Preliminary results of single centre experience with the "release and perfuse technique" during aortic arch surgery.

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Abstract

Background and aim of the study To evaluate whether the release and perfuse technique implies a circulatory arrest time comparable with or shorter than those of standard Frozen Elephant Trunk technique in aortic arch surgery. **Methods** We retrospectively reviewed the records of patients who had undergone aortic arch repair with Release and Perfuse Technique (RPT) or standard Frozen Elephant Trunk (FET) at our Institution between January 2018 and May 2021. Primary endpoints were the comparison of circulatory arrest time, perioperative variables, and complications between two groups. A propensity score weighting approach was used for data analysis. **Results** A total of 41 patients underwent aortic arch surgery were analyzed:15 (37%) and 26 (63 %) in RPT and FET group, respectively. The use of RPT showed a significant shorter circulatory arrest times than FET: 9 min vs 58 min ($P < 0.001$), respectively. The median lactates peak in the first 24h post intervention was 2.6 for RPT group and 5.4 mmol/L for FET group, ($P < 0.0001$). When compared with the FET, RPT is associated with significant reduction in the use of packed red blood cells ($P < 0.0001$), fresh frozen plasma ($P < 0.0001$), platelet concentrate ($P < 0.0001$), and fibrinogen ($P < 0.004$). The median ICU stay was 3 and 9 days ($P = 0.011$), whereas the median hospital stay was 12 and 18.5 days ($P=0.004$) in the RPT and FET groups, respectively. Thirty-day mortality and postoperative outcomes were comparable between the two groups. **Conclusions** Considering the anatomical limitations related to the use of this technique, the RPT appears to be safe, feasible, and effective in reducing the circulatory arrest time during aortic arch surgery. Nevertheless, further studies are required to demonstrate its safety and efficacy.

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Patient consent statement and Permission to reproduce material from other sources

It is declared that every reasonable effort was made to obtain written informed consent to participate in this study. Notably, the use of data for scientific and research purposes is already included in the written informed consent agreements in use at our Centre. The local ethic committee approved of the study design, consent process, and review and analysis of the data.

We also guarantee the respect of anonymity and professional secrecy and use the collected data and the statistical analysis solely for the scientific purposes granted in accordance with the law in force (GDPR).

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Author contributions statement

Antonio Piperata: Conceptualization, data collection, writing.

Nicolas d'Ostrevy: Data collection.

Olivier Busuttil: Data collection.

Thomas Modine : Review and editing, supervision

Giulia Lorenzoni: statistical analysis

Danila Azzolina: statistical analysis

Louis Labrousse : Supervisor

Mathieu Pernot: Project administration, critical revision of article, approval of article, supervisor.

ABSTRACT

Background and aim of the study

To evaluate whether the release and perfuse technique implies a circulatory arrest time comparable with or shorter than those of standard Frozen Elephant Trunk technique in aortic arch surgery.

Methods

We retrospectively reviewed the records of patients who had undergone aortic arch repair with Release and Perfuse Technique (RPT) or standard Frozen Elephant Trunk (FET) at our Institution between January 2018 and May 2021. Primary endpoints were the comparison of circulatory arrest time, perioperative variables, and complications between two groups. A propensity score weighting approach was used for data analysis.

Results

A total of 41 patients underwent aortic arch surgery were analyzed:15 (37%) and 26 (63 %) in RPT and FET group, respectively. The use of RPT showed a significant shorter circulatory arrest times than FET: 9 min vs 58 min ($P < 0.001$), respectively. The median lactates peak in the first 24h post intervention was 2.6 for RPT group and 5.4 mmol/L for FET group, ($P < 0.0001$). When compared with the FET, RPT is associated with significant reduction in the use of packed red blood cells ($P < 0.0001$), fresh frozen plasma ($P < 0.0001$), platelet concentrate ($P < 0.0001$), and fibrinogen ($P < 0.004$). The median ICU stay was 3 and 9 days ($P = 0.011$), whereas the median hospital stay was 12 and 18.5 days ($P=0.004$) in the RPT and FET groups, respectively. Thirty-day mortality and postoperative outcomes were comparable between the two groups.

Conclusions

Considering the anatomical limitations related to the use of this technique, the RPT appears to be safe, feasible, and effective in reducing the circulatory arrest time during aortic arch surgery. Nevertheless, further studies are required to demonstrate its safety and efficacy.

Abbreviations

ACP : Antegrade Cerebral Perfusion

AVR: Aortic Valve Replacement

COPD : Chronic Obstructive Pulmonary Disease

CPBS : Covariate Balance Propensity Score

CPB : Cardio-Pulmonary Bypass

CT : Computer Tomography

ET : Elephant Trunk

FET : Frozen Elephant Trunk

ICU : Intensive Care Unit

LVEF : Left Ventricle Ejection Fraction

RPT : Release and Perfuse Technique

INTRODUCTION

The modern evolution of the classic Elephant Trunk (ET) technique is the Frozen Elephant Trunk

(FET), which is the result of technical and device modifications over decades with the main purpose to reduce complications (1,2). Although FET allows to perform a complete single-stage treatment in extended thoracic aortic disease, the early outcome is still suboptimal due to the complex surgical technique, patient's anatomy, and different pathological settings (2,3).

In this context, the problem of circulatory arrest time is still unsolved, and the standard FET, although safe, does not ensure satisfactory abdominal protection (4). Thus, to reduce the circulatory arrest time, many simplifications of the technique have been proposed. These include the proximalization of the distal anastomosis from zone 3 to zone 2, endovascular techniques or the use of new devices (5-11).

Our group recently described the simplified FET called "release and perfuse technique" (RPT) using the Thoraflex Hybrid prosthesis (Vascutek Terumo, Inchinnan, Scotland, UK) to minimize the circulatory arrest time (12). This technique does not require additional surgical skills or device, but it simply consist in the lower body reperfusion before starting the distal anastomosis.

In this work we compared the preliminary results of the use of RPT with those of standard FET in our single centre experience with the main objective of contributing to the introduction of a new possible strategy in the armamentarium of aortic arch surgery.

Materials and Methods

Study population

From January 2018 we started to use the Thoraflex Hybrid prosthesis for FET procedures at our Institution. Up to June 2021, a total of 41 patients were successfully treated with this prosthesis, and fifteen of them were treated with the use of the RPT, introduced in October 2019.

Baseline and preoperative characteristics of the overall population are shown in Table 1.

The primary indication for surgery included acute type A aortic dissection (ATAAD), chronic type B aortic dissection, and chronic aneurysms. Cerebral protection was ensured through the antegrade selective cerebral perfusion with mild-to-moderate hypothermia. The analysis of the surgical outcomes was performed by reviewing electronic health records, and the results are presented according to the different aortic diseases.

Operative technique

The Release and Perfuse Technique (RPT):

The surgical protocol applied in Bordeaux University Hospital has been previously described in detail (12,13). Here we propose a short explanation of the procedure. All operations were performed by senior surgeons with extensive experience in aortic arch surgery at our department using standard general anesthesia. The cardiopulmonary bypass (CPB) is established by the right axillary artery and central venous cannulation as previously described (13). During the cooling of the patient, the arterial cannula (20 Fr, EOPA, Medtronic, Minneapolis, MN, USA) is inserted into the fourth branch of the Thoraflex Hybrid and then securitized. At the target temperature, CPB flow is reduced, the supra-aortic vessels are clamped, and standard CPB is switched to unilateral brain perfusion. The arch is then completely opened and inspected. The prosthesis is then introduced in an antegrade fashion in the descending aorta and released (figure 1). Two 4-0 polypropylene U-stitches with pledgets are used to fix the sewing collar of Thoraflex with the aortic wall.

At this point, a second arterial line is connected to the cannula previously placed into the fourth branch of Thoraflex. The antegrade blood flow is slowly restored to fill the abdominal and descending aorta. Once the prosthesis is completely full of blood, de-airing is done, and the proximal part of the prosthesis and its branches are clamped (figure 1). The full arterial flow is now slowly restarted to perfuse the lower body, and the patient progressively rewarmed. The distal anastomosis is performed between the incorporating sewing collar of the Thoraflex and the aorta, starting from the previously prepared 2 U-stitches (figure 2).

The supra-aortic vessels are anastomosed to the branches of the graft, and the operation is completed with an aortic root procedure if necessary.

Classic frozen elephant trunk (FET)

All patients underwent median sternotomy. The CPB is established by right axillary artery and central venous cannulation. Once the target temperature was reached, a period of circulatory arrest followed, allowing for inspection of the aortic arch, the deployment of Thoraflex Hybrid prosthesis and the distal anastomosis. The cerebral protection is allowed through the antegrade perfusion by clamping the supra-aortic vessels just before the opening of the aortic arch.

Once the distal anastomosis is completed, CPB is reinstituted through the side branch of Thoraflex Hybrid prosthesis. The supra-aortic branches are anastomosed, and aortic root procedure added if necessary.

Indication and choice of the strategy

During the study period, the choice of which strategy to use in case of aortic arch surgery was made based on the anatomical characteristics of each patient. The first step was the evaluation of the feasibility of the RPT. For each patient the decision to perform RPT was discussed in a group of experienced surgeons which made an accurate and meticulous investigation of the descending aortic landing zone size, as assessed by computer tomography (CT) scan. This step was mandatory before choosing the stent-graft's size in case of RPT.

Whenever the endoleaks were anticipated during the CT scan evaluation (including the lack of appropriate collar at the landing zone or an aortic lumen diameter too large for performing a stent oversizing), the RPT was considered infeasible then the strategy switched to classic FET.

Figure 3 reports the criteria used to choose the stent-graft size. The aim is to perform an over-sizing of about 15% in case of degenerative aortic aneurysms, and about 5-10% derived from the maximal diameter of true lumen in case of aortic dissection, in order to avoid any aortic injury caused by radial force of the stent on the aortic wall.

STATISTICAL ANALYSIS

The descriptive statistics have been reported summarizing the continuous data as I quartile, median, and III quartiles; categorical data are instead reported as a percentage and absolute frequencies. Wilcoxon-type tests were performed for continuous variables and the Pearson chi-square test, or Fisher-exact test whatever appropriate, for categorical variables.

A Covariate Balance Propensity Score (CBPS)[14] estimation has been estimated accounting for baseline confounding variables. The features included in the CBPS computation were: 1) Age, 2)Gender, 3)dissection type, 4)Aortic aneurysm, 5)High blood pressure, 6)Dyslipidemia, 7)Diabetes, 8)Preoperative intubation 9)REDO surgery, 10)Preoperative stroke, 11)Baseline COPD, 12)EUROSCORE, 13)LVEF. The CBPS balancing performance has been assessed via visual inspection of the mean difference (MD) plot (Figure 4). The variable having a post propensity estimated MD lower than 0.1 (15) were considered unbalanced after the CBPS estimation. The common support propensity score density plot has been also reported (figure 4). The overlap across the propensity densities between intervention groups indicates that the individuals who received the intervention have comparable propensity distributions with respect to those who did not. This is an indication of a suitable CBPS estimation balance (16).

Logistic regression model estimates for binary endpoints and linear regression model estimates for continuous one have been carried out. The models have been adjusted for propensity score via Inverse Probability Weights (IPW) estimation. The p-values for multiple outcomes have been adjusted via Benjamini-Hochberg correction. Analyses have been conducted with R 3.4.2 with rms and WeightIt packages.

RESULTS

From January 2018 we started to use the Thoraflex Hybrid prosthesis for FET procedures, and from October 2019 we introduced the release and perfuse technique. During this period, a total of 41 (76% males) was successfully treated with this prosthesis. Baseline and preoperative characteristics of the overall population are shown in Table 1.

The use of RPT was associated with significantly shorter circulatory arrest time [9 (8-13) min vs 58 (48-65) min, ($p < 0.0001$)]. The median lowest core temperature was 29°C (28–31) for RPT and 26.5 °C (25–27) for FET group, ($p < 0.0001$). Tables 2 and 3 show the intraoperative and postoperative details. There was no significant difference between the 2 cohorts in terms of 30-day mortality ($P = 0.185$). The RPT revealed a significantly reduced use of number of packed blood transfusion during the operative time and the first 24 hours compared with FET. These include red blood cells [1 (0-1) vs 4 (3.2-5.8), ($p < 0.0001$)], fresh frozen plasma [0.5 (0-1) vs 3 (2-4), ($p < 0.0001$)], platelets [0 (0-0) vs 3 (3-4), ($p<0.0001$)], and fibrinogen [2 (2-2.5) gr vs 3 (3-4.8) gr, ($p = 0.004$)].

The median lactates peak reported during the first 24h post intervention was 2.6 for RPT group and 5.4 mmol/L for FET group, ($p < 0.0001$).

The use of RPT was associated with shorter intensive care unit stay ($p=0.011$) and hospital stay ($p = 0.004$), compared with FET. No others statistical differences were reported between two cohorts in terms of post-operative complications.

CONCUSION

Since its introduction in clinical practice, the FET technique with modern hybrid prostheses has represented an important milestone in the treatment of complex lesions of the thoracic aorta (1).

However, the main limitation of this technique is related to the circulatory arrest time which includes the deployment of the prosthesis and the time required to perform the distal anastomosis (2-3).

The most important finding of our work is that the RPT can significantly reduce the circulatory arrest time by performing the distal anastomosis during the antegrade lower body reperfusion. This finding could support and explain few more favourable consequences.

Firstly, the RPT reducing the circulatory arrest time and therefore the visceral ischemic time, is associated with a significant lower postoperative lactates values. This can be considered an indirect parameter of effective abdominal perfusion. Secondly, the significatively shorter circulatory arrest times expose patients to hypothermia for shorter periods, reducing all the risks related to low temperatures (17-19). The effects are undoubtedly translated into reduced blood transfusions and an easier hemostasis phase. Lastly, minimizing all these criticisms could play a key role in reducing postoperative complications and the length of hospitalization.

It is important to highlight that our results showed a significantly shorter times of CPB and Crossclamp in the RPT group. In our opinion, this finding, although significant, does not constitute an advantage related to the use of the RPT technique. In fact, the FET group compared with RPT group includes more combined procedure as 2 cases of cabg, 1 case of AVR, 1 case of Bentall. Furthermore, one of 3 cases of valve sparing performed in FET group required a second aortic cross clamp to correct the valve repair. We are aware that in such a small series as ours here proposed, the timing required to perform these concomitant procedures in the standard FET group had a significant impact in increasing CPB and crossclamp times.

Regarding the technical aspect of the RPT, we want to highlight that, despite our short experience, we have not reported any case of aortic injury or endoleaks at the level of the landing zone. Moreover, after deploying the Thoraflex prosthesis, full blood flow through the side branch was achieved in all patients without reporting any case of backflow at the level of the sewing collar. However, in case of occurrence, we propose to reduce the pump output until a bloodless surgical field is obtained, sufficient to perform the distal anastomosis.

In addition, the RPT can be easily performed even in complicated settings, such as type A aortic dissection, type B aortic dissection, and chronic aneurysm, without requiring specific surgical's skills or other devices. Up to now several surgical groups have proposed various modifications of the classic FET procedure with the common goal of reducing the circulatory arrest time. These include the proximalization of the distal anastomosis from zone 3 to zone 2, and 1 or the use of new prostheses (5-11). Di Eusanio and colleagues (20) had recently published a hybrid technique to perform complex aortic arch surgery avoiding circulatory arrest time and remaining normothermic. This technique involving the use of balloon endoclamping and femoral cannulation seems to be promising, and it represents the last effort of surgical community to resolve the problem of circulatory arrest time during aortic arch surgery (20-22).

Similar to the RPT, Senage et al. (23) have recently described a modified FET technique in which the lower body reperfusion precedes the distal anastomosis. Despite some technical differences with the RPT (i.e. the proximalization of the distal anastomosis and the use of two tourniquets to avoid backflow on the operative field) this approach appears to be feasible in specific anatomic settings.

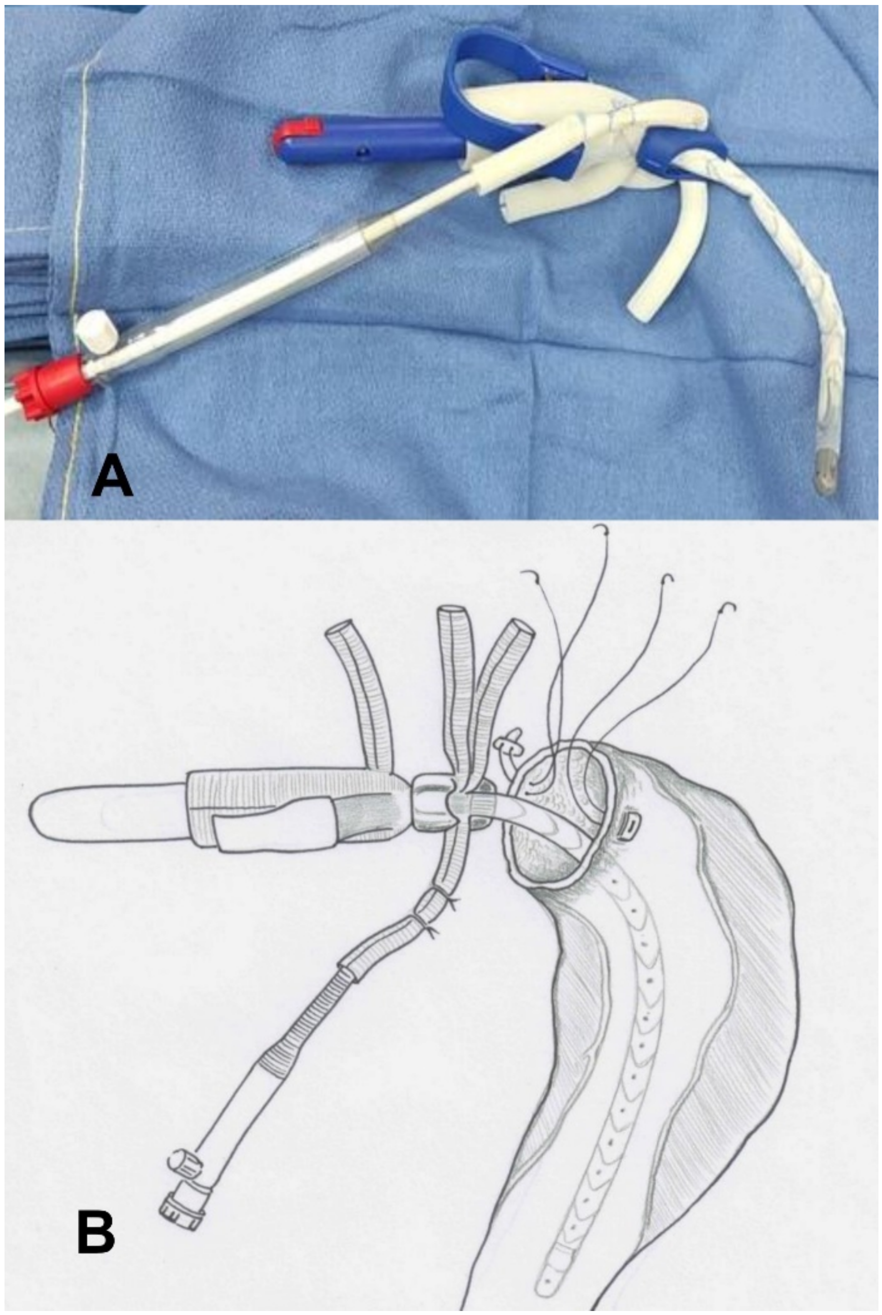
The technique that we proposed represents another "fish in the sea", but despite the limitations related to the seal of the landing zone, the RPT appears to be safe and effective in reducing the circulatory arrest time. Moreover, there is an undisputed need to simplify the complex aortic procedures and endovascular techniques are playing a key role in evolving in this direction (22). In this context, we strongly believe that our technique could represent an important contribution and impetus in pursuing this goal, having the advantage to simplify the classic FET procedure.

Limitations

The main limitation of the study is its retrospective rather than randomized nature. In addition, we are aware that only 41 patients (15 of them with RPT) including and mixing different aortic diseases cannot give a solid scientific value to this work, and the propensity score analysis performed can only partially mitigate this limitation. Moreover, the results are influenced by surgeons' skills and periprocedural context. For this reason, further studies with larger samples are needed to demonstrate its safety and efficacy.

Figure Legends

Figure 1



Title: Thoraflex Hybrid prosthesis

A: The prosthesis preparation; **B:** the insertion of the prosthesis into the thoracic aorta.

Figure 2

Title : The Release and Perfuse Technique. The prosthesis is deployed, cerebral branches are clamped, and the abdominal flow is restored through the side branch of the Thoraflex.

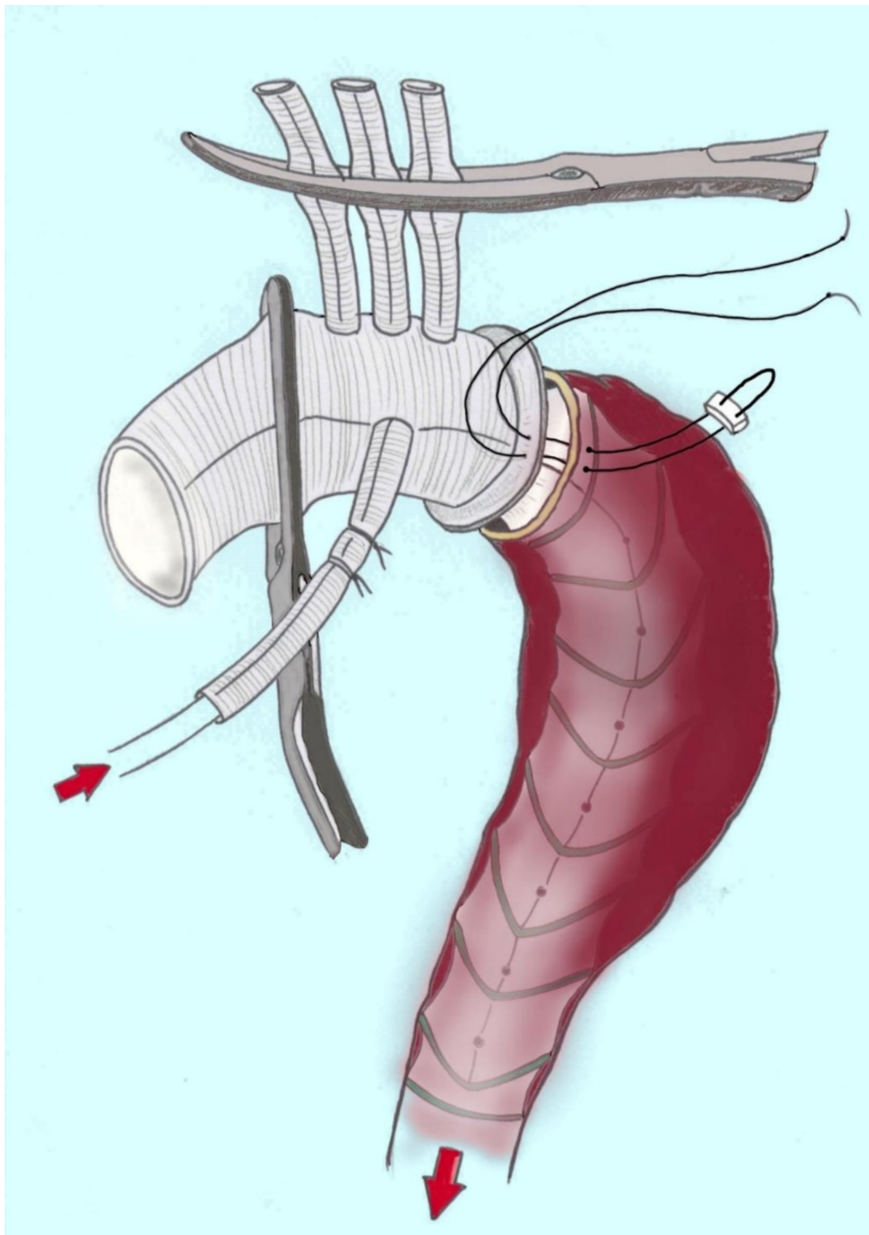


Figure 3

Title : Criteria for choosing the size of the prosthesis

Size of aortic landing zone (mm)	Size of the Thoraflex stent graft (mm)	
	Chronic aneurysm	Acute aortic dissection
36	40	40
35	40	38
34	40	36
33	38	36
32	38	34
31	36	34
30	36	32
29	34	32
28	34	30
27	32	30
26	30	28
25	28	28

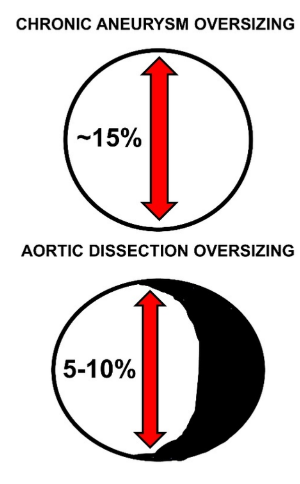
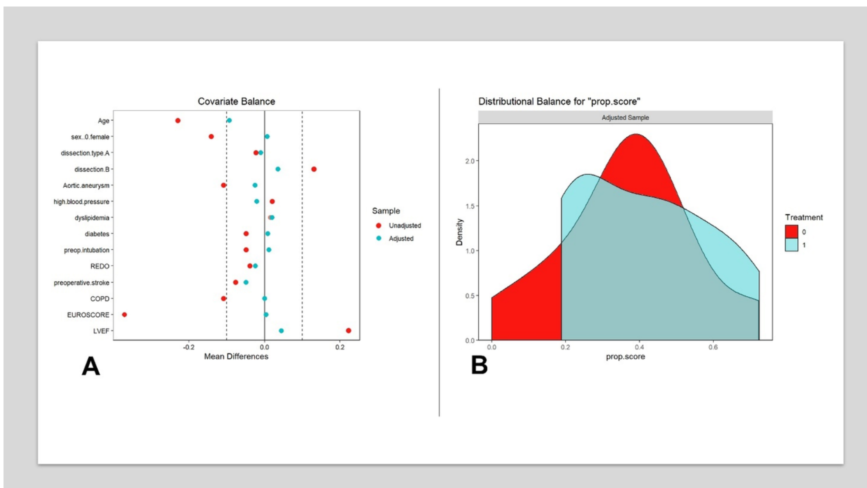


Figure 4

Title : The propensity score weighting analysis



A : The used variables. **B** : the visual inspection of propensity score balancing estimation.

Tables

Table 1.

Baseline characteristics

Variable	RP technique (15)	Classic FET (26)	Combined (41)	P value
Indication for surgery TAAD TBAD Chronic aneurysm	6 (40%) 6 (40%) 3 (20%)	11 (42%) 7 (27%) 8 (31%)	17 (41%) 13 (32%) 11 (27%)	0.885 0.386 0.453
Age	67 (57-71)	68 (60-73)	68 (58-72)	0.496
Males	10 (67%)	21 (81%)	31 (76%)	0.311

Variable	RP technique (15)	Classic FET (26)	Combined (41)	P value
Previous cardiac surgery	0	1 (4%)	1 (2%)	0.442
Hypertension	13 (87%)	22 (85%)	35 (85%)	0.858
COPD	3 (20%)	8 (31%)	11 (27%)	0.453
Dyslipidaemia	6 (40%)	10 (38%)	16 (39%)	0.923
Diabetes	1 (7%)	3 (12%)	4 (10%)	0.613
Genetic aortic syndrome	0	0	0	-
LVEF	60 (60-65)	60 (58-65)	60 (58-65)	0.686
Preoperative Neurological dysfunction	0	2 (8%)	2 (5%)	0.271
Preoperative intubation	1 (7%)	3 (12%)	4 (10%)	0.613
Euroscore II (%)	10 (8-12)	12 (10-13)	11 (9-12)	0.096

Continuous data are reported as median (I, III quartiles); categorical data are reported as a percentage and absolute frequencies. COPD: chronic obstructive pulmonary disease; LVEF: left ventricle ejection fraction; TAAD: type A aortic dissection; TBAD: type B aortic dissection.

Table 2.

Operative details

Variable	RP technique (15)	Classic FET (26)	Combined (41)	P value
Cardiopulmonary bypass time (min)	157 (147-200)	288 (274-306)	274 (175-296)	<0.0001
Cross-clamp time (min)	65 (51-118)	143 (129-161)	134(102-149)	<0.0001
Circulatory arrest (min)	9 (8-13)	58 (48-65)	46 (13-61)	<0.0001
Core body temperature (°C)	29 (28-31)	26.5 (25-27)	27 (26-28)	<0.0001
Aortic valve replacement (n°)	0	1 (4%)	1 (2%)	0.442
Valve sparing (DAVID) (n°)	4 (27%)	3 (12%)	7 (17%)	0.215
Coronary artery bypass (n°)	0	2 (8%)	2 (5%)	0.271
Bentall (n°)	1 (7%)	2 (8%)	3 (7%)	0.903
Intraoperative death (n°)	0	0	0	-

Continuous data are reported as median (I, III quartiles); categorical data are reported as a percentage and absolute frequencies.

Table 3.

Postoperative characteristics

Variable	RP technique (15)	Classic FET (26)	Combined (41)	P value
30-day mortality	1 (7%)	4 (15%)	5 (12%)	0.185
ICU stay (days)	3 (2-8)	9 (6-13)	7 (4-11)	0.011
Hospital stays (days)	12 (11-16)	19 (16-27)	17 (12-24)	0.004
Permanent neurologic deficit (n°) *	1 (7%)	3 (12%)	4 (10%)	0.488
Transient neurologic dysfunction (n°) **	1 (7%)	2 (8%)	3 (7%)	0.633
Reoperation for bleeding (n°)	1 (7%)	3 (12%)	4 (10%)	0.488

Variable	RP technique (15)	Classic FET (26)	Combined (41)	P value
Myocardial infarction (n°)	1 (7%)	0	1 (2%)	0.183
Multi-organ failure (n°)	1 (7%)	3 (12%)	4 (10%)	0.613
Acute kidney failure (n°)	1 (7%)	5 (19%)	6 (15%)	0.273
Pulmonary infection (n°)	1 (7%)	3 (12%)	4 (10%)	0.613
Limb ischemia (n°)	0	1 (4%)	1 (2%)	0.442
Mediastinitis (n°)	0	1 (4%)	1 (2%)	0.442
Digestive ischemia (n°)	0	2 (8%)	2 (5%)	0.271
Digestive hemorrhage (n°)	0	1 (4%)	1 (2%)	0.442
Lactates peak in the first 24 h (mmol/L)	2.6(2.2-2.9)	5.4 (4.7-6.3)	4.7 (2.8-5.8)	<0.0001
Packed red blood cells	1 (0-1)	4 (3.2-5.8)	3 (1-4)	<0.0001
Fresh frozen plasma	0.5 (0-1)	3 (2-3)	2 (1-3)	<0.0001
Platelet concentrate	0	3 (3-4)	3 (0-4)	<0.0001
Fibrinogen (gr)	2 (2-2.5)	3 (3-4.8)	3 (2-4)	<0.004

Continuous data are reported as median (I, III quartiles); categorical data are reported as a percentage and absolute frequencies. The P values are adjusted after propensity score weighting. ICU: intensive care unit. * Permanent neurologic deficit was defined as the presence of stroke, motor deficit (confirmed at CT/MRI control) or coma; ** Transient neurologic dysfunction was defined as the presence of reversible postoperative deficit before discharge, including confusion, delirium and motor deficits with no signs of stroke at computed tomography (CT) scan.

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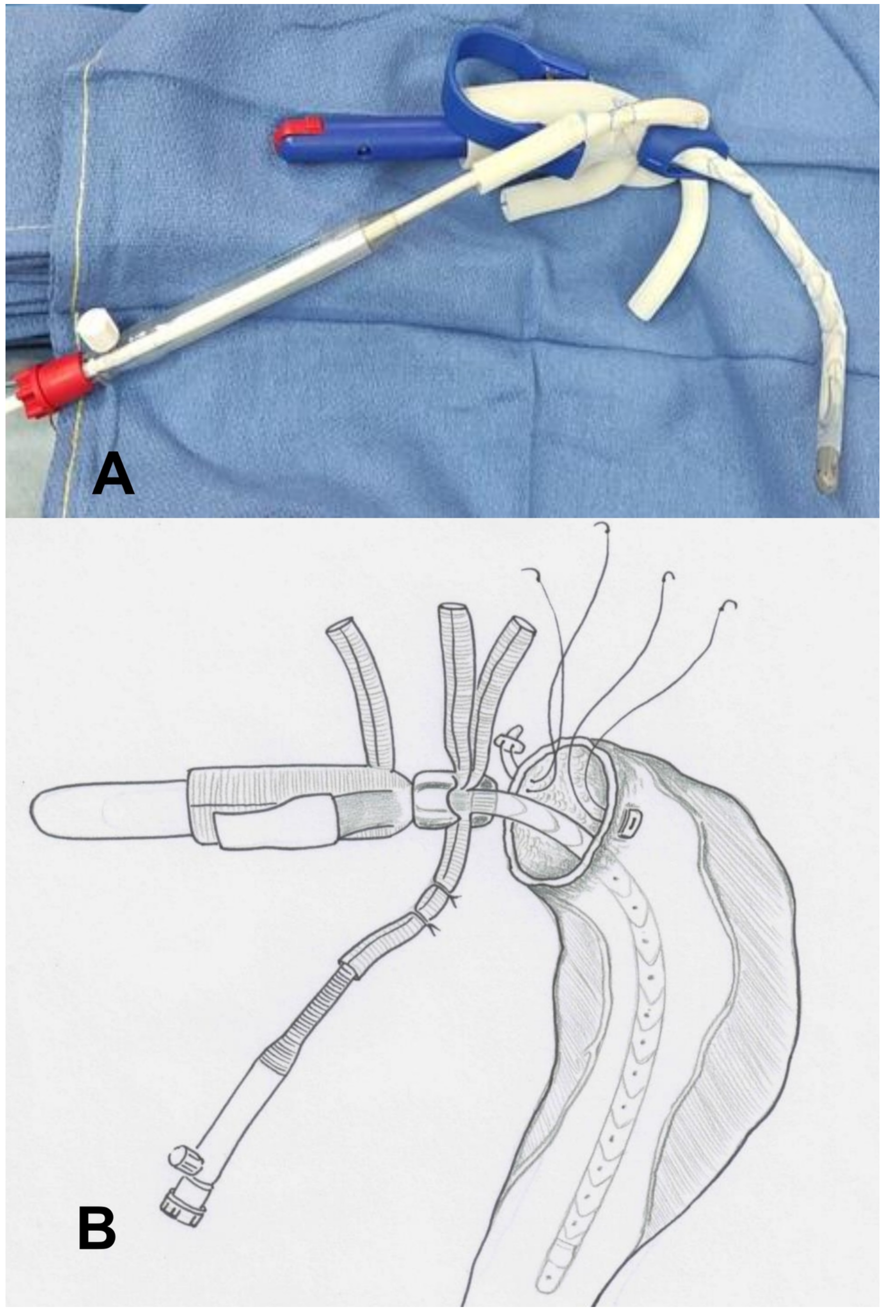
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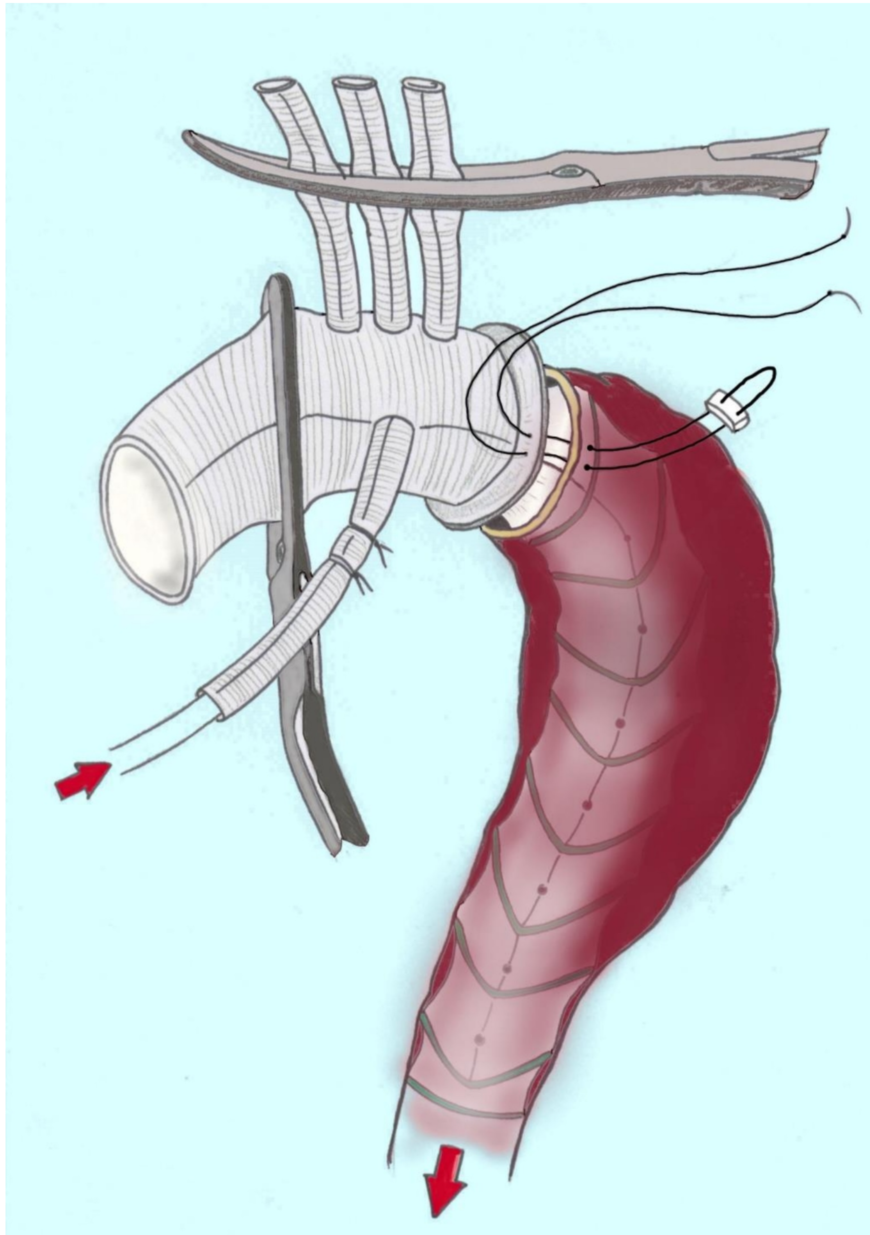

Size of aortic landing zone (mm)	Size of the Thoraflex stent graft (mm)	
	Chronic aneurysm	Acute aortic dissection
36	40	40
35	40	38
34	40	36
33	38	36
32	38	34
31	36	34
30	36	32
29	34	32
28	34	30
27	32	30
26	30	28
25	28	28