Inter-Stage Mortality in Two-Stage Elephant Trunk Surgery

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Abstract

Purpose: Diffuse mega-aorta is challenging. Prior studies have raised concerns regarding the safety of the open two-stage elephant trunk (ET) approach for extensive thoracic aortic aneurysm (TAA), specifically in regard to inter-stage mortality. This study evaluates the safety of the two-stage ET approach for management of extensive TAA. Methods: Between 2003–2018, 152 patients underwent a Stage I ET procedure by a single surgeon (mean age 64.5±14.8). Second stage ET procedure was planned in 60 patients (39.4%) and to-date has been performed in 54 patients (90%). (In the remaining patients, the elephant trunk was prophylactic for the long-term, with no plan for near-term utilization). Results: In-hospital mortality after the Stage I procedure was 3.3% (5/152). In patients planned for Stage II, the median inter-stage interval was 5 weeks (range: 0-14). Of the remaining six patients with planned, but uncompleted Stage II procedures, five patients expired from various causes in the interval period (inter-stage mortality of 8.3%). There were no cases of aortic rupture in the inter-stage interval. Stage II was completed in 58 patients (including 4 unplanned) with 30-day morality of 10.3% (6/58). Seven patients developed strokes after Stage II (12%), and three patients (5.1%) developed paraplegia. Conclusions: The overall mortality, including Stage I, inter-stage interval, and Stage II was 18.6%. This cumulative mortality for the open two-staged ET approach for treatment of extensive TAA is acceptable for aortic disease of this severity. Fear of inter-stage rupture should not preclude the aggressive Two-Stage approach to management of extensive TAA.

INTRODUCTION

Mega-aorta syndrome is a relatively rare disease, with aneurysmal dilatation afflicting the ascending aorta, the aortic arch, the descending aorta and variable portions of the abdominal aorta[1]. This condition usually requires extensive surgical intervention, with poor prognosis if left untreated (39% five-year survival in patients with untreated aneurysms) [2]. Traditionally, open surgical treatment has been the standard treatment of this syndrome, although adjuvant endovascular therapy is increasingly being applied.

Thirty-seven years have passed since Dr. Borst and colleagues first operated on their patients with mega-aorta syndrome using the Elephant Trunk (ET) technique [3]. This brilliant technique negated the need for proximal cross clamping of the descending aorta, facilitated the second procedure, shortened clamp time, and significantly decreased bleeding [4]. Thereafter, the technique was modified by pioneer surgeons to facilitate the distal anastomosis by inverting the graft within itself in the descending aorta [2], introducing a hybrid procedure with a new collared graft [5] and converting the elephant trunk into a “frozen” elephant trunk [6].

However, studies have raised concerns regarding the safety of the open two-staged ET approach for extensive thoracic aortic aneurysm (TAA), specifically in regard to inter-stage mortality[7].

The purpose of this study is to evaluate the safety of the two-stage ET approach for management of extensive TAA.

PATIENTS AND METHODS

After approval from the Human Investigation Committee of the Yale University School of Medicine, we searched the database of the Yale Aortic Institute—containing 3914 patients with thoracic aortic disease–for patients who underwent the ET procedure. We identified 152 patients between 2003–2018 who underwent a Stage I ET procedure by the senior author (JAE). Baseline characteristics were reviewed. In some patients, the elephant trunk of the Stage I procedure was placed for prompt use as the cornerstone of an upcoming Stage II procedure for cogent descending aortic disease. In other patients, the elephant trunk was placed prophylactically for possible late use in case of further descending disease progression (Figure 1). All patients were followed for a median of 52 months (quartile 1–3; 22.7 – 96.5). Data on morbidity and mortality of both Stage I and Stage II procedures were recorded during the follow up period, and long-term mortality was ascertained using the Aortic Institute method described previously [8].

Surgical technique.

Surgical technique has been described in detail previously[4]. During the first stage, axillary cannulation is usually used for inflow for cardiopulmonary bypass, so as to avoid retrograde embolization of aortic debris under retrograde femoral perfusion. Under straight deep hypothermic arrest (DHCA) at 18°C during, aortic arch replacement is performed, with elephant trunk deployment. For the elephant trunk construction, a Dacron graft is brought to the surgical field and invaginated into itself. An anastomosis is performed between the aortic tissue and the full thickness of the invaginated graft, leaving the elephant trunk itself dangling in the descending aorta (Figure 2)[4]. The inner portion of the inverted elephant trunk is then everted and used for the aortic arch replacement. The arch vessels are then reconstructed and attached to the new Dacron aortic arch. Aortic Zone 2 was our preferred site for the aortic arch anastomosis (just before the left subclavian artery. During rewarming, the arch graft is sutured to the ascending aorta or to another graft replacing the ascending aorta. The patient is rewarmed and weaned from cardiopulmonary bypass.

During the second stage, typically 3 to 6 weeks later, a left thoracotomy or thoracoabdominal incision is made in a curvilinear fashion. In our institution, we prefer left atrial to femoral bypass for the Stage II procedure. Recently, we have switched from a centrifugal pump without oxygenator to the full heart-lung machine with an oxygenator for our descending and thoracoabdominal procedures [9]. When the distal aorta is clamped, bypass is instituted, and vertical aortotomy is done in the descending aorta at the level of the elephant trunk graft, which is then retrieved by the finger-thumb technique and clamped [10] (Figure 3). We then pull down gently on the elephant trunk, as a considerable longitudinal portion of the elephant trunk graft may still be up in the aortic arch. A proximal graft-to-graft anastomosis is performed to provide the required length of graft for reaching to the distal extent of the aortic resection. We perform the distal anastomosis and visceral anastomoses as required. The subclavian artery is transected and grafted (8 or 10 mm Dacron graft) during the Stage II procedure. The remaining aortic tissue is usually wrapped around the anastomosed graft, and the thoracotomy/thoraco-abdominal incision is closed in a standard fashion (Figure 4

Statistics.

Statistical analysis was performed using Stata software version 15.1 (College Station, TX: StataCorp LLC.) and Excel (Windows Excel 2016, Microsoft, Redmond, Washington). Continuous variables were tested for normality distribution with the Kolmogorov-Smirnov test and were expressed as a mean with standard deviation (SD). Independent t-tests were performed for normally distributed variables, or Mann-Whitney U tests otherwise. Categorical variables were presented as frequencies with percentages, and analyzed by Chi-square test or Fisher's exact test, as appropriate. Analysis of adverse events was performed and tabulated. Kaplan-Meier curves were used to display the survival for stage- I and II ET procedures.

RESULTS

Stage I Procedure

We identified 152 patients who underwent an ET procedure, with a mean age of 64± 14 years and a mean maximal aortic diameter of 5.3±0.6. Among the total population, 50.6% were females. The large majority of patients (n=125, 82%) carried a diagnosis of hypertension, and 15.8% had baseline neurologic abnormalities, including prior strokes (n=15). Patient characteristics are listed in Table 1.

Stage I procedure was carried out in all patients either electively (n=119, 78%), urgently (n=29, 19%) or on an emergent basis (n=4, 3%). Indications for aortic repair were either aortic aneurysm (n=97, 64%), aortic dissection (n=44, 29%) or other acute aortic syndromes (PAU or rupture, n=11, 7%). DHCA was conducted in all patients, with a mean duration of 41±16 minutes, and average cardiopulmonary bypass time of 161±41 minutes (Table 2).

Operative mortality (30 day or in-house) was 3.3% (5/152). Of these, two patients had fatal strokes, 2 patients died from multi-organ failure, and 1 patient expired due descending aortic rupture prior to planned Stage II repair. All 147 surviving patients were triaged to either Stage II repair or long-term monitoring. The median interval between surgery date and death was 12 days.

Complications: After the Stage I procedure, post-operative stroke (confirmed by computed tomography or magnetic resonance imaging) occurred in 7 patients (4.6%). Of these, 2 patients expired within 30 days. Re-exploration for bleeding was required in 14 patients (9%) and 4 patients (2.6%) required renal replacement therapy (RRT).

Inter-Stage Interval

60 patients were planned for Stage II, and inter-stage mortality (after discharge) occurred in 5 patients (8.3%). Of these, 1 patient had a fatal intracerebral hemorrhage, 1 patient had pulseless cardiac arrest due to exacerbation of heart failure, and 3 patients died of severe overwhelming sepsis (causes were; severe influenza pneumonia, methicillin-resistant staphylococcus bacteremia, and bacterial pneumonia in a patient with tracheostomy). There were no cases of aortic rupture in the inter-stage interval.

Stage II Procedure

In patients who were planned for Stage II (n=60, 41%), 54/60 patients (90%) underwent repair, while 6/60 patients (10%) did not (5 patients expired and 1 patient was lost to follow-up) . In patients who were not planned for early Stage II (n=87, 59%), 4/87 patients eventually required repair for progression of aneurysm disease (4.6%). Ultimately, 58/152 patients (38%) underwent Stage II repair. Figure 5 depicts the distribution of cases throughout the study period.

Stage II repair was conducted electively in 50 patients (86%) and urgently in 8 patients (14%). Aortic repair was confined to the descending aorta in 43 patients (74%) while 15 patients (26%) had thoracoabdominal repair. A cerebrospinal fluid drain was utilized in 37/58 patients (64%). In patients planned for Stage II, the median inter-stage interval was 5 weeks (range: 0-14) (Table 3).

In patients who underwent Stage II procedure (n=58), operative mortality (30-day or in-house) occurred in 6 patients (10.3%). One patient expired intraoperatively, 2 patients suffered fatal strokes, and 3 patients expired due to post-operative complications (causes were: acute respiratory distress syndrome (ARDS), septic shock from ischemic colitis, and hemorrhagic shock due to bleeding). Post-operative strokes occurred in 7 patients (12%) and post-operative paraplegia occurred in 3 patients (5.1%). Re-exploration for bleeding was required in 4 patients (7%) and 1 patient (1.7%) required renal replacement therapy (RRT).

Overall Outcome: Stage I, Inter-Stage, and Stage II

The overall mortality rate, including Stage I (0%), inter-stage interval (5 (8.3%)), and Stage II (6 (10.3%) was 18.6%. Figure 6 shows the Kaplan-Meier survival curves for the entire cohort, and for patients who underwent either Stage I only, and both stages.

When analyzing the adverse events, we chose a composite of 30-day mortality, stroke, paraplegia, myocardial infarction, and occurrence of RRT. Univariate analysis after stage I showed a trend towards increasing events in patients with history of smoking (53% vs. 43%) coronary artery disease (26% vs 15%) or baseline neurologic abnormalities (40% vs. 13%), as well as with prolonged intraoperative cardiopulmonary bypass or DHCA time (Table 4).

COMMENT

Before advent of the ET procedure, the earlier techniques (clamping the descending aorta or aortic arch for Stage II, or performing Stage II under DHCA through a left thoracotomy) carried a significant risk of hemorrhage. Hemorrhage could easily occur during dissection of the enlarged, fragile upper descending aorta, especially after inflammation from a preceding aortic arch replacement. The back wall of the aorta or the pulmonary artery could easily be injured in surrounding the upper descending aorta.[11]. Multiple ET modifications have been suggested and tried, and reports on the mid and long-term post-operative mortality are becoming available.

One-step repair of the entire aorta through a clamshell [12], trans-mediastinal [13], or left posterolateral thoracotomy [14] have been attempted in order to avoid the need for two separate operations. However these challenging techniques have achieved only limited clinical application due to multiple factors, including long operating time, higher pulmonary complications rates (ranging from 15 to 50%), and near inability to repair segments below the diaphragm [15].

The staged ET procedure is thought to decrease the pulmonary complications and negates the need for proximal descending aorta dissection, hence avoiding injury to adjacent anatomic structures such as the pulmonary artery, esophagus, and phrenic nerve [4].

Frozen elephant trunk is another technique introduced in 2003 [6] utilizing a custom-made prosthesis. The proximal portion consists of a Dacron sleeve for traditional surgical anastomosis; and the distal part consists of a stent graft [16]. Experience with the frozen elephant trunk is rapidly accumulating. It can be said, in summary, that the initial operation is generally well tolerated, but a risk of paraplegia is incurred, especially with all but the shortest stent portions [17]. In contrast, paraplegia is quite unlikely with a non-frozen Stage I elephant trunk (except with very long elephant trunks) . In support of the frozen elephant trunk option is the issue that the conventional elephant trunk (used in our experience) can be difficult to retrieve and utilize as a proximal landing zone for a later endovascular extension.

Indeed, subjecting patients to two major surgeries carries real risks of morbidity and mortality. Several retrospective reports have discussed the mortality rates for each stage. In our cohort, the operative and 30-day mortality rate after Stage I in 152 patients was 3.3%, with reported rates ranging from 2% to 14% [7, 11, 18, 19]. Our inter-stage mortality rate in patients awaiting Stage II was 8.3%, with reports ranging between 2% and 11% [7, 20, 21]. This comes in a patient population with 31.6 % having undergone a previous cardiac surgery before Stage I. Fortunately, most of our patients who were planned for Stage II eventually underwent repair. We had only 1 patient who was lost to follow up and 5 patients who expired, not from rupture, advocating for earlier rather than later second stage [7]. It is notable that in the inter-stage period – beyond the first 30-days – there were no cases of aortic rupture. Our mortality rate in the second stage performed in 58 patients was 10.3%, which again is consistent with previous reports [7, 11, 18]. The continued mortality of 6 patients within the first year after completion of Stage II shows how serious is the disease of mega-aorta, often with substantial non-aortic comorbidities. In our patients, prophylactic placement of an elephant trunk was performed in 87 patients in whom the descending aorta was mildly dilated. To date, four patients eventually required repair, and a secure upper landing zone was already present for replacement of their descending aorta[21].

Aortic diameter remains a significant predictor of rupture and dissection in TAA [22, 23] however, it is difficult to predict the operative mortality and morbidity following repair. The lack of statistical significance in our variable analysis is understandable due to low number of events, which is a problem encountered in previous studies and metanalyses [24]. Our results showed increased composite adverse events in patients with prior neurologic abnormalities including prior strokes. Not surprisingly, smoking, coronary artery disease and prolonged clamp time were also factors associated with increased complications after Stage I, although this failed to reach statistical significance.

With advanced techniques of neuronal protection, the risk of spinal cord injury (SCI) and strokes has decreased. During Stage I, we used straight DHCA for cerebral protection, which we have shown to be safe and effective for a duration of 50 minutes or less [15]. We do not usually use antegrade cerebral perfusion [25]. In our study, the rate of strokes after Stage I was 4.6%.

Our paraplegia rates were low (3 patients). Routine visualization of the anterior spinal artery prior to repair may have contributed to these low paraplegia rates [26]. Utilization of a spinal drain to keep the lumbar pressure at 5 to 12 mm Hg postoperatively in descending, thoracoabdominal, and thoracic endovascular aortic repair (TEVAR) has been shown effective in reducing the risk of spinal cord injury [27].

An important point to consider has to do with choosing an appropriate length of the elephant trunk (10-15 cm) to avoid thrombus around the graft yet permit easy accessibility at Stage II. It is important to avoid entrapment of the graft in the false lumen in patients with chronic dissection [20].

Some centers apply a stent graft in the descending aorta prior to discharge instead of a later Stage II open repair [28]. Although this hybrid approach has gained popularity, there remain serious questions about the durability of these stents and the unique associated complications—especially endoleaks– often mandating later re-operation.

Enthusiasm regarding ET staged repair may have waned over the years due to complexity and fear of the inter-stage mortality; however, we feel that the inter-stage mortality rates and overall outcomes are acceptable for a disease of this severity. Long-term survival finds our results durable.

LIMITATIONS

This study is limited by its retrospective nature and by referral bias inherent in a single specialty center study. Statistical significance of predictors of adverse outcome could not be achieved due to low number of adverse events and overall relatively small cohorts. The results reported in this study are representative only of referral centers with concentrated experience in these procedures.

Despite advantages in the approach to the mega-aorta, there are also certain inherent disadvantages of the Two-Stage elephant trunk procedure. (a) Stage I requires a suitable landing zone in the aortic arch for the elephant trunk anastomosis. Although workable neck is usually able to be found, this can be problematic in the advanced mega aorta. In our practice, we use the Sienna graft for such cases; the Sienna graft has a "skirt" that can accommodate virtually any aorta. (b) The elephant trunk can be difficult to engage at a second stage endovascular completion. We have uniformly used an open second stage. Also, grafts are now available in Europe (E-Vita (Jotec) and Thoraflex (Terumo)) and under investigation in the United States that can be deployed at the time of the original procedure to stent the descending aorta (albeit incurring a risk of paraplegia with all but the shortest grafts)[16].

CONCULUSION

Several decades later after its conception, the Two-Stage Elephant Trunk technique remains a reliable, safe, and reproducible approach for treatment of extensive aortic disease (mega-aorta). The cumulative mortality of the stage I, inter-stage, and stage II procedures is acceptable for disease of this severity. Fear of the inter-stage mortality should not preclude an aggressive Two-Stage approach to management of extensive TAA.

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TABLES

Table 1. Patient characteristics

Variable	N	%
Total cohort	152	
Mean age at the time of surgery (year)	64.5±14.7	
Race		
White	127	83.6%
African American	20	13.2%
Hispanic	3	2%
Asian	2	1.3%
Female (%)	77	50.7%
Height (cm)	168.4±14.1	
Weight (Kg)	82.0±21.8	
Body surface area (m^2)	1.93±0.28	
Maximal aortic diameter (cm)	5.31±0.98	
Hypertension (%)	125	82.2%
Diabetes mellites (%)	15	9.9%
Dyslipidemia (%)	67	44.1%
History of smoking (%)	67	44.1%
Marfan syndrome (%)	7	4.6%
Neurological comorbidities (%)	24	15.8%
Chronic renal dysfunction (%)	18	11.8%
Pulmonary comorbidities (%)	33	21.7%
Coronary artery disease (%)	25	16.4%
Previous Cardiac Surgery (%)	48	31.6%
Primary Diagnosis as Dissection (%)	49	32.2%

Table 2. Stage I repair

	N	%
Total Cohort	152	
Timing of surgical intervention		
Elective	119	78.29%
Urgent	29	19.08%
Emergent	4	2.63%
Preoperative diagnosis		
Aortic Aneurysm	97	63.82%
Aortic dissection	44	28.95%
Aortic rupture	5	3.29%
Penetrating aortic ulcer	6	3.95%
Aortic Valve Replacement (%)		
None	102	67.1%
Bioprosthetic	29	19.1%
Mechanical	21	13.8%
Composite Graft replacement (%)	17	11.2%
Concomitant CABG (%)	14	9.2%
Cardiopulmonary bypass time (min)	161.85±30.48	
Aortic Cross-clamp time (min)	84.14±35.96	
DHCA time (min)	42.13±8.90	
30-day mortality	5	3.29%
Post-operative stroke	7	4.61%
Post-operative myocardial infarction	1	0.66%
Prolonged ventilation > 48 hours	16	10.53%
Renal failure requiring dialysis	4	2.63%
Re-exploration after Stage I	14	9.21%

CABG = coronary artery bypass grafting, DHCA = deep hypothermic circulatory arrest.

Table 3. Stage II repair

	N	%
Stage II	58	38.16%
Median inter-stage Interval (months)	4	
Median inter-stage interval (days)	139	
Stage II planned	54	93.10%
Stage II initially not planned	4	6.90%
Timing		
Elective	50	86.21%
Urgent	8	13.79%
Extent of repair		
Descending aorta	43	74%

	N	%
Thoracoabdominal aorta	15	26%
Utilization of spinal drain	37	64%
30-day Mortality	6	10.34%
Post-operative stroke	7	12.07%
Post-operative paraplegia	3	5.17%
Aortic re-interventions	3	5.1%
All cause 1-year mortality after stage II	12	20.6%
Prolonged ventilation > 48 hours	13	22.41%
Renal failure requiring dialysis	2	3.45%
Re-exploration after Stage II	4	6.90%
Mesenteric ischemia	1	1.72%

Table 4. Univariate analysis of predictors of adverse events after stage I repair

	No Composite Adverse Events	Composite Adverse Events*	*P*
Total cohort	137	15	
Mean age at the time of surgery (year)	64.5±14.2	64.9±19.8	0.911
Race			0.664
White	114 (83.2)	13 (86.7)	
AA	19 (13.9)	1 (6.7)	
Hispanic	2 (1.5)	1 (6.7)	
Asian	2 (1.5)	0 (0.0)	
Female (%)	68 (49.6)	9 (60.0)	0.624
Height (cm)	168.5±14.3	167.8±12.8	0.858
Weight (Kg)	81.2±19.3	78.0±23.2	0.574
Maximal Aortic Size (cm)	5.3±1.0	5.3±1.0	0.874
Hypertension (%)	114 (83.2)	11 (73.3)	0.552
Diabetes (%)	13 (9.5)	2 (13.3)	0.986
Dyslipidemia (%)	63 (46.0)	4 (26.7)	0.247
History of smoking (%)	59 (43.1)	8 (53.3)	0.627
Marfan syndrome (%)	6 (4.4)	1 (6.7)	1
Neurological comorbidities (%)**	18 (13.1)	6 (40.0)	0.02
Chronic renal dysfunction (%)	15 (10.9)	3 (20.0)	0.542
Pulmonary comorbidities (%)	30 (21.9)	3 (20.0)	1
CAD (%)	21 (15.3)	4 (26.7)	0.449
Previous Cardiac Surgery (%)	45 (32.8)	3 (20.0)	0.469
Primary Diagnosis as Dissection (%)	46 (33.6)	3 (20.0)	0.437
Timing of surgical intervention (%)			

	No Composite Adverse Events	Composite Adverse Events*	*P*
Elective	109 (79.6)	10 (66.7)	
Urgent	26 (19.0)	3 (20.0)	
Emergent	2 (1.5)	2 (13.3)	
Aortic Valve Replacement (%)			
None	93 (67.9)	9 (60.0)	
Bioprosthetic	26 (19.0)	3 (20.0)	
Mechanical	18 (13.1)	3 (20.0)	
Composite Graft replacement (%)	15 (10.9)	2 (13.3)	1
Concomitant CABG (%)	12 (8.8)	2 (13.3)	0.911
Cardiopulmonary bypass time (min)	160.6±29.6	173.1±36.5	0.131
Aortic Cross-clamp time (min)	82.9±35.7	94.7±38.0	0.229
DHCA time (min)	41.9±8.6	44.3±11.7	0.329

AA= African American, BSA = body surface area, CAD = coronary artery disease, CABG = coronary artery bypass grafting, DHCA = deep hypothermic circulatory arrest.

*Composite adverse events including 30-day mortality, stroke, paraplegia/paresis, myocardial infarction, and renal replacement therapy.

** *$P < 0.05$.*

FIGURE LEGENDS

Figure 1. Flowchart showing the patient breakdown.

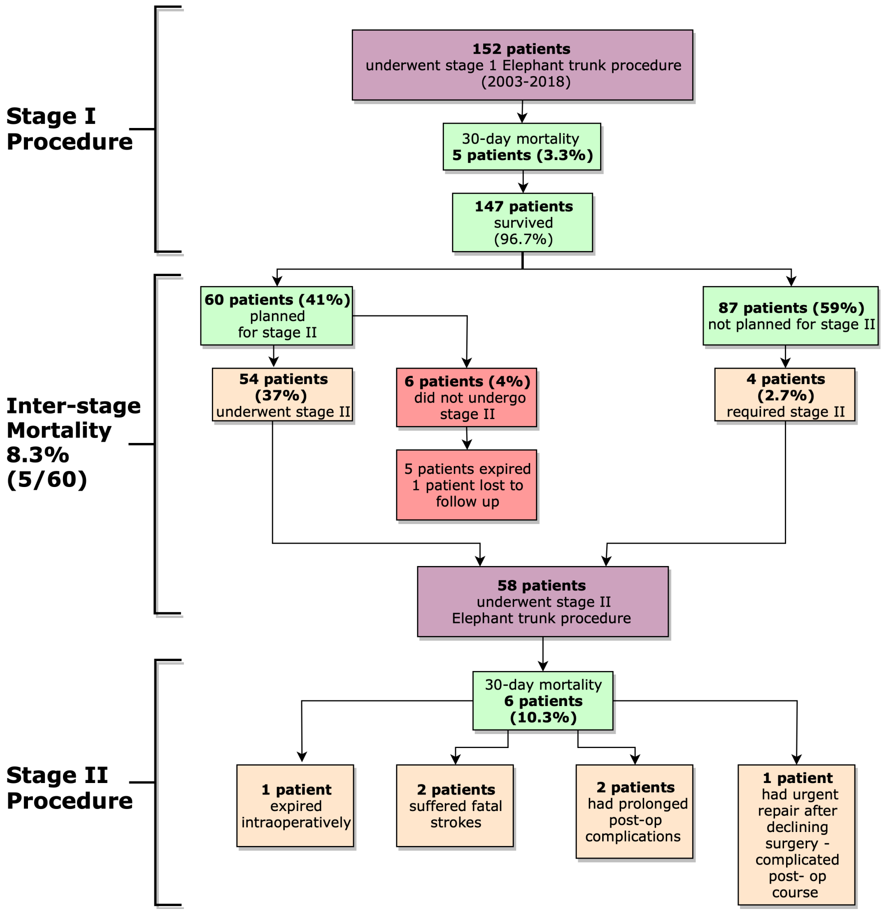
Figure 2. The elephant trunk: (A) Implantation and Suturing; (B) Head vessels and graft to graft anastomosis. (Reprinted with permission from Velasquez CA, Zafar MA, Saeyeldin A, Bin Mahmood SU, Brownstein AJ, Erben Y, et al. Two-Stage Elephant Trunk approach for open management of distal aortic arch and descending aortic pathology in patients with Marfan syndrome. Ann Cardiothorac Surg. 2017;6(6):712-20.)

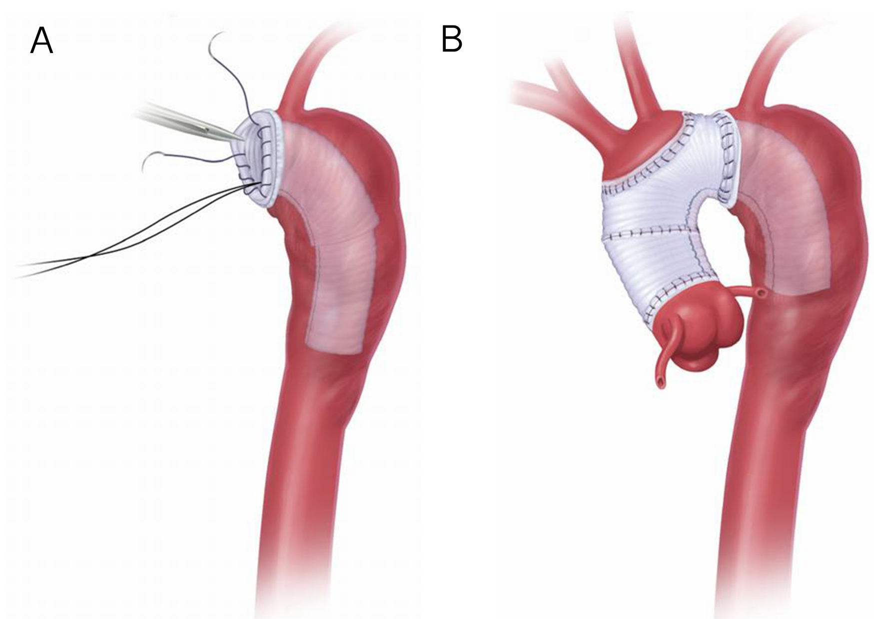
Figure 3. Finger-thumb technique for retrieval of the elephant trunk. (Reprinted with permission from Velasquez CA, Zafar MA, Saeyeldin A, Bin Mahmood SU, Brownstein AJ, Erben Y, et al. Two-Stage Elephant Trunk approach for open management of distal aortic arch and descending aortic pathology in patients with Marfan syndrome. Ann Cardiothorac Surg. 2017;6(6):712-20.)

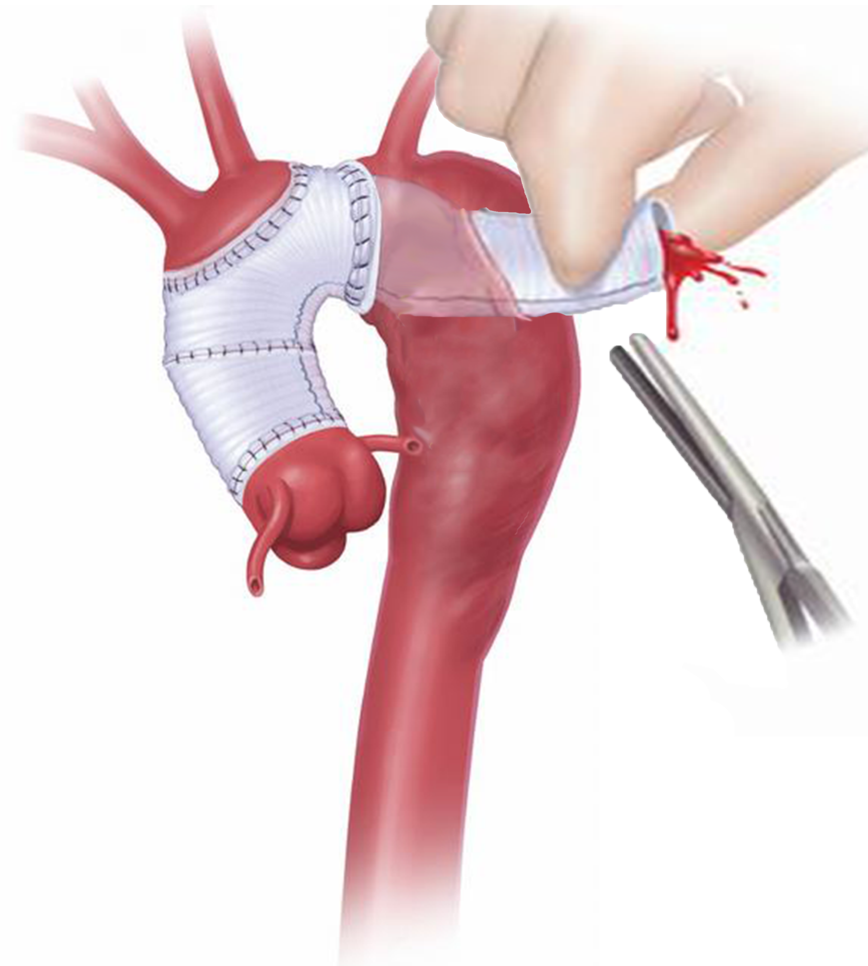
Figure 4. Completion of the elephant trunk procedure. (A) anastomosis to the descending aorta; (B) Replacement of the thoracoabdominal aorta. (Reprinted with permission from Velasquez CA, Zafar MA, Saeyeldin A, Bin Mahmood SU, Brownstein AJ, Erben Y, et al. Two-Stage Elephant Trunk approach for open management of distal aortic arch and descending aortic pathology in patients with Marfan syndrome. Ann Cardiothorac Surg. 2017;6(6):712-20.)

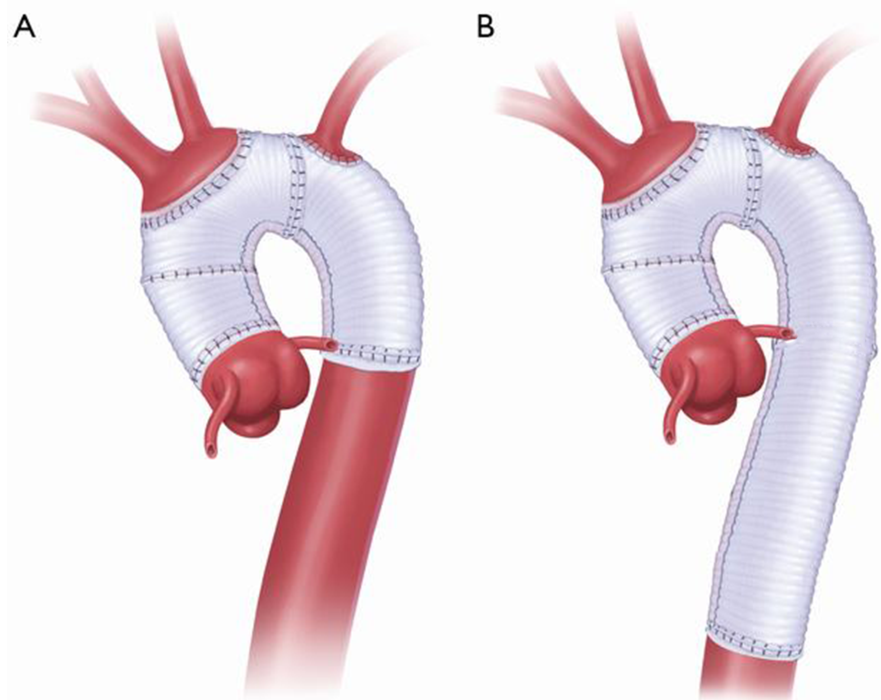
Figure 5. Distribution of cases throughout the study period.

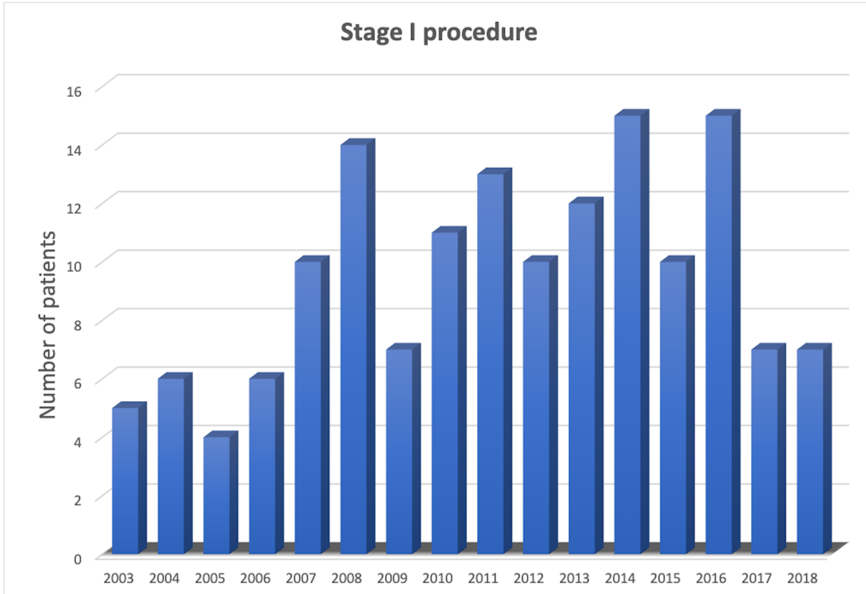
Figure 6. Kaplan Meir Curves; A) for the whole cohort, B) for patients who underwent stage I only, C) for patients who underwent both stages I and II.

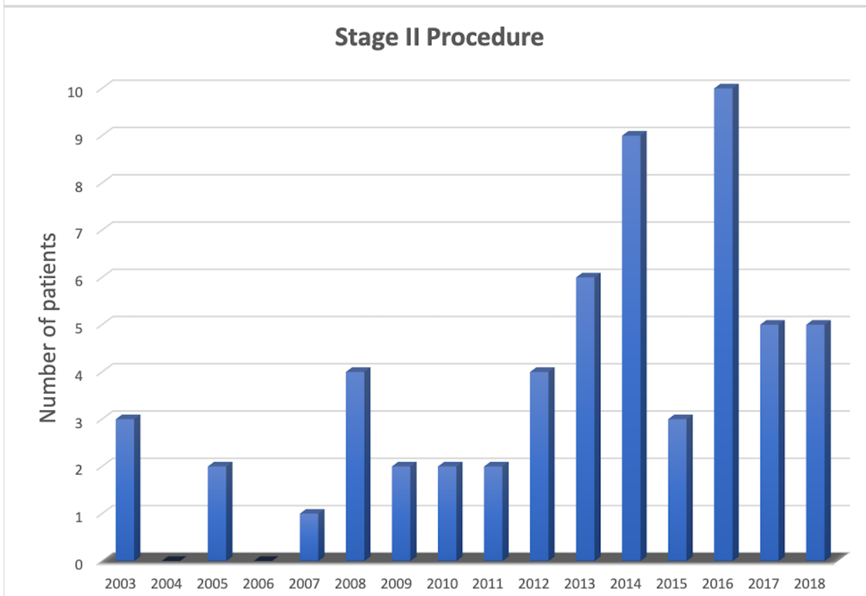

Stage I Procedure
152 patients underwent stage 1 Elephant trunk procedure (2003-2018)
30-day mortality 5 patients (3.3%)
147 patients survived (96.7%)
Inter-stage Mortality 8.3% (5/60)
60 patients (41%) planned for stage II
87 patients (59%) not planned for stage II
54 patients (37%) underwent stage II
6 patients (4%) did not undergo stage II
4 patients (2.7%) required stage II
5 patients expired 1 patient lost to follow up
58 patients underwent stage II Elephant trunk procedure
Stage II Procedure
30-day mortality 6 patients (10.3%)
1 patient expired intraoperatively
2 patients suffered fatal strokes
2 patients had prolonged post-op complications
1 patient had urgent repair after declining surgery - complicated post- op course

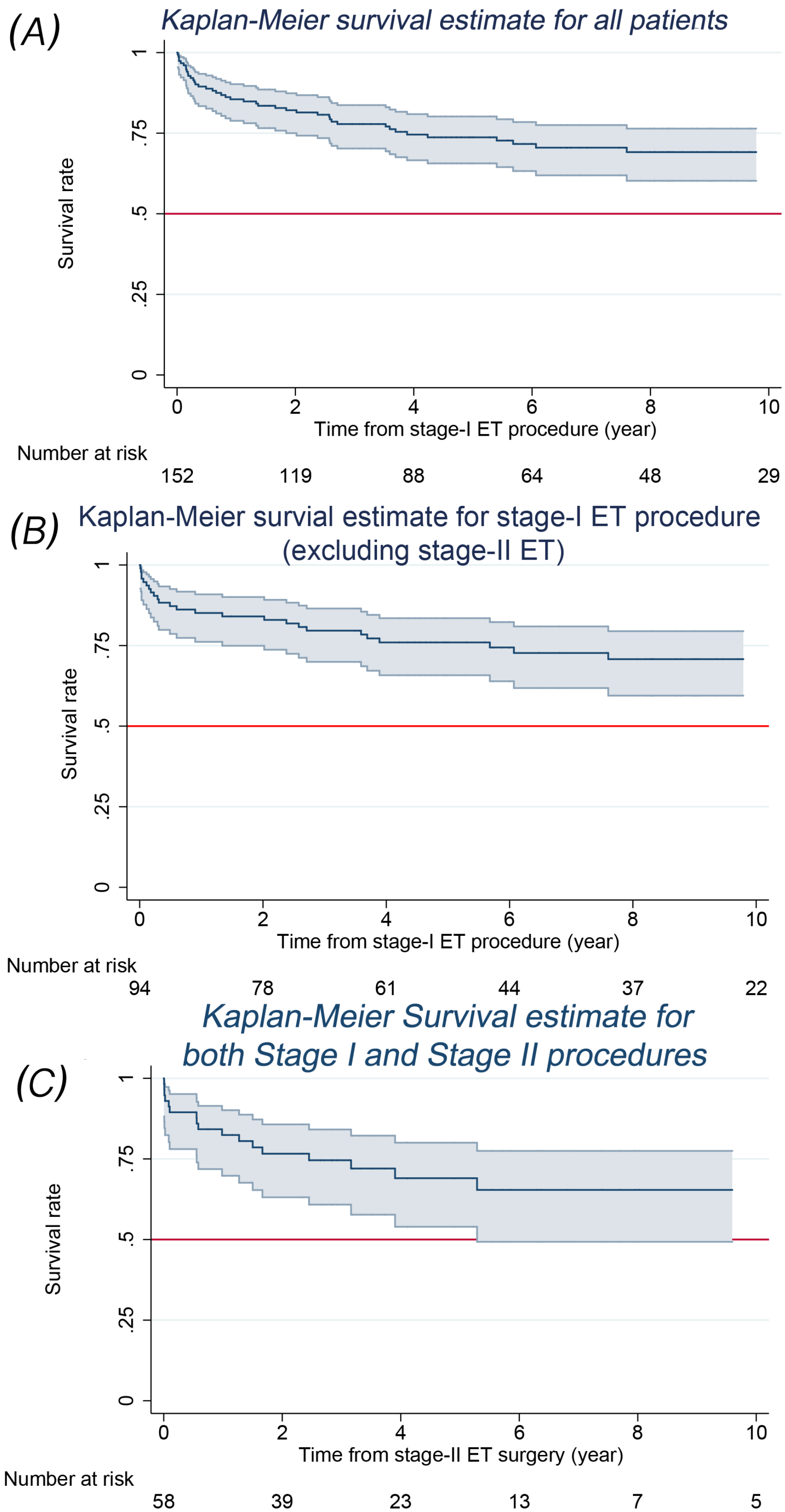

A
B




A
B


Stage I procedure
Number of patients
0
2
4
6
8
10
12
14
16
2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018


Stage II Procedure
Number of patients
0
1
2
3
4
5
6
7
8
9
10
2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018


(A)
Kaplan-Meier survival estimate for all patients
Survival rate
0
.25
.5
.75
1
0
2
4
6
8
10
Time from stage-I ET procedure (year)
Number at risk
152
119
88
64
48
29
(B)
Kaplan-Meier survial estimate for stage-I ET procedure
(excluding stage-II ET)
Survival rate
0
.25
.5
.75
1
0
2
4
6
8
10
Time from stage-I ET procedure (year)
Number at risk
94
78
61
44
37
22
Kaplan-Meier Survival estimate for
both Stage I and Stage II procedures
(C)
Survival rate
0
.25
.5
.75
1
0
2
4
6
8
10
Time from stage-II ET surgery (year)
Number at risk
58
39
23
13
7
5