Long Stent Graft for Frozen Elephant Trunk Repair in Acute Type A Aortic Dissection

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Long stent graft for frozen elephant trunk repair in acute type A aortic dissection

Running Head: Safety and efficacy in long stent graft

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Abstract

Background: The frozen elephant trunk (FET) technique has become an important tool in the treatment of acute type A aortic dissection. The aim of this study was to evaluate the effect of long FET on spinal cord injury (SCI) and distal aortic remodeling after acute type A aortic dissection based on clinical and radiological outcomes.

METHODS: From January 2018 to November 2019, 158 patients [mean age 51.8 years (range 32 - 78 years), 88.6% male] with acute type A aortic dissection were treated by FET with 100 mm (*n*=113) or 150 mm (*n*=45) open hybrid stent graft prosthesis. Patients were divided into two groups according to the length of FET. The clinical and radiological outcomes of the patients were reviewed retrospectively.

RESULTS: Postoperative outcomes did not differ significantly: in-hospital mortality (9.7% *vs* 6.7%, *P*=0.758) and SCI (5.3% *vs* 2.2%, *P*=0.674). Aortic remodeling, which was evaluated by aortic diameter, true lumen diameter, false lumen diameter and the rate of false lumen complete thrombosis, was more positive in long FET group in the descending thoracic aorta during the follow-up period. At the abdominal level, there was no statistically significant difference between the two groups. In the long FET group, the level of complete false lumen thrombosis was more extensive during the follow-up period.

CONCLUSIONS: The long version of FET does not increase the risk of SCI in patients with acute type A aortic dissection. The application of long FET can achieve better results in terms of remodeling of the thoracic aorta in the short- and medium-term follow-up.

Key words: Frozen elephant trunk, Aortic dissection, False lumen thrombosis, Aortic remodeling

Background

The frozen elephant trunk (FET) technique has become an important tool in the treatment of various aortic diseases including acute type A aortic dissection [1-3]. This technique is used to close intimal tears in the proximal part of the descending aorta, to direct the blood flow in the true lumen (TL) and to seal the false lumen (FL) to prevent its dilatation [4-5]. However, 0-24% of patients develop spinal cord injury (SCI) after surgery [6-9], and 20-38% of patients develop negative remodeling of the distal descending aorta during follow-up, which may require secondary opening or endovascular repair to prevent rupture [10-12]. For the surgical concept dominated by closed intimal tears, whether the length of FET affects SCI and remodeling of the downstream aorta is still controversial.

In this study, we evaluated the effect of long FET on SCI and distal aortic remodeling after acute type A aortic dissection using clinical and radiological outcomes.

PATIENTS AND METHODS

Patients

From January 2018 to November 2019, 158 patients (140 males, 88.6%) with acute type A aortic dissection were treated by FET with open hybrid stent graft prosthesis (Cronus®, MicroPort Medical, Shanghai, China) at our institution. Mean age was 51.8 years (range 32 - 78 years). All patients were divided into two groups according to the length of FET inserted. A total of 113 patients were treated with the short version (short FET: 100 mm), and 45 patients were treated with the long version (long FET: 150 mm). All diagnoses were assessed by preoperative computed tomography angiography (CTA) and echocardiography. The clinical and radiological outcomes of patients were reviewed retrospectively. The preoperative characteristics of these patients are shown in Table 1. Clinical outcomes in all subjects were evaluated and aortic remodeling in 123 patients (87 short FET and 36 long FET) was investigated. The inclusion criteria were as follows: (i) patients were diagnosed with acute type A aortic dissection; (ii) dissection involved the aortic arch and descending aorta; and (iii) no previous surgical repair or endovascular repair of the descending aorta. When aortic remodeling was analyzed, 35 patients were excluded as they did not undergo CTA after surgery due to renal insufficiency (12, 7.6%), no preoperative CTA data(2, 1.2%), endoleak (5, 3.1%), hospital mortality (14, 8.9%), or lost to follow-up (2, 1.2%). This retrospective study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (No. GDREC2019840H(R1)). Individual written informed consent was obtained from each patient before surgery. All methods were performed in accordance with the guidelines and regulations.

Surgical technique

All surgical procedures were performed through a median sternotomy. The right axillary artery with or without the right femoral artery were exposed for arterial cannulation, and the superior and inferior vena cava were exposed for intravenous cannulation, and cardiopulmonary bypass was performed. Bladder temperature was cooled to 25-28℃, followed by circulatory arrest of the lower body with moderate hypothermia. Cerebral protection was achieved by unilateral or bilateral anterograde perfusion, and myocardial protection was achieved by intermittent anterograde perfusion of cold blood cardioplegic solution. After completion of aortic root repair, the aortic arch was laterally severed to the left subclavian level, and the FET stent was implanted into the true lumen of the aortic arch and descending aorta and deployed. The aortic arch was treated using the island technique or the branched prosthetic graft. At the end of the procedure, the aortic arch graft was anastomosed with the ascending aortic or root graft. Cerebrospinal fluid drainage was only performed in patients with paraplegia or paresis after surgery.

Data collection and follow-up

Clinical data were obtained from databases and outpatient or telephone follow-up. Clinical follow-up ended in July 2020 and was complete in 98.7% of patients. The median (1st–3rd quartile) follow-up time was 17 months (12–22 months).

All patients without renal insufficiency were required to undergo CTA before surgery, after 1 month, 3 months, 1 year and annually thereafter. Aortic remodeling (Figure 1) was measured by the aortic lumen (AL), TL, FL diameter, and FL thrombosis at the following six levels: level 1 (L1) at the level of the pulmonary artery bifurcation, which is usually covered by a stent after surgery; level 2 (L2) at the level of the tenth thoracic vertebra, which is not usually covered by the stent in the thoracic aorta; level 3 (L3) at the level of the diaphragm, which is the thoracic and abdominal aorta transition areas; level 4 (L4) at the level of the celiac trunk; level 5 (L5) at the level of the left renal artery; and level 6 (L6) at the level of the abdominal aorta bifurcation. AL and TL diameters were measured by the maximum length perpendicular to the free internal diaphragm. FL diameter was calculated by subtracting the TL diameter from the aortic diameter. According to the degree of FL patency, the degree of thrombosis was divided into three categories: no thrombosis, partial thrombosis and complete thrombosis.

The level of thoracic vertebrae corresponding to the distal end of the stent graft and distal complete thrombosis were measured by postoperative CTA.

Statistical analysis

The results are shown as *n* (%), mean±standard deviation or median (P25,P50). Statistical analysis was performed with SPSS 25.0 software (IBM Corp., USA). The Shapiro–Wilk test was used to verify the normal distribution. The Student's *t*-test was used to compare the groups of continuous variables with normal distribution, and the Mann–Whitney U-test was used to compare the groups of continuous variables without normal distribution or rank variable. The log-rank test was used to calculate statistical differences in the Kaplan–Meier survival estimates. Differences were considered significant when two-tailed *P*-values were < 0.05.

RESULTS

Preoperative data

Patient demographics and baseline characteristics are shown in Table 1. A total of 113 patients (99 males, 87.6%, aged 51.9±7.8 years) were treated with the short FET. Forty-five patients (41 males, 91.1%, aged 50.2±9.4 years) were treated with the long FET. The primary entry tears were located in the ascending aorta in 58 (51.3%) short FET and in 28 (62.2%) long FET, the aortic arch in 53 (46.9%) short FET and in 14 (31.1%) long FET. The remaining primary entry tears were located in the descending aorta. Baseline data were comparable between the two groups.

Intraoperative data

Patient intraoperative data are shown in Table 2. Concomitant procedures mainly included root replacement (31.1% *vs* 35.4%, *P*=0.608), root repair (62.2% *vs* 36.3%, *P*=0.003) and coronary artery bypass grafting (6.7% *vs* 9.7%, *P*=0.758) were not significantly different in the long FET and short FET group. The mean cardiopulmonary bypass time (251±61.0 *vs* 245.5±58.9 min, *P*=0.601) and hypothermic circulatory arrest time (22.9±11.0 *vs* 21.85±5.9 min, *P*=0.569) were equivalent, while cross-clamp time (147.7±38.7 *vs* 128.1±38.2 min, *P*=0.011) was shorter in the short FET group. The mean distal stent graft at the level of the thoracic vertebra was significantly longer in the long FET group (T8.5 *vs* T6.8, *P*<0.001).

Postoperative data

Patient postoperative data are summarized in Table 3. There was no significant difference between the two groups in overall in-hospital mortality [3/45 (6.7%) *vs* 11/113 (9.7%), *P*=0.758]. Major postoperative complications, including re-exploration due to bleeding, renal insufficiency requiring hemodialysis, stroke and endoleak were not significantly different between the two groups. Remarkably, paraplegia after surgery was also comparable in the long FET and short FET group [1/45 (2.2%) *vs* 6/113 (5.3%), *P*=0.674]. All patients with spinal paraplegia were treated with cerebrospinal fluid drainage, glucocorticoid and neurotrophic drugs. Three of these patients recovered from spinal paraplegia after treatment.

Aortic diameter changes at the downstream aorta

The changes in AL, TL and FL diameters at each level of the downstream aorta are presented in Figure 2. There was no significant difference in the preoperative aortic diameter of each segment of the downstream aorta between the two groups. At the level of L1, the increase in TL diameter and the reduction in FL diameter were greater in the long FET group at 1 month, 3 months and 12 months after surgery. The change in AL diameter was not significantly different between the two groups. At the level of L2, the postoperative AL and FL diameters were significantly smaller in the long FET group compared to those in the short FET group at 3 months and 12 months after surgery. At the level of L3, the AL and FL diameters were smaller in the long FET group at 12 months after surgery. At the level of L4, L5 and L6, the postoperative AL, TL and FL diameters were not significantly different between the two groups.

Thrombosis of the false lumen

The rate of complete FL thrombosis at each level after surgery is shown in Figure 3. At one month after surgery, the rate of complete FT thrombosis was higher at the level of L2 (83% *vs* 61%, P=0.022) and L3 (70% *vs* 45%, P=0.020) in the long FET group. At 3 months after surgery, the rate of complete FL thrombosis was higher at the level of L2 (78% *vs* 51%, P=0.050) in the long FET group. At 12 months after surgery, the rate of complete FL thrombosis at all levels showed higher trend in the long FET group; however, the difference was not statistically significant between the two groups.

The distal level of postoperative complete thrombosis of the FL was significantly different between the two groups, as shown in Table 4. In the long FET group, the level of complete FL thrombosis was more extensive at 1 month (T10 vs T11, P=0.019), 3 months (T10 vs T12, P=0.042) and 12 months (T10 vs L3, P=0.047).

Follow-up

During the follow-up period, none of the patients required re-operation of the distal aorta. Kaplan-Meier survival curves are shown in Figure 4. Follow-up survival was not significantly different between the two groups.

DISCUSSION

In acute type A aortic dissection, the use of FET has become an effective surgical strategy over the past few decades [4,11,13]. This technique is used to seal the tear in the proximal descending aorta, enlarge the TL, and shrink the FL. The main advantages of this technique are to stabilize a range of descending aorta dissections, reduce the possibility of re-intervention, and exclude the occurrence of retrograde aortic dissection [7,14]. Moreover, the FET technique can be used for secondary opening and endovascular repair if necessary, as it offers a better landing zone for endovascular completion and makes an open surgical completion possible [15].

Although FET has shown encouraging results in the treatment of acute type A aortic dissection [1-3,12], SCI is still considered one of the most devastating complications after surgery. As shown in the literature, the incidence of SCI ranges from 0 to 24% [6-9]. In the present study, 7/158 (4.4%) of patients developed postoperative SCI. Traditionally, postoperative SCI was thought to be caused by the occlusion of critical intercostal arteries which perfuse the spinal cord, particularly the Adamkiewicz artery [7]. Flores and colleagues [7] recommended that a distal landing zone of T7 or lower was an independent risk factor for SCI in multivariate analysis. Similarly, Mizuno and colleagues [16] reported that the incidence of SCI was significantly higher when the distal landing zone was T8.

However, in our series, the long FET group had a mean distal landing zone of T8.5, which did not increase the incidence of SCI compared with the short FET group (2.2% *vs* 5.3%, P=0.674). This suggested that no significant increase in the incidence of SCI was observed when more intercostal arteries were occluded. This result is similar to that of Hoffman and colleagues [8], who reported that the risk of SCI was not increased even when the FET reached T10-12. They also considered that total occlusion of the intercostal arteries down to T10-12 may reduce the risk of SCI for future interventions

[8]. Kozlov and colleagues [17] also recommended that an additional thoracic stent graft implanted down to the celiac artery after FET, which covered more intercostal arteries, would not increase the incidence of SCI. This result can be explained by the collateral network theory suggested by Griepp and colleagues [18], which is based on the fact that the spinal cord is fed by intercostal arteries, and branches of the vertebral and iliac arteries. When the extensive coverage of intercostal arteries was occluded by FET, the remaining intercostal arteries, vertebral arteries, and iliac arteries, along with their collateral network, gradually adapted and continued to provide adequate blood to the spinal cord [18].

As a matter of fact, the descending aorta still changes dynamically after surgery. Postoperative dilatation of the distal aorta is the major factor that threatens the survival of patients. As mentioned in other literature [13,19], in the thoracic segment, the TL increased, the FL decreased, and the total diameter remained stable compared with pre-operation, while in the abdominal segment, the TL remained stable, the FL and AL diameter increased gradually. In our series, the results in both the long FET and short FET groups were similar to those mentioned above. It should be noted that the long FET group showed better remodeling in the postoperative changes of the thoracic levels. In the descending thoracic aorta, the TL remained stable due to the covered stent, while the FL gradually formed thrombosis due to proximal occlusion and progressive obliteration [20]. The better remodeling effect in the long FET group may have been due to the fact that more of the TL was stabilized by the stent, and the longer FL was occluded to form a thrombosis and gradually absorbed.

In addition to the increase in the TL and the decrease in the FL, complete thrombosis of the FL is also one of the main indicators of favorable aortic remodeling [21]. In the absence of complete thrombosis of the FL, the wall of the FL would not be able to withstand the internal aortic pressure, leading to subsequent dilatation. A residual patent FL in the downstream aorta was reported as a predictor of both distal aortic enlargement and late mortality [22-24]. Actually, the rate of complete thrombosis of the FL varies at different levels of the downstream aorta [13,25]. It has been reported that the rate of complete thrombosis of the FL along the stent in the early postoperative period is 70–100%, whereas the probability of FL complete thrombosis at the level of the abdominal aorta is only 14–37% [17,25]. In our study, we observed a similar trend to the above in terms of complete thrombosis of the FL of the descending aorta in both groups. The rate of complete FL thrombosis at the thoracic levels showed a higher trend in the long FET group. While in the abdominal segment, there was no statistically significant difference in thrombosis levels between the two groups.

As Hoffman and colleagues [8] reported, the longer version of the FET allows more extensive aortic dissection to be repaired, and can limit the residual type B aortic dissection to a shorter level. At the distal aorta, proximal occlusion is eliminated due to reentry of the dissection and the branching vessels of the abdominal aorta. This may explain the lower rate of complete thrombosis at the abdominal level.

Limitations

Our study had some limitations. The design of the study was retrospective, and the follow-up was relatively short. Nonetheless, we consider our results to be meaningful. A larger patient sample and longer follow-up results will be reported in a future study.

CONCLUSION

It is encouraging that the long FET did not increase the risk of SCI in the treatment of patients with acute type A aortic dissection. In addition, the application of long FET can achieve better results in remodeling of the thoracic aorta in the short- and medium-term follow-up.

Abbreviations

FET: frozen elephant trunk; TL: true lumen; FL: false lumen; SCI: spinal cord injury; CTA: computed tomography angiography; LAL: all lumen of the long FET, LTL: true lumen of the long FET, LFL: false lumen of the long FET, SAL: all lumen of the short FET, STL: true lumen of the short FET, SFL: false lumen of the short FET. SFET: short frozen elephant trunk, LFET: long frozen elephant trunk.

Declarations

This retrospective study was approved by the ethics committee of Guangdong Provincial People’s Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China. Written informed consent was obtained from the patients and their legal relatives.

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Not applicable.

Authors’ contributions

WCJ, ZWQ and PJH contributions to conceptualization and design, or acquisition of data, or analysis and interpretation of data, involved in drafting, reviewing and editing the manuscript; HJ and CGT contributions to acquisition of data, involved in reviewing and editing the manuscript; WM, HJS and FRX analysis and interpretation of data, involved in reviewing and editing the manuscript; FXP revising it critically for important intellectual content. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This retrospective study was approved by the ethics committee of Guangdong Provincial People’s Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China (No. GDREC2019840H(R1)). Written and informed consent was obtained from the patients included in this study.

Consent for publication

Not applicable.

Competing interests

Not applicable.

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TABLES

Table 1: Patient characteristics

Table 2: Intraoperative characteristics

Table 3: Clinical and aortic outcome

Table 4: The distal level of complete thrombosis thrombosis

FIGURES

Figure 1: Computed tomographic angiography showed aortic imaging after frozen elephant trunk.

Figure 2: Aortic, true lumen and false lumen diameter change at each level of the descending aorta at each time period. LAL: all lumen of the long FET, LTL: true lumen of the long FET, LFL: false lumen of the long FET, SAL: all lumen of the short FET, STL: true lumen of the short FET, SFL: false lumen of the short FET.

Figure 3:Rate of complete false lumen thrombosis in each level after surgery. SFET: short frozen elephant trunk, LFET: long frozen elephant trunk.

Figure 4: Kaplan–Meier estimates of survival probability.

Table 1: Patient characteristics

Variables	Total (n=158)	Short FET (n=113)	Long FET (n=45)	P-value
Age (years), mean ± SD	51.4±8.3	51.9±7.8	50.2±9.4	.255
Male gender, n (%)	140（88.6）	99（87.6）	41(91.1)	.532
Time from onset to surgery (day), median [IQR]	4 (2,8)	4 (2,7)	4.5 (2,10)	.358
Hypertension, n (%)	114（72.2）	84（74.3）	30（66.7）	.332
Diabetes Mellitus,n(%)	6（3.8）	4（3.5）	2（4.4）	1.000
Smoking history, n (%)	23（14.6）	18（16.1）	5（11.1）	.427
Marfan’s syndrome,n (%)	3（1.9）	2（1.8）	1（2.2）	1.000
Coronary artery disease,n (%)	8（5.1）	5（4.4）	3（6.7）	.689
History of stroke,n (%)	8（5.1）	6（5.3）	2（4.4）	1.000
Aortic regurgitation, n (%)				
Moderate	33(20.9)	25(22.1)	8(17.8)	.208
Severe	20(12.7)	11(9.7)	9(20.0)	
Location of primary entry tear, n(%)				
Ascending aorta	86(54.4)	58(51.3)	28(62.2)	.081
Aortic arch	67(42.4)	53(46.9)	14(31.1)	
Descending aorta	5(3.1)	2(1.8)	3(6.7)	
Distal extent of aortic dissection, n(%)				
Thoracic descending aorta	11（7.0）	7（6.2）	4（8.9）	.294
Aorta abdominalis	25（15.8）	21（18.6）	4（8.9）	
Iliac artery	122（77.2）	85（75.2）	37（82.2）	

Table 2. Intraoperative Characteristics

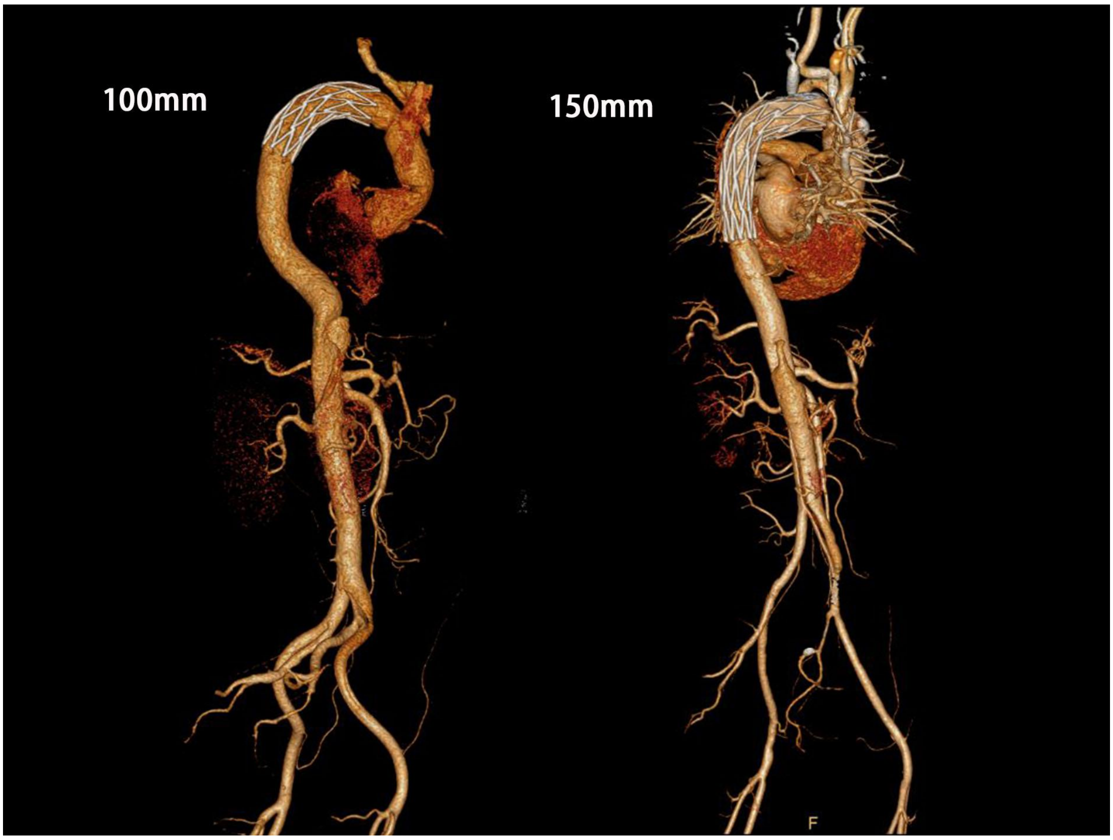
Variables	Total (n=158)	Short FET (n=113)	Long FET (n=45)	P-value
Cardiopulmonary bypass time (min), mean ± SD	247.8±59.5	245.5±58.9	251±61.0	.601
Cross-clamp time (min), mean ± SD	135.6±39.4	128.1±38.2	147.7±38.7	.011
hypothermic circulatory arrest time (min), mean ± SD	22.3±8.2	21.85±5.9	22.9±11.0	.569
Concomitant procedures，n(%)				
Root replacement	54(34.2)	40(35.4)	14(31.1)	.608
Root repair	69(43.7)	41(36.3)	28(62.2)	.003
Coronary artery bypass grafting	14(8.9)	11(9.7)	3(6.7)	.758
Proximal anastomosis zone, n (%)				
Z1	26（21.5）	20（22.7）	6（18.2）	.588
Z2	95（78.5）	68（77.3）	27（81.8）	
Distal stent graft at the level of thoracic vertebra, mean ± SD	**T7.3±1.0**	**T6.8±0.7**	**T8.5±0.7**	**.000**

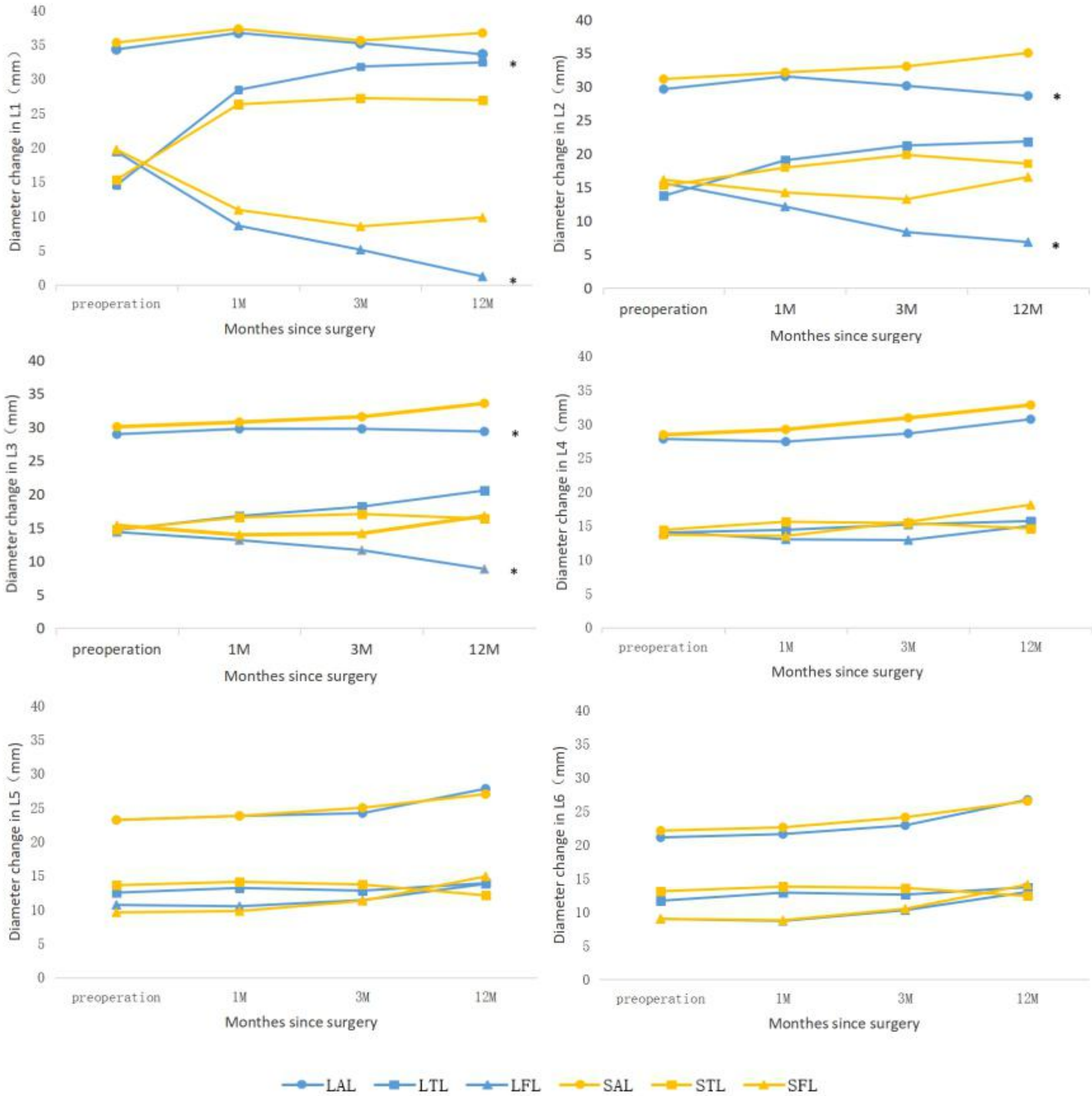
Table 3. Clinical and aortic outcome

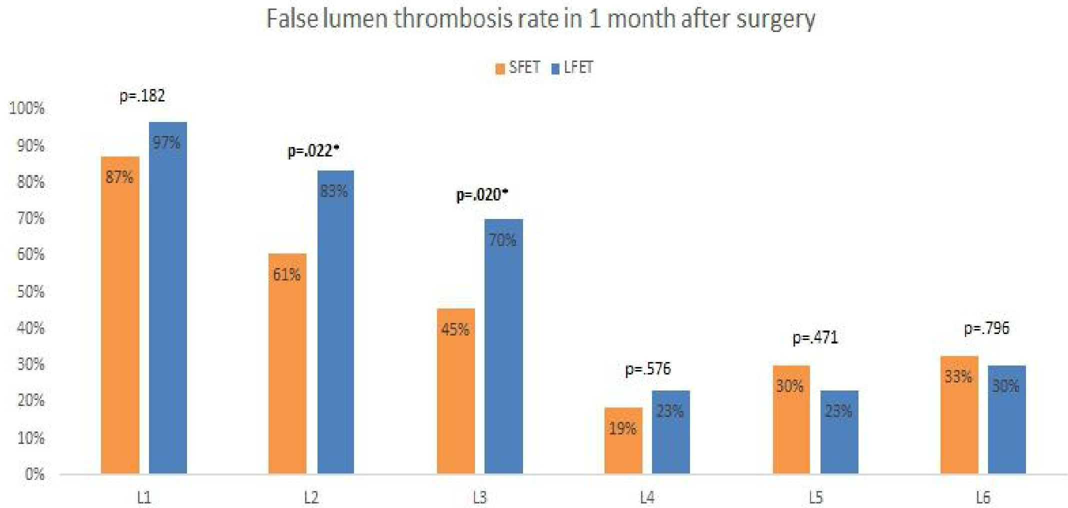
Variables	Total (n=158)	Short FET (n=113)	Long FET (n=45)	P-value
Re-exploration for bleeding，n(%)	6（3.8）	3（2.7）	3（6.7）	.353
Stroke，n(%)	20（12.7）	14（12.4）	6（13.3）	.872
Paraplegia，n(%)	**7（4.4）**	**6（5.3）**	**1（2.2）**	**.674**
Renal failure，n(%)	42（26.6）	32（28.3）	10（22.2）	.434
Endoleak，n(%)	5 (3.1)	3 (2.7)	2 (4.4)	.624
ICU stay among survivors (days), mean ± SD	8（5，11）	8（5，11）	8（5，11）	.987
Hospital stay among survivors (days), mean ± SD	23（18，31）	22（17，29）	24（20，36）	.066
Operative mortality，n(%)	14（8.8）	11（9.7）	3（6.7）	.758

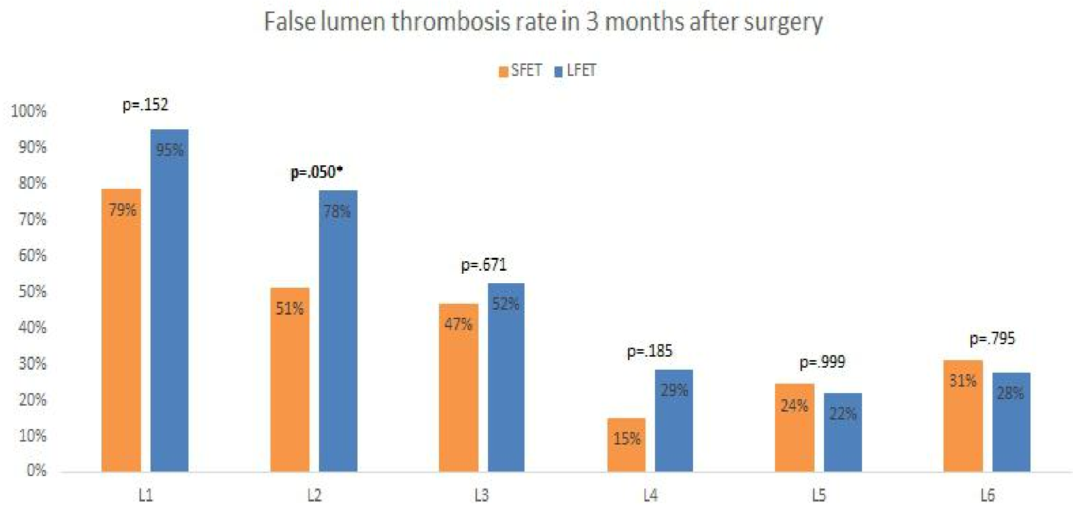
Table 4. The distal level of complete thrombosis.

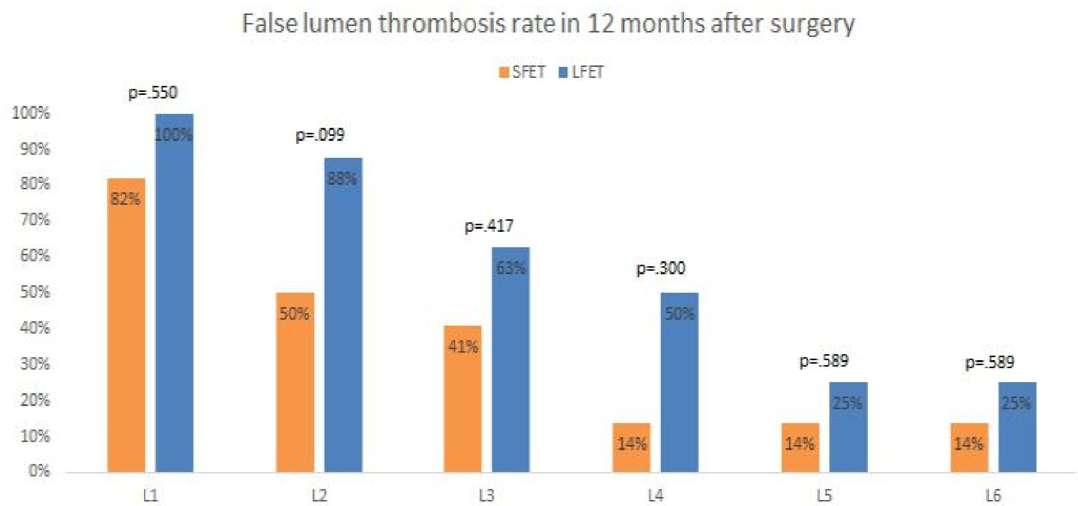
Variables	Short FET	Long FET	P-value
1 month	**T10 (T8, T12)**	**T11 (T10, T12)**	**.019**
3 months	**T10 (T7, T12)**	**T12 (T9, L3)**	**.042**
12 months	**T10 (T7, T12)**	**L1 (T10, L3)**	**.047**

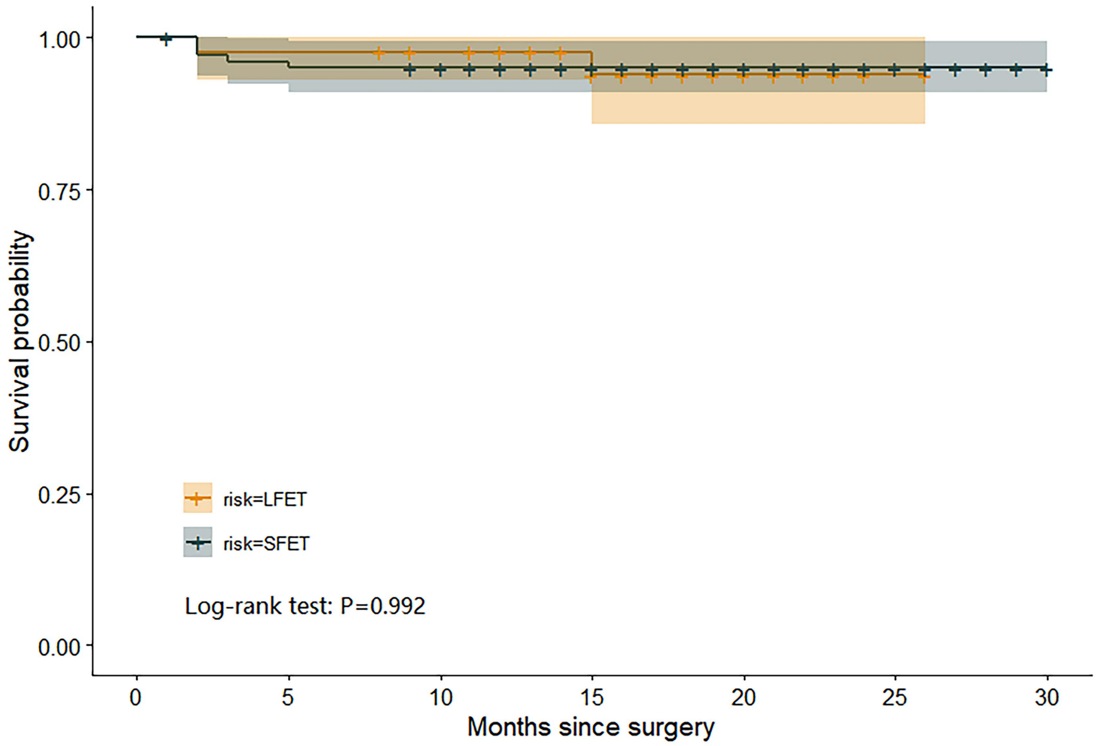

100mm
150mm
F


Diameter change in L1（mm）
Diameter change in L2（mm）
Diameter change in L3（mm）
Diameter change in L4（mm）
Diameter change in L5（mm）
Diameter change in L6（mm）
0
5
10
15
20
25
30
35
40
preoperation
1M
3M
12M
Monthes since surgery
*
LAL
LTL
LFL
SAL
STL
SFL


False lumen thrombosis rate in 1 month after surgery
SFET
LFET
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
p=.182
87%
97%
p=.022*
61%
83%
p=.020*
45%
70%
p=.576
19%
23%
p=.471
30%
23%
p=.796
33%
30%
L1
L2
L3
L4
L5
L6


False lumen thrombosis rate in 3 months after surgery
SFET
LFET
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
p=.152
79%
95%
p=.050*
51%
78%
p=.671
47%
52%
p=.185
15%
29%
p=.999
24%
22%
p=.795
31%
28%
L1
L2
L3
L4
L5
L6


False lumen thrombosis rate in 12 months after surgery
SFET
LFET
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
p=.550
82%
100%
p=.099
50%
88%
p=.417
41%
63%
p=.300
14%
50%
p=.589
14%
25%
p=.589
14%
25%
L1
L2
L3
L4
L5
L6


1.00
0.75
0.50
0.25
0.00
Survival probability
risk=LFET
risk=SFET
Log-rank test: P=0.992
0
5
10
15
20
25
30
Months since surgery

Figures

Figure 1

Computed tomographic angiography showed aortic imaging after frozen elephant trunk

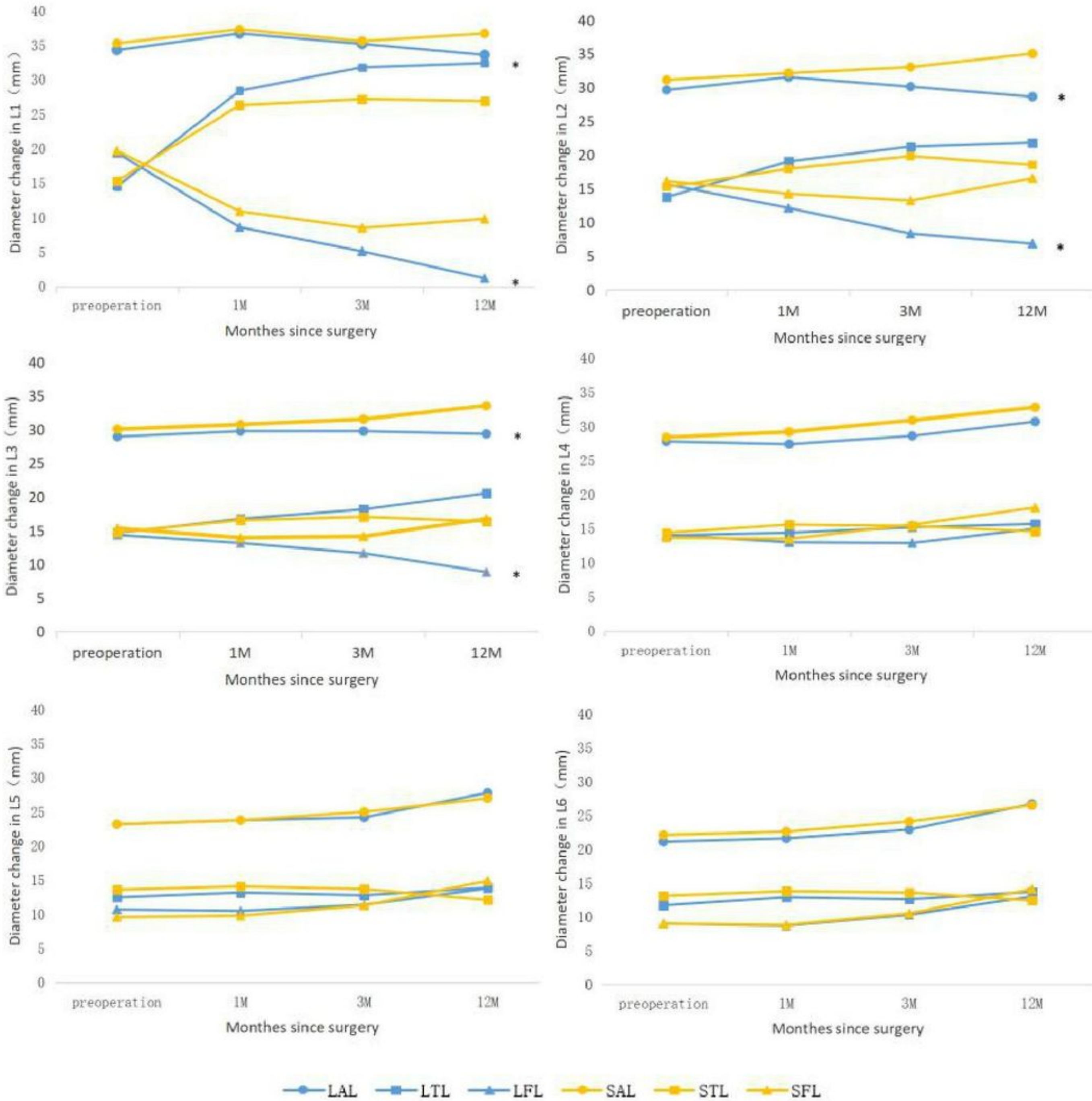


Figure 2

Aortic, true lumen and false lumen diameter change at each level of the descending aorta at each time period. LAL: all lumen of the long FET,LTL: true lumen of the long FET,LFL: false lumen of the long FET,SAL: all lumen of the short FET, STL: true lumen of the short FET,SFL: false lumen oftheshortFET.

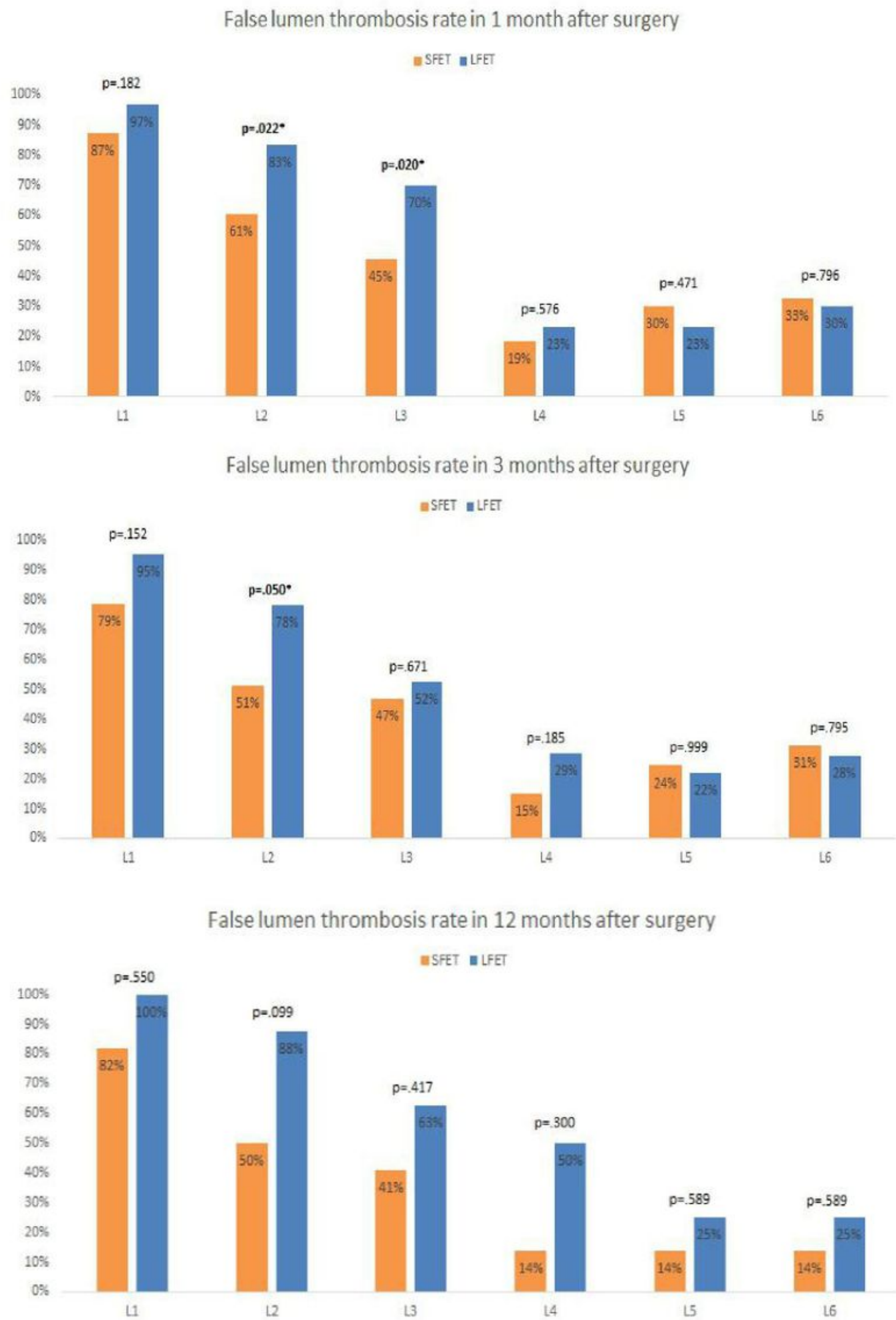


Figure 3

Rate of complete false lumen thrombosis in each level after surgery. SFET: short frozen elephanttrunk,LFET:longfrozenelephanttrunk

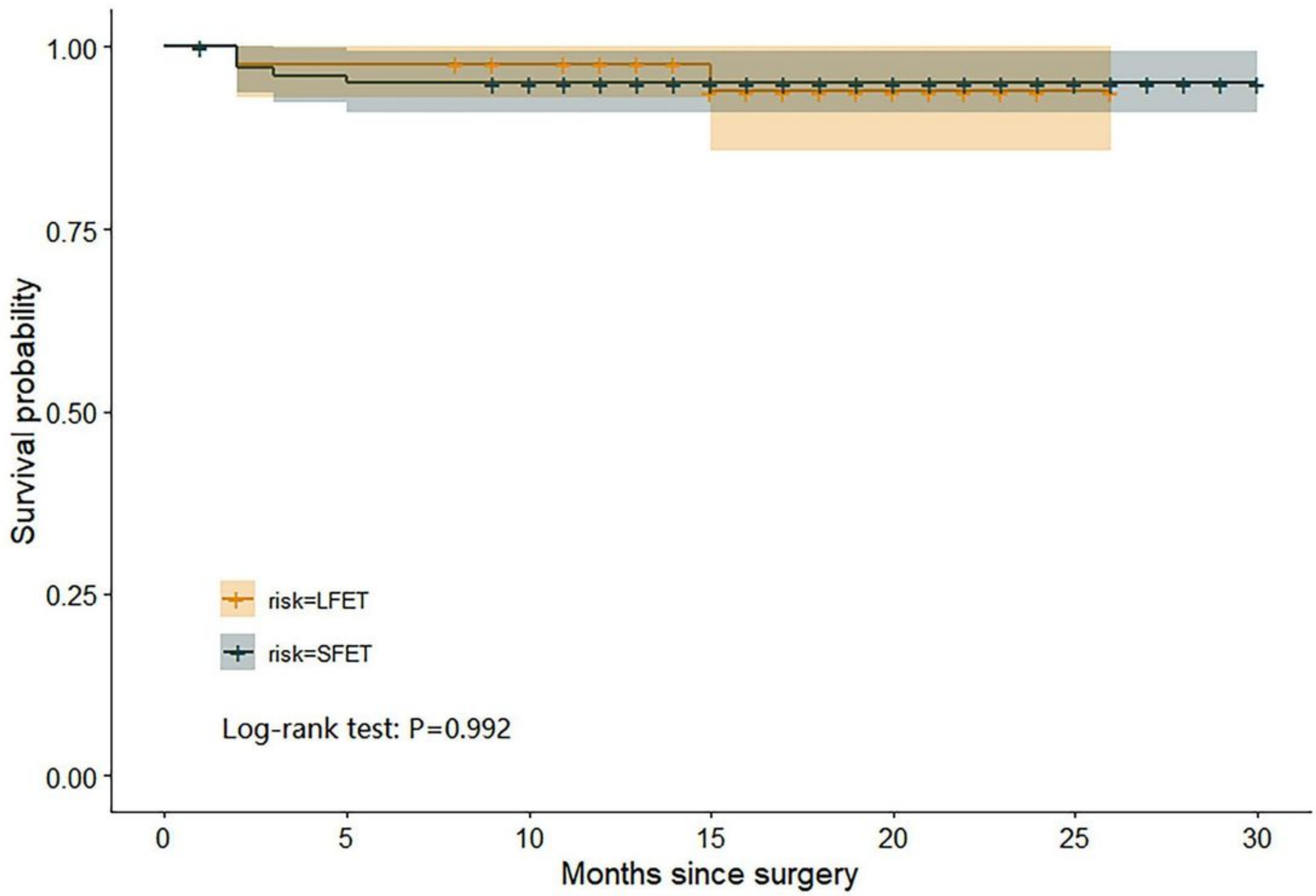


Figure 4

Kaplan–Meier estimates of survival probability