anatomical factors, graft material, underlying diseases, age and gender on the development of graft leg thrombosis were evaluated. Anatomical measurements were evaluated in terms of their predictive power for graft leg thrombosis by Receiver Operating Characteristic (ROC) analysis.

**Results:** The prevalence of graft leg occlusion was significantly associated with some anatomical factors, especially increased aortic neck angle (OR=1.07,  $p<0.001$ ) and descent to the external iliac artery (OR=13.43,  $p<0.001$ ). Polytetrafluoroethylene (PTFE) grafts were associated with a reduced risk of graft leg occlusion (OR=0.26,  $p=0.002$ ). ROC analysis showed that aortic neck angle had the highest predictive accuracy for GLT (AUC=0.817,  $p<0.001$ ). There were no significant differences in age, gender, smoking status, diabetes, and hypertension as comorbidities. Peripheral artery disease was shown to increase the risk.

**Conclusion:** Our findings highlight the role of aortic anatomy and graft material selection in the risk of graft leg thrombosis. The use of PTFE grafts appears to be protective against graft leg thrombosis. This information highlights the importance of personalized surgical planning and postoperative management to optimize patient outcomes. Future research should focus on developing models that include these factors.

**Keywords:** Aneurysm, endovascular, graft occlusion

### INTRODUCTION

Endovascular aneurysm repair (EVAR), which started to be used in the 90s, has now become the first treatment option due to its low blood loss, short hospital stay, and much lower mortality and morbidity rates than open surgery [1,2]. However, as time progressed, it was reported that re-intervention rates were high in patients who underwent EVAR [3]. Complications such as

endoleak, graft migration and graft leg occlusion are frequently encountered [4,5]. With the developments in technology, the development of lower profile and more flexible grafts has paved the way for EVAR treatment in more difficult aortic anatomies, and the indications have expanded compared to the early times. Expanding indications may be associated with potentially increased rates of subsequent complications.

### CITATION

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Extremity graft occlusion after EVAR is responsible for approximately 1 in 3 of reinterventions and is an important cause of rehospitalization [6,7]. If left undiagnosed and untreated, it can lead to serious morbidity and mortality. Extremity thrombosis after EVAR has an incidence between 0% and 10.6%. It has been reported that especially patients who underwent EVAR with anatomy outside the graft usage instructions, patients with calcification in the iliac arteries, and patients requiring extension to the external iliac artery are at risk for graft leg thrombosis [8,9]. It has also been reported that the graft material used may play a role in the presence of stenosis [10].

Studies on graft leg occlusion after EVAR with large patient groups are limited. Therefore, this study was planned in a large patient group and long-term follow-up. The main purpose of the study is to retrospectively examine the causes of graft leg occlusions observed after EVAR in aneurysms. In particular, it aims to investigate the relationship between graft leg occlusions and graft type, gender, descent to the external iliac artery, presence of peripheral artery disease and anatomical factors. This study aims to contribute to the development of strategies to prevent these complications by identifying factors that increase the risk of graft occlusion.

## MATERIAL AND METHODS

A total of 512 patients who underwent endovascular stent graft repair for abdominal aortic aneurysm between July 2010 and December 2023 were included in this study. While 60.7% (311) of the patients were male and 39.3% (201) were female, the average age was  $74.4 \pm 8.1$  years.

### Exclusion Criteria

- Thoracoabdominal aneurysms (57 patients),
- Juxtarenal aneurysms (13 patients),
- Isolated iliac artery aneurysms (41 patients).

The study was started with the 27.12.2023 dated and 27/365 numbered approval of Ordu University Clinical Research Ethics Committee.

The radiological images and pre-procedure, during-procedure and post-procedure data of all patients were recorded prospectively in the created database and analyzed retrospectively. An informed consent form was obtained from all patients before the procedure.

### Surgery Technique

After all patients were provided with the necessary sterilization conditions in the angiography unit, femoral artery was explored with incisions made from both groins.

5000 units of heparin were applied to the patients. The procedure was performed by selecting the leg to which the main body would be sent according to anatomical suitability with the guide wires endoscopy. Angiography and measurements were performed to determine the renal artery level with a pigtail catheter from the other leg before. The graft was placed based on the renal artery level with a stiff wire support from the leg to which the main body would be sent. Then, the iliac extension was placed from the other leg. Control angiography was performed and balloon dilatation was performed to the joints if necessary. Standard heparinization procedures were performed by the same team consisting of anesthesiologists and cardiovascular surgeons. Post-procedure control angiography was performed on each patient. Two types of stent grafts made of Polyester and Polytetrafluoroethylene (PTFE) were used in the patients. Aortobiiliac stent grafts were placed in all patients.

In the study, patients with aortic neck angle of  $\geq 60$  degrees, aortic neck diameter of  $\geq 28$  mm, aortic neck length of  $\leq 20$  mm, and patients with external iliac artery diameter of  $\leq 9$  mm were considered as patients with poor aortic anatomy. After discharge, patients with normal renal function were followed up with Computerized tomography (CT) angiography at 1, 6, and 12 months, while other patients were followed up with color Doppler ultrasonography.

### Statistical Analysis

Continuous variables were analyzed based on their distribution, represented either as mean $\pm$ standard deviation for normally distributed data or median with range for non-normally distributed data.

The normality of continuous variables was meticulously evaluated using the Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests, ensuring the selection of suitable statistical tests for further analysis. The Pearson Chi-Square test was applied to evaluate differences in categorical variables across groups, using 2x2 contingency tables with expected cell frequencies of five or more. In cases where cell frequencies were less than five, Fisher's Exact Test was employed to maintain accuracy in statistical inference. For larger contingency tables with low expected frequencies, the Fisher Freeman Halton extension of Fisher's Exact Test was utilized.

For continuous variables, the method of analysis was determined by their distribution. The Independent Samples T-Test was used for normally distributed data, while the Mann-Whitney U test was applied for data not adhering to normal distribution criteria.

The statistical analyses were performed using the latest versions of Jamovi (Version 2.3.28) and JASP (Version 0.18.3) software, with a predefined significance level of 0.05 for all tests.

RESULTS

In the study in which a total of 512 patients were included, aortobiiliac grafts were successfully placed in all patients. Technical success was 100%. No mortality was observed during the operation or within 30 days. The average follow-up period was 95.5 months (range 14–160-SD: 38,89) and extremity graft thrombosis was detected in a total of 43 patients (8.39%). Of the patients who developed thrombosis, symptoms were claudication in 35 patients and signs of acute

ischemia in 4 patients, and 4 patients were detected by CT angiography during routine follow-up.

Significant differences were observed in the prevalence of peripheral artery disease among comorbid pathologies between patients with graft limb thrombosis and those without, indicated by a p value of 0.001. However, there was no significant difference in terms of age, gender, smoking status, presence of comorbidities such as Coronary Artery By-pass Grafting (CABG), Diabetes Mellitus (DM), Hypertension (HT), Carotid Artery Disease (CAD), Chronic Obstructive Pulmonary Disease (COPD), Cerebrovascular Accident (CVA), Chronic Kidney Disease (CKD), malignancy (p>0.05 for each) (Table 1). HT was found to be the most common comorbid disease with 54.7%..

Table 1. Comparative and descriptive analysis of demographic and clinical characteristics based on the presence of graft limb thrombosis

|                            | Overall (n=512) | Presence of graft limb thrombosis |                | p-values |
|----------------------------|-----------------|-----------------------------------|----------------|----------|
|                            |                 | Absent (n=496)                    | Present (n=43) |          |
| Age†                       | 74.4±8.1        | 74.2±8.1                          | 76.2±7.5       | 0.109**  |
| Gender‡                    |                 |                                   |                |          |
| Female                     | 201 (39.3)      | 186 (39.7)                        | 15 (34.9)      | 0.652*   |
| Male                       | 311 (60.7)      | 283 (60.3)                        | 28 (65.1)      |          |
| Smoking, yes‡              | 182 (35.5)      | 164 (35.0)                        | 18 (41.9)      | 0.461*   |
| Comorbidities‡             |                 |                                   |                |          |
| CABG, present              | 52 (10.2)       | 50 (10.7)                         | 2 (4.7)        | 0.294*   |
| DM, present                | 126 (24.6)      | 114 (24.3)                        | 12 (27.9)      | 0.734*   |
| HT, present                | 280 (54.7)      | 255 (54.4)                        | 25 (58.1)      | 0.753*   |
| Carotid, present           | 37 (7.2)        | 36 (7.7)                          | 1 (2.3)        | 0.350*   |
| Peripheral artery, present | 35 (6.8)        | 26 (5.5)                          | 9 (20.9)       | 0.001*   |
| CAD, present               | 59 (11.5)       | 53 (11.3)                         | 6 (14.0)       | 0.616*   |
| COPD, present              | 87 (17.0)       | 80 (17.1)                         | 7 (16.3)       | 0.999*   |
| CVA, present               | 17 (3.3)        | 16 (3.4)                          | 1 (2.3)        | 0.999*   |
| CKD, present               | 15 (2.9)        | 14 (3.0)                          | 1 (2.3)        | 0.999*   |
| Malignancy, present        | 14 (2.7)        | 13 (2.8)                          | 1 (2.3)        | 0.999*   |

Table 1 employs a range of statistical analyses to examine the demographic and clinical characteristics in relation to the presence of graft limb thrombosis among participants; the † symbol denotes values are expressed as mean±standard deviation, illustrating continuous variables; the ‡ symbol indicates that data are presented as counts and percentages (n (%)), highlighting categorical variables; statistical significance between groups for categorical variables was assessed using the Pearson Chi-Square test or Fisher's Exact test, as denoted by \*, in cases where expected frequencies were low, Fisher's Exact test provided accurate assessment; differences in continuous variables between two groups were analyzed using the Independent Samples t test, indicated by \*\*, to compare mean values

The average abdominal aortic aneurysm diameter of the patients was found to be 65.3 mm (50-120 mm). The average aortic neck angle was recorded as 48.0°, aortic neck diameter as 26.3 mm and neck length as 23.0 mm. The median diameters of the right and left common iliac arteries were 18.3 mm and 19.3

mm, respectively. External iliac artery descent was performed in 60 patients (11.7%). Poor aortic anatomy was present in 297 patients (58%). There was iliac artery angulation in 152 patients (29.7%).

Polyester graft material was used in 306 patients (59.8%) and PTFE graft was used in 206 patients (40.2%). In terms of anesthesia preferences, general anesthesia was preferred in 51 patients (10.0%), while spinal anesthesia was preferred in 461 patients (90.0%). During follow-up, endoleak was detected in 111 patients (21.7%); Type 1 endoleak predominantly accounted for 81.1% (90 patients) of cases, followed by Type 2 with 13.5% (15 patients) and Type 3 with 5.4% (6 patients). Secondary intervention was required in 108 patients (21.1%). At the end of the follow-up period, 454 (88.7%) patients were alive and 58 (11.3%) patients had died. Deaths during follow-up occurred at an average of 8 years after surgery. The main cause was stroke (26 patients, 44.8%), followed by myocardial infarction (23 patients, 39.7%), lung cancer (5 patients, 8.6%), stomach cancer (2 patients, 3.4%) and aneurysm rupture (2 patients, 3.4%).

The average duration of extremity graft thrombosis was found to be 45 (16-180 days) days. According to statistical analysis, patients with extremity graft thrombosis exhibited significantly increased rates of iliac angulation, endoleak presence, Type 1 endoleak formation, polyester graft use, and secondary procedure requirement compared to patients without thrombosis ( $p<0.05$  for each category). Type 2 leak was more common in patients without thrombosis, whereas Type 3 leak rates were similar between both groups. Additionally, patients with thrombosis faced longer surgery and hospital stay ( $p=0.034$  and  $p=0.006$ , respectively) than those without thrombosis. As a secondary intervention for the patients with thrombosis, femoro-femoral bypass was performed in 35 of them (Figure 1), while PTCA was applied in 8 of them and blood supply was restored.



**Figure 1.** CT angiography appearance of a patient who underwent femoral-femoral bypass

No significant difference was observed between the two groups in terms of follow-up period, amount of contrast used, secondary procedures (including balloon angioplasty and

additional stent), choice of anesthesia, mortality rates, time to mortality and causes of death ( $p>0.05$  for each) (Table 2).

**Table 2. Comparative analysis of clinical and procedural variables in patients with and without graft limb thrombosis**

|                                  | Overall (n=512)    | Presence of graft limb thrombosis |                    | p-values          |
|----------------------------------|--------------------|-----------------------------------|--------------------|-------------------|
|                                  |                    | Absent (n=496)                    | Present (n=43)     |                   |
| Iliac deployment, yes‡           | 152 (29.7)         | 109 (23.2)                        | 43 (100.0)         | <0.001*           |
| Endoleak presence, yes‡          | 111 (21.7)         | 85 (18.1)                         | 26 (60.5)          | <0.001*           |
| Endoleak type‡                   |                    |                                   |                    |                   |
| Type 1                           | 90 (81.1)          | 64 (75.3)                         | 26 (100.0)         | <b>0.014*</b>     |
| Type 2                           | 15 (13.5)          | 15 (17.6)                         | 0 (0.0)            |                   |
| Type 3                           | 6 (5.4)            | 6 (7.1)                           | 0 (0.0)            |                   |
| Follow-up duration (months)§     | 95.5 [14.0–160.0]  | 95.0 [14.0–160.0]                 | 96.0 [18.0–150.0]  | 0.823**           |
| Operation time (minutes)§        | 50.0 [30.0–110.0]  | 50.0 [30.0–110.0]                 | 55.0 [35.0–80.0]   | <b>0.034**</b>    |
| Hospital stay (days)§            | 1.0 [1.0–3.0]      | 1.0 [1.0–3.0]                     | 2.0 [1.0–3.0]      | <b>0.006**</b>    |
| Contrast use (cc)§               | 100.0 [40.0–150.0] | 100.0 [40.0–150.0]                | 105.0 [40.0–135.0] | 0.552**           |
| Graft limb thrombosis onset day§ | 45.0 [16.0–180.0]  | -                                 | 45.0 [16.0–180.0]  | -                 |
| Secondary procedure status, yes‡ | 108 (21.1)         | 65 (13.9)                         | 43 (100.0)         | <0.001*           |
| Secondary procedure type‡        |                    |                                   |                    |                   |
| Balloon                          | 47 (43.5)          | 27 (41.5)                         | 20 (46.5)          | 0.755*            |
| Bypass                           | 35 (32.4)          | 0 (0.0)                           | 35 (81.4)          | <0.001*           |
| Cuff                             | 34 (31.5)          | 32 (49.2)                         | 2 (4.7)            | <0.001*           |
| Additional stent                 | 6 (5.6)            | 6 (9.2)                           | 0 (0.0)            | 0.079*            |
| PTCA                             | 8 (7.4)            | 0 (0.0)                           | 8 (18.6)           | <0.001*           |
| Number of secondary procedures‡  |                    |                                   |                    |                   |
| 1                                | 86 (79.6)          | 65 (100.0)                        | 21 (48.8)          | <b>&lt;0.001*</b> |
| 2                                | 22 (20.4)          | 0 (0.0)                           | 22 (51.2)          |                   |
| Graft type‡                      |                    |                                   |                    |                   |
| Polyester                        | 306 (59.8)         | 270 (57.6)                        | 36 (83.7)          | <b>0.001*</b>     |
| PTFE                             | 206 (40.2)         | 199 (42.4)                        | 7 (16.3)           |                   |
| Anesthesia type‡                 |                    |                                   |                    |                   |
| General                          | 51 (10.0)          | 44 (9.4)                          | 7 (16.3)           | 0.177*            |
| Spinal                           | 461 (90.0)         | 425 (90.6)                        | 36 (83.7)          |                   |
| Mortality‡                       |                    |                                   |                    |                   |
| Alive                            | 454 (88.7)         | 415 (88.5)                        | 39 (90.7)          | 0.805*            |
| Deceased                         | 58 (11.3)          | 54 (11.5)                         | 4 (9.3)            |                   |
| Time of event (year)§            | 8.0 [2.1–13.0]     | 8.5 [2.1–13.0]                    | 7.0 [5.0–12.0]     | 0.688**           |
| Cause of event‡                  |                    |                                   |                    |                   |
| Stroke                           | 26 (44.8)          | 24 (44.4)                         | 2 (50.0)           | 0.570*            |
| Myocardial infarction            | 23 (39.7)          | 22 (40.7)                         | 1 (25.0)           |                   |
| Lung cancer                      | 5 (8.6)            | 4 (7.4)                           | 1 (25.0)           |                   |
| Gastric cancer                   | 2 (3.4)            | 2 (3.7)                           | 0 (0.0)            |                   |
| Rupture                          | 2 (3.4)            | 2 (3.7)                           | 0 (0.0)            |                   |

Table 2 provides a detailed comparative analysis of clinical and procedural variables among patients, segmented by the occurrence of graft limb thrombosis; the ‡ symbol indicates that data are expressed as counts and percentages (n (%)) to convey categorical information; the § symbol indicates that values are reported as medians with their respective ranges [Minimum-Maximum], applied to continuous variables; the symbol \* marks the use of the Pearson Chi-Square test, Fisher's Exact test, or the Fisher Freeman Halton test, which assess the significance of differences in categorical variables across groups; the \*\* symbol signifies the application of the Mann-Whitney U test for evaluating disparities in median values between two independent groups, focusing on continuous variables

Pairwise comparisons focusing on the presence of graft limb thrombosis revealed that patients with thrombosis had a significantly higher aortic neck angle than those without thrombosis ( $p<0.001$ ). Aortic neck angle greater than  $60^\circ$  was also seen significantly more frequently in patients with thrombosis ( $p<0.001$ ). In addition, larger aortic neck diameter was associated with thrombosis ( $p=0.044$ ), and it was noteworthy that the external

iliac artery diameter was smaller in patients with thrombosis ( $p=0.044$ ). It was observed that the incidence of extremity graft thrombosis was higher in patients with poor aortic anatomy ( $p=0.006$ ) and in patients with descent to the external iliac artery ( $p<0.001$ ). There was no significant difference between patients with and without thrombosis in terms of aneurysm diameter, neck length, and right and left iliac artery diameters ( $p>0.05$ ) (Table 3).

**Table 3. Comparative and descriptive analysis of ECO measure in patients with and without graft limb thrombosis**

|                                                            | Overall (n=512)   | Presence of graft limb thrombosis |                   | p-values           |
|------------------------------------------------------------|-------------------|-----------------------------------|-------------------|--------------------|
|                                                            |                   | Absent (n=496)                    | Present (n=43)    |                    |
| <b>Aneurysm location, abdominal<sup>‡</sup></b>            | 512 (100.0)       | 496 (100.0)                       | 43 (100.0)        | -                  |
| <b>Aneurysm diameter (mm)<sup>§</sup></b>                  | 65.3 [50.0–120.6] | 65.3 [50.0–120.6]                 | 66.2 [55.0–110.4] | 0.440**            |
| <b>Aortic neck angle (<math>^\circ</math>)<sup>§</sup></b> | 48.0 [10.0–101.0] | 45.0 [10.0–101.0]                 | 65.0 [30.0–86.0]  | <b>&lt;0.001**</b> |
| <b>Aortic neck angle (<math>^\circ</math>)<sup>‡</sup></b> |                   |                                   |                   |                    |
| $\leq 60^\circ$                                            | 381 (74.4)        | 366 (78.0)                        | 15 (34.9)         | <0.001*            |
| $> 60^\circ$                                               | 131 (25.6)        | 103 (22.0)                        | 28 (65.1)         |                    |
| <b>Aortic neck diameter (mm)<sup>§</sup></b>               | 26.3 [12.0–45.0]  | 26.3 [12.0–45.0]                  | 26.8 [20.0–38.0]  | <b>0.044**</b>     |
| <b>Aortic neck diameter (mm)<sup>‡</sup></b>               |                   |                                   |                   |                    |
| $\leq 28$ mm                                               | 336 (65.6)        | 312 (66.5)                        | 24 (55.8)         | 0.212*             |
| $> 28$ mm                                                  | 176 (34.4)        | 157 (33.5)                        | 19 (44.2)         |                    |
| <b>Neck length (mm)<sup>§</sup></b>                        | 23.0 [8.0–45.0]   | 23.0 [8.0–45.0]                   | 22.0 [10.0–42.0]  | 0.178**            |
| <b>Neck length (mm)<sup>‡</sup></b>                        |                   |                                   |                   |                    |
| $\geq 20$ mm                                               | 408 (79.7)        | 377 (80.4)                        | 31 (72.1)         | 0.273*             |
| $< 20$ mm                                                  | 104 (20.3)        | 92 (19.6)                         | 12 (27.9)         |                    |
| <b>Poor aortic anatomy, yes<sup>‡</sup></b>                | 297 (58.0)        | 263 (56.1)                        | 34 (79.1)         | <b>0.006*</b>      |
| <b>Right iliac artery diameter (mm)<sup>§</sup></b>        | 18.3 [10.0–49.0]  | 18.3 [11.0–49.0]                  | 17.4 [10.0–42.2]  | 0.821**            |
| <b>Left iliac artery diameter (mm)<sup>§</sup></b>         | 19.3 [11.0–52.0]  | 19.3 [11.0–52.0]                  | 18.6 [13.0–42.2]  | 0.841**            |
| <b>External iliac artery engagement, yes<sup>§</sup></b>   | 60 (11.7)         | 37 (7.9)                          | 23 (53.5)         | <b>&lt;0.001*</b>  |
| <b>External iliac artery diameter (mm)<sup>§</sup></b>     | 9.0 [7.0–12.0]    | 9.0 [7.0–12.0]                    | 9.0 [7.0–11.0]    | <b>0.044**</b>     |

Table 3 details the echocardiographic (ECO) measurements and their comparative analysis across patients with and without graft limb thrombosis; data are presented using specific symbols to indicate the statistical methodologies applied; the <sup>‡</sup> symbol represents data shown as counts and percentages (n (%)) for categorical variables; the <sup>§</sup> symbol is used to denote median values alongside their ranges [Minimum-Maximum] for continuous variables; statistical significance for categorical differences was evaluated using the Pearson Chi-Square test, as indicated by \*; the Mann-Whitney U test, marked by \*\*, assessed differences in median values between two independent samples for continuous variables

Univariate analysis results revealed that several factors significantly increased the risk of graft limb thrombosis. These factors were defined as increased aortic neck angle (Odds Ratio [OR]=1.07; 95% Confidence Interval [CI]: 1.05 to 1.09;  $p<0.001$ ), increased aortic neck diameter (OR=1.11; 95% CI: 1.01-1.21;  $p=0.029$ ), presence of descent to the external iliac artery (OR=13.43; 95% CI: 6.76-26.69;  $p<0.001$ ), endoleak formation (OR=6, 91; 95% CI: 3.59-

13.3;  $p<0.001$ ) and the presence of peripheral artery disease (OR=4.51; 95% CI: 1.96-10.39;  $p<0.001$ ). Notably, the use of PTFE grafts was associated with a significant reduction in risk (OR=0.26; 95% CI: 0.12 to 0.61;  $p=0.002$ ). Conversely, surgery time (OR=1.03; 95% CI: 0.99-1.05;  $p=0.056$ ), neck length (OR=0.97; 95% CI: 0.92-1.02;  $p=0.278$ ) and patient age (OR=1.03; 95% CI: 0.99 to 1.07;  $p=0.129$ ) did not show statistical significance.

In multivariate analysis, both an increase in the aortic neck angle (OR=1.05, 95% CI=1.02-1.09, p=0.001) and an increase in aortic neck diameter (OR=1.14, 95% CI=1.01-1.29, p=0.036) were significant predictors. Additionally, engagement of the external iliac artery was strongly associated with outcome (OR=18.03, 95% CI=7.37 to 44.14, p<0.001) and significantly increased the risk of limb thrombosis (OR=7.47, 95% CI=2.37-23.57, p<0.001). Conversely, the use of PTFE type grafts significantly reduced this risk (OR=0.23, 95% CI=0.08-0.7, p=0.009). The significance of the presence of endoleak was not maintained in the multivariable model (OR=2.45, 95% CI=0.84-7.12, p=0.100) (Table 4).

| Table 4. Risk factors for graft limb thrombosis: Results of logistic regression analysis |                                |          |                                  |          |
|------------------------------------------------------------------------------------------|--------------------------------|----------|----------------------------------|----------|
| Logistic regression predicting<br>"Presence of graft limb thrombosis"                    | Univariate logistic regression |          | Multivariate logistic regression |          |
|                                                                                          | OR [95% CI]                    | p-values | OR [95% CI]                      | p values |
| Aortic neck angle (°)                                                                    | 1.07 [1.05–1.09]               | <0.001   | 1.05 [1.02–1.09]                 | 0.001    |
| Aortic neck diameter (mm)                                                                | 1.11 [1.01–1.21]               | 0.029    | 1.14 [1.01–1.29]                 | 0.036    |
| Neck length (mm)                                                                         | 0.97 [0.92–1.02]               | 0.278    | -                                | -        |
| External iliac artery engagement: yes vs. no                                             | 13.43 [6.76–26.69]             | <0.001   | 18.03 [7.37–44.14]               | <0.001   |
| Endoleak presence: yes vs. no                                                            | 6.91 [3.59–13.30]              | <0.001   | 2.45 [0.84–7.12]                 | 0.100    |
| Operation time (minutes)                                                                 | 1.03 [0.99–1.05]               | 0.056    | -                                | -        |
| Graft type: PTFE vs. polyester                                                           | 0.26 [0.12–0.61]               | 0.002    | 0.23 [0.08–0.70]                 | 0.009    |
| Age                                                                                      | 1.03 [0.99–1.07]               | 0.129    | -                                | -        |
| Peripheral artery disease: present vs. absent                                            | 4.51 [1.96–10.39]              | <0.001   | 7.47 [2.37–23.57]                | <0.001   |

Table 4 elucidates the logistic regression analysis conducted to identify risk factors associated with graft limb thrombosis, presenting both univariate and multivariate logistic regression outcomes; the Odds Ratio (OR) and 95% Confidence Interval (CI) are used to quantify the strength and precision of associations between variables and the presence of graft limb thrombosis; a '-' symbol is utilized to indicate variables not included in the multivariate model due to insignificance or redundancy; the significance of each association is denoted by the p-value, with a lower p-value (<0.05) indicating a statistically significant relationship between the risk factor and the occurrence of graft limb thrombosis

Receiver Operating Characteristic (ROC) analysis provided information regarding the diagnostic performance of various anatomical measurements. The aortic neck angle exhibited an Area Under the Curve (AUC) of 0.817 (95% CI: 0.780 to 0.849; p<0.001). The optimal cutoff point of >55° provided 83.72% sensitivity and 71% specificity. The AUC of aortic neck diameter was 0.593 (95% CI: 0.549 to 0.636; p=0.049); this showed 72.09% sensitivity and 46.06% specificity at a cutoff of >25.72 mm. Aortic neck length exhibited an AUC of 0.562 (95% CI: 0.518 to 0.605; p=0.181), with a cutoff point of ≤24 mm, a sensitivity of 69.77% and a specificity of 44.99%. External iliac artery diameter, with an AUC of 0.651 (95% CI: 0.517 to 0.770; p=0.034), achieved 82.61% sensitivity and 40.54% specificity at the cutoff point of ≤9 mm (Table 5).

| Table 5. Diagnostic performance of vascular and anatomical measurements in predicting graft limb thrombosis: results of ROC analysis |       |             |             |         |               |          |
|--------------------------------------------------------------------------------------------------------------------------------------|-------|-------------|-------------|---------|---------------|----------|
|                                                                                                                                      | AUC   | Sensitivity | Specificity | Cut Off | 95% CI        | p-values |
| Aortic neck angle (°)                                                                                                                | 0.817 | 83.72       | 71          | >55     | 0.780 – 0.849 | <0.001   |
| Aortic neck diameter (mm)                                                                                                            | 0.593 | 72.09       | 46.06       | >25.72  | 0.549 – 0.636 | 0.049    |
| Neck length (mm)                                                                                                                     | 0.562 | 69.77       | 44.99       | ≤24     | 0.518 – 0.605 | 0.181    |
| External iliac artery diameter (mm)                                                                                                  | 0.651 | 82.61       | 40.54       | ≤9      | 0.517 – 0.770 | 0.034    |

Table 5 details the results of Receiver Operating Characteristic (ROC) analysis, evaluating the diagnostic performance of various vascular and anatomical measurements in predicting graft limb thrombosis; the Area Under the Curve (AUC) reflects the diagnostic ability of each measurement, with values closer to 1.0 indicating higher diagnostic accuracy; sensitivity and specificity percentages are provided alongside optimal cut-off points for each measurement, offering insights into the effectiveness of these variables in identifying patients at risk for graft limb thrombosis; the 95% Confidence Interval (CI) for AUC values illustrates the range within which the true AUC is expected to lie with 95% certainty; a lower p-value (<0.05) indicates a statistically significant predictive capability of the measurement

The main findings obtained in this study are summarized as follows:

- ✓ Increase in aortic neck angle significantly increases the risk of graft leg thrombosis (Univariate OR=1.07,  $p<0.001$ ; Multivariate OR=1.05,  $p=0.001$ ), which increases the likelihood of developing graft leg thrombosis with aortic neck angle. This suggests that there is a strong correlation between
- ✓ Similarly, increased aortic neck diameter was significantly associated with an increased risk of graft leg thrombosis (Univariate OR=1.11,  $p=0.029$ ; Multivariate OR=1.14,  $p=0.036$ ).
- ✓ Descent into the external iliac artery significantly increases the risk of graft limb thrombosis (Univariate OR=13.43,  $p<0.001$ ; Multivariate OR=18.03,  $p<0.001$ ), highlighting this as a critical factor.
- ✓ Presence of endoleak showed a significant association with graft limb thrombosis in univariate analysis (OR=6.91,  $p<0.001$ ), but did not remain significant in multivariate analysis (OR=2.45,  $p=0.100$ ).
- ✓ Peripheral artery disease is a significant determinant of graft limb thrombosis, and its presence nearly doubles the risk (Univariate OR=4.51,  $p<0.001$ ; Multivariate OR=7.47,  $p<0.001$ ).
- ✓ Use of PTFE grafts was associated with a significantly reduced risk of graft limb thrombosis (Univariate OR=0.26,  $p=0.002$ ; Multivariate OR=0.23,  $p=0.009$ ), indicating a protective effect.
- ✓ ROC analysis revealed that aortic neck angle had the highest diagnostic accuracy in predicting graft limb thrombosis (AUC=0.817, Sensitivity=83.72%, Specificity=71%,  $p<0.001$ ).

## DISCUSSION

Although EVAR provides great advantages in treatment, graft-related complications and secondary interventions are increasing during follow-up. Graft leg occlusion, one of the most serious complications after EVAR, usually occurs with sudden onset of lower extremity claudication or rest pain. It is a rare but serious complication and requires a secondary procedure. It has been reported as the 3rd most common reason for hospitalization after EVAR [11]. In data obtained from Eurostar registry, graft occlusion is the most common indication for extraanatomical revascularization and has been reported as a procedure that increases morbidity, hospitalization and cost [12].

In a study conducted with 460 patients, a graft leg occlusion rate of 7.2% was detected during follow-up, while in another study conducted with 66 patients, a graft leg occlusion rate of 10.6% was detected [13,14]. In another multicenter study conducted recently with 924 patients, it was reported that a 5.9% rate of graft leg occlusion was generally observed within the first year [15]. In this study, the rate of graft leg occlusion was found to be 8.3%, and the occlusions occurred within the first year, with an average of 45 days, and were found to be compatible with the literature. In the studies of Sivamurth et al. [16], it was reported

that occlusion generally developed within the first 6 months.

Different theories regarding the factors causing graft leg occlusion are still up to date. It has been stated that longitudinal changes in aneurysm morphology after EVAR, especially in patients with angled and curved anatomy, may cause bending of the stent graft (accordion effect) over time. Additionally, it has been reported that artificial straightening of especially long and angled iliac vessels with a stent graft may cause vascular occlusion by folding over the graft in the long term [17].

In a review that analyzed 9 different studies, it was reported that angulation of the iliac arteries was an important cause of graft leg occlusion [18]. In our series, all 43 patients who developed graft leg occlusion also had iliac angulation and it was statistically significant ( $p<0.001$ ). Wang et al. [13] divided the causes of graft leg occlusion into 3 main categories: anatomical, graft-related and combined. Among anatomical factors, the rate of graft leg occlusion is more common when used in patients with anatomical factors other than those specified in the manufacturer's instructions for use (such as aortic neck angle of  $>60$  degrees, aortic neck diameter of  $>28$  mm). Among graft-related factors, graft migration and especially low radial force stand out. In the study of Woody et al. [11], it was shown that poor anatomy caused graft leg occlusion due to bending of the graft in the iliac arteries. In another study, it was defined that the incidence of graft leg occlusion after EVAR was higher in the presence of at least one non-instruction-related anatomical factor [19]. Other studies have also shown that poor aortic anatomy increases the risk of graft leg occlusion [20,21].

In our study, it was revealed that an increase in the aortic neck angle significantly increased the likelihood of developing graft leg thrombosis in both univariate (OR=1.07,  $p<0.001$ ) and multivariate analysis (OR=1.05,  $p=0.001$ ). Additionally, ROC analysis showed that the aortic neck angle had the highest diagnostic value in predicting graft leg occlusion ( $p<0.001$ ). Similarly, it was revealed by univariate and multivariate analysis that an increase in aortic neck diameter also increased the risk of graft leg thrombosis, consistent with the literature.

It has been reported by some authors that extending the graft leg to the external iliac artery also increases the risk of graft leg occlusion [22,23]. It has been emphasized that especially the diameter of the external iliac artery being  $<10$  mm may further increase the risk [9]. When the graft is extended to the external iliac artery, the risk of graft leg occlusion also increases as smaller diameter devices are used and are exposed to high compression and are more likely to bend [18]. In a recent study, it was shown that descent to the external iliac artery and artery diameter of  $<10$  mm significantly increase the risk of graft leg occlusion [15]. In our study, graft leg occlusion developed in 23 patients who underwent descent to the external iliac artery, and in univariate analysis (OR=13.43,  $p<0.001$ ), it was shown that descent to the

external iliac artery significantly increased the risk of graft limb occlusion, consistent with the literature.

Since there is a study in the literature reporting that the presence of endoleak also contributes to the development of graft leg occlusion, we wanted to focus on this issue [9]. In our study, 26 of 43 patients (60.5%) who developed graft leg occlusion also had endoleak. While this situation showed a significant relationship with graft leg occlusion in univariate analysis, this did not remain significant in multivariate analysis.

It has been reported that the presence of underlying peripheral artery disease may lead to graft leg occlusion during follow-up [24]. In our series, the presence of peripheral artery disease was shown to be an important factor in determining the risk of graft leg occlusion in both univariate and multivariate analyses and almost doubled the risk. Detecting the presence of peripheral artery disease in patients planned for EVAR may have a significant impact on preventing graft leg occlusion.

One of the important factors in the development of graft leg occlusion is the type of graft used. There are not many studies comparing different stent graft types in terms of graft leg occlusion in the long term. In a study conducted with 924 patients, it was reported that graft leg occlusion was observed in only 1 patient in whom PTFE coated stent graft was used [15]. In another study conducted with PTFE-coated stent graft, 0% graft leg occlusion was reported, and this graft was recommended to be used in difficult anatomies [25]. In another study, it was reported that the majority of cases of graft leg occlusion were seen in patients treated with polyester-covered stent graft [21]. In this study, it was demonstrated in univariate ( $OR=0.26$ ,  $p=0.002$ ) and multivariate ( $OR=0.23$ ,  $p=0.009$ ) analyses that the use of PTFE-coated grafts significantly reduced the risk of graft leg occlusion. We believe that the use of PTFE-coated grafts, especially in difficult anatomies, would be more rational to prevent graft leg occlusion.

PTCA, thrombolysis, thrombectomy and extraanatomic bypasses can be applied in the treatment of graft leg occlusion. Thrombolysis treatment has disadvantages such as being time-consuming, causing embolism, bleeding, and causing new endoleak due to thrombosis in the aneurysm sac. In thrombectomy, there are risks such as separation of graft components and graft migration [24]. The authors recommend extraanatomic bypass due to patency rates over 90% [26]. In a recent study, high primary and secondary patency rates were reported, and extraanatomically femoro-femoral bypass is recommended in the treatment of graft leg occlusion [27]. We applied femoro-femoral bypass in the treatment of 35 of the 43 patients who developed occlusion, and we did not encounter any reocclusion during follow-up.

In light of the findings of our study, we can say that aortic anatomy, graft type, extending the graft to the external iliac artery, and the presence of underlying peripheral artery disease are serious risk

factors in the development of graft leg occlusion after EVAR. The study makes significant contributions to the literature by quantitatively demonstrating that the aortic neck angle and extension to the external iliac artery are important determinants of graft leg thrombosis. Through rigorous logistic regression and ROC analyses, we not only highlighted the predictive accuracy of these anatomical factors but also demonstrated that the risk of graft leg thrombosis is reduced with the use of PTFE grafts. We would like to emphasize that in order to minimize graft leg occlusion, the appropriate patient and graft type should be selected before the operation, the aortic anatomy should be revealed in detail, and if possible, patients who do not meet the instructions for use criteria should be avoided. Developing a treatment strategy by identifying patients at risk in advance will reduce complications and costs that may arise later. In the context of graft leg thrombosis, the results and analysis of our study show significant parallels with the literature, focusing specifically on the complex etiology of graft leg thrombosis and the factors that cause graft leg occlusion.

### Limitations

Although the study makes significant contributions to the understanding of GLT, it is acknowledged that there are some limitations that should be taken into account. First, the retrospective nature of the analysis may introduce inherent biases related to patient selection and data collection, potentially affecting the generalizability of the findings. Additionally, the study's sample size, although significant, was limited to a single institution. This could limit the applicability of the results to different populations with different clinical and demographic characteristics.

Moreover, the study focused predominantly on anatomical and procedural variables, possibly overlooking the influence of systemic factors such as patient comorbidities and medication use that may also influence the risk of graft limb occlusion. The complex interplay between these systemic factors and surgical intervention require further investigation.

Finally, although the statistical methods used in the study are comprehensive, they are based on the assumption that the models chosen accurately reflect the underlying biological phenomena. Future studies using prospective designs and multicenter collaborations may increase the robustness of the findings and contribute to a more nuanced understanding of graft limb occlusion.

In conclusion, our study provides important information on risk factors associated with GLT, providing a solid foundation for future research aimed at improving preventive and management strategies. Recognizing the limitations of this research will be crucial in guiding the design and conduct of subsequent studies to address remaining gaps in knowledge and improve patient care in vascular surgery.

## CONCLUSION

Our findings in our comprehensive study highlight the significant impact of anatomical factors such as the angle and diameter of the aortic neck, as well as the extension of the graft to the external iliac artery, on the risk of developing GLT. Furthermore, we have demonstrated that material selection plays an important role in reducing this complication. We believe that solid evidence has emerged supporting the need for personalized preoperative planning and selection of graft materials tailored to the patient's specific anatomical profile. In conclusion, our study provides important information on the risk factors associated with graft limb occlusion, providing a solid basis for future research aimed at improving preventive and management strategies.

**Ethics Committee Approval:** The approval of Ordu University Faculty of Medicine Clinical Research Ethics Committee, dated 27.12.2023 and decision no. 27/365 was obtained.

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