# Total aortic arch replacement using a frozen elephant trunk device: Results of a 1-year US multicenter trial

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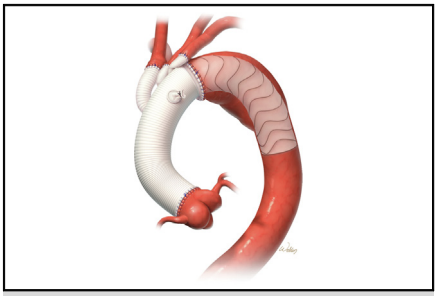
## ABSTRACT

**Objective:** In this prospective US investigational device exemption trial, we assessed the safety and 1-year clinical outcomes of the Thoraflex Hybrid device (Terumo Aortic) for the frozen elephant trunk technique to repair the ascending aorta, aortic arch, and descending thoracic aorta.

**Methods:** For the trial, which involved 12 US sites, 65 patients without rupture were recruited into the primary study group, and 9 patients were recruited into the rupture group. All patients underwent open surgical repair of the ascending aorta, aortic arch, and descending thoracic aorta in cases of aneurysm and/or dissection. The primary end point was freedom from major adverse events (MAE), defined as permanent stroke, permanent paraplegia/paraparesis, unanticipated aortic-related reoperation (excluding reoperation for bleeding), or all-cause mortality.

**Results:** In the primary study group, 2 patients were lost to follow-up at 1 year. Freedom from MAE at 1 year was 81% (51/63). Seven patients (11%) died (including 2 before 30 days or discharge), 3 patients (5%) suffered permanent stroke, and 3 (5%) developed permanent paraplegia/paraparesis. Twenty-six patients (41%) underwent planned extension procedures, including 22 endovascular procedures within a median of 122 (interquartile range, 64-156) days. In the aortic rupture group, 2 patients were lost to follow-up at 1 year. Freedom from MAE at 1 year was 71% (5/7). One patient (14%) died, 2 patients (29%) had permanent stroke, and none had permanent paraplegia/paraparesis. No extension procedures were performed in the rupture group.

**Conclusions:** One-year results with the Thoraflex Hybrid device are acceptable. Long-term data are necessary to assess the durability of these repairs. (J Thorac Cardiovasc Surg 2022;■:1-12)



The Thoraflex device (Terumo Aortic) facilitates definitive thoracic aortic repair in select patients.

### CENTRAL MESSAGE

The Thoraflex Hybrid device (Terumo Aortic) enables treatment of extensive thoracic aortic disease through either a single procedure or a staged approach that includes a subsequent endovascular or open procedure.

### PERSPECTIVE

Using the Thoraflex device (Terumo Aortic) for total aortic arch replacement is a promising and versatile approach to repair in patients with extensive thoracic aortic disease. The use of this hybrid device might provide a stable landing zone for subsequent downstream endovascular aortic repair. One-year results are acceptable, but long-term data will be necessary to assess the durability of these repairs.

See Commentary on page XXX.

ADULT

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**Abbreviations and Acronyms**
ET = elephant trunk
FDA = Food and Drug Administration
FET = frozen elephant trunk
IRB = institutional review board
MAE = major adverse events
POD = postoperative day
IQR = interquartile range

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Frozen elephant trunk (FET) repair has emerged as a major technical advancement in the treatment of complex thoracic aortic disease, concurrently treating the ascending aorta, aortic arch, and descending thoracic aorta. Unlike conventional elephant trunk (ET) procedures,[1-6] the FET technique, in which a stent graft is delivered antegrade inside the trunk, enables treatment of the entire aortic pathology during a single procedure or can facilitate a subsequent endovascular procedure.[7-11] Initially, FET prostheses were made by hand by combining polyester grafts and endovascular stent grafts until prefabricated FET hybrid devices became available. The first-generation Thoraflex Hybrid device (Terumo Aortic) has been available on the European market since 2012. At the time of the study reported, there was no FET device approved for use in the United States.

The FET experience in the United States has primarily consisted of off-label use of thoracic endografts combined with total or partial aortic arch replacement using a polyester graft.[12-14] The Thoraflex Hybrid device (Terumo Aortic; Figure 1) offers a single-device option for FET repair by combining a gelatin-sealed woven polyester graft component with a nitinol self-expanding stent graft component and enables single-stage FET repair of the ascending aorta, aortic arch, and proximal descending thoracic aorta. In 2015, the study, "Evaluation of the Thoraflex Hybrid Device for Use in the Repair or Replacement of the Ascending Aorta, Aortic Arch and Descending Aorta in an Open Surgical Procedure," was launched in the United States to assess the effectiveness, safety, and clinical outcomes of the Thoraflex Hybrid device in the treatment of aortic disease affecting the aortic arch. The secondary objectives were to: (1) assess the safety and early clinical outcomes in patients who receive an extension procedure within 1 year of Thoraflex Hybrid implantation, and (2) assess the safety and clinical outcomes of patients who receive a Thoraflex Hybrid device for treatment of aortic rupture. On April 29, 2020, the Thoraflex Hybrid device received breakthrough device designation from the US Food and Drug Administration (FDA), and on April 20, 2022, the device received FDA approval for the treatment of patients with complex aortic arch disease. Herein, we report the results of the Thoraflex Hybrid study that led to FDA approval.

## METHODS

### Study Enrollment

The trial received institutional review board approval at each of the 12 participating sites and was registered at ClinicalTrials.gov (NCT02724072). Informed consent was obtained from each patient before enrollment. All patients provided written informed consent for the publication of study data. Inclusion criteria for the primary group consisted of having 1 of the following pathologies: acute dissection, chronic dissection, or aortic aneurysm. Inclusion criteria for the rupture group consisted of having either aortic rupture or high risk of imminent rupture in the opinion of the treating surgeon. Patients with connective tissue disorders were eligible for enrollment. Of the 83 patients who provided informed consent for the study, 9 failed subsequent screening and were excluded for reasons including the presence of other medical, social, or psychological problems precluding enrollment, and patient withdrawal of consent (see Figure E1 for the Consolidated Standards of Reporting Trials [CONSORT] diagram). Seventy-four patients were enrolled in the study and underwent device implantation between August 2016 and May 2018; these included 65 patients without rupture in the primary study group and 9 patients in the aortic rupture group.

Preoperative characteristics of enrolled patients are summarized in Table 1. In the primary study group, the median age of patients was 68 years (interquartile range [IQR], 56-74]), and 66% (43/65) were men. The surgical histories of

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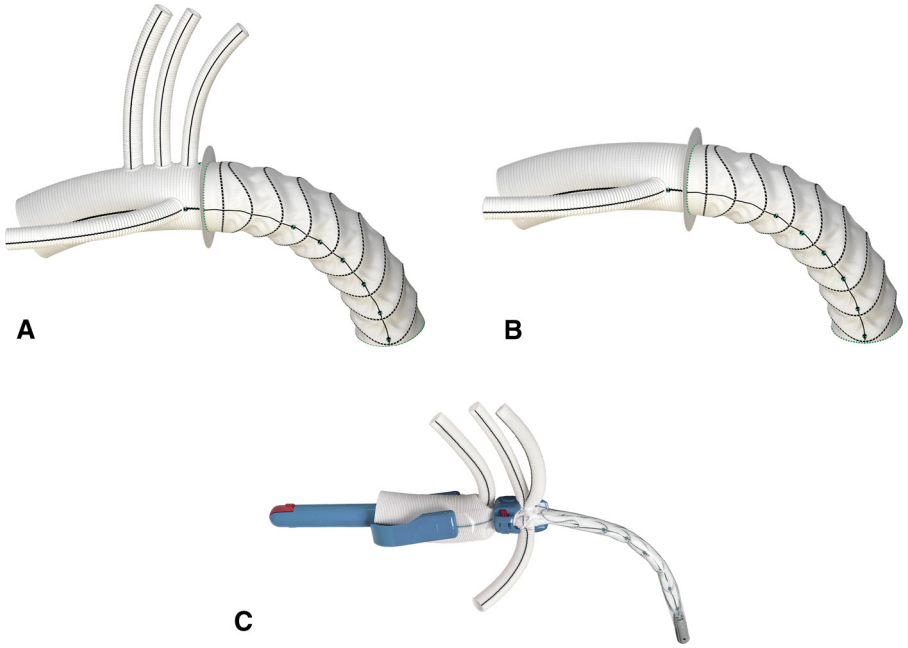


**FIGURE 1.** The Thoraflex Hybrid device (Terumo Aortic) is available as (A) a branched Plexus device or (B) a nonbranched Ante-Flo device. Both models have a side branch to provide aortic perfusion during reconstruction. The system (C) for the Thoraflex Hybrid device features a handle for manual deployment. Upon deployment, the sheath compressing the stent graft portion is split and removed. Used with permission from Terumo Aortic.



these patients included previous proximal aortic surgery (n = 31) and previous coronary artery bypass grafting (n = 8). In the primary group, 27 patients had aneurysm only (without dissection) as an indication for surgery, and 37 patients had chronic dissection (Figure 2). In the aortic rupture group, the median age of patients was 70 (IQR, 49-75) years, and 78% (7/9) were men; 2 patients (22%) had aneurysm only (without dissection) as an indication for surgery, 6 (67%) had an acute dissection, and 1 had a chronic dissection. Two of the 9 patients had an aortic rupture when enrolled; the remaining 7 patients in this study arm were included because the treating surgeon considered the patients at high risk of imminent rupture.

### The Device and Surgical Techniques

The Thoraflex Hybrid device is a 1-piece hybrid prosthesis that incorporates a polyester graft for the proximal repair and a nitinol stent graft component for the descending aorta; thus, this enables a single-stage FET repair of the ascending aorta, the entire aortic arch, and the proximal descending thoracic aorta. All patients in this study received the second-generation Thoraflex Hybrid device, which is a modification of the first-generation device. The second-generation device is manufactured in several sizes and 2 configurations. The Plexus version includes 3 branch grafts to facilitate arch vessel attachment, and the Ante-Flo version does not have arch branches (Figure 1). The device is supplied preloaded in a delivery system to facilitate accurate deployment. The delivery system is available in 2 sizes on the basis of shaft and stent graft length (100 mm and 150 mm).

Operative details for the patients are provided in Table 2. Surgical techniques for FET repair and use of the Thoraflex Hybrid device varied depending on the participating institution. All procedures were performed through a median sternotomy while the patient was receiving cardiopulmonary bypass. The general approach involved initiating hypothermic circulatory arrest, opening the ascending aorta and transverse aortic arch, and then inserting the distal end of the delivery device antegrade through the transected aorta into the lumen of the descending thoracic aorta (Figure 3). After positioning the device, the stent graft portion was deployed, and the delivery system was separated and removed from the graft. The device was secured by suturing the collar portion of the product to the distal native aortic remnant. The ascending aorta and aortic arch were replaced with the proximal, nonstented graft portion of the device. Overall, the Plexus configuration was used in 76% of cases (56/74); the most common concomitant procedures were aortic valve repair or replacement (n = 20), aortic root replacement (n = 14), and coronary artery bypass (n = 12).

### Study Definitions and Follow-up

In this report, we provide postoperative results at discharge or within 30 days and at 12 months. The primary end point was freedom from major adverse events (MAEs) occurring ≤1 year after the procedure. This composite end

**TABLE 1. Preoperative characteristics of Thoraflex Hybrid study patients (N = 74) stratified according to study group**

| Variable | Primary group (n = 65) | Aortic rupture group (n = 9) |
|---|---|---|
| Age at consent, y | 68 (56-74) | 70 (49-75) |
| Male sex | 43 (66) | 7 (78) |
| Ethnicity | | |
| Hispanic or Latino | 5 (8) | 2 (22) |
| Not Hispanic or Latino | 57 (88) | 7 (78) |
| Not reported or unknown | 3 (5) | 0 |
| Race | | |
| Asian | 6 (9) | 0 |
| Black or African American | 12 (19) | 2 (22) |
| White | 44 (68) | 7 (78) |
| Other | 3 (5) | 0 |
| Aneurysm only (without dissection)* | 27 (40) | 2 (22) |
| Aortic dissection | 38 (58) | 7 (78) |
| Acute/subacute dissection | 1 (2) | 6 (67) |
| Chronic dissection | 37 (57) | 1 (11) |
| DeBakey type I | 33 (51) | 7 (78) |
| DeBakey type III | 5 (8) | 0 |
| Suspected or confirmed genetic disorder | 5 (8) | 1 (1) |
| Current or former smoker | 39 (60) | 6 (67) |
| Hypertension | 57 (88) | 9 (100) |
| Hypercholesterolemia | 37 (57) | 4 (44) |
| Hyperlipidemia | 36 (55) | 4 (44) |
| Diabetes | 6 (9) | 0 |
| Coronary artery disease | 24 (37) | 2 (22) |
| Previous coronary artery bypass surgery | 8 (12) | 1 (11) |
| Previous angioplasty or stent | 4 (6) | 0 |
| Previous myocardial infarction | 4 (6) | 0 |
| Congestive heart failure | 10 (15) | 1 (11) |
| Previous stroke | 8 (12) | 0 |
| Transient ischemic attack | 4 (6) | 0 |
| Chronic obstructive pulmonary disease | 10 (15) | 2 (22) |
| Renal insufficiency† | 7 (11) | 3 (33) |
| History of renal failure‡ | 2 (3) | 0 |
| Previous paraplegia | 1 (2)§ | 0 |
| Previous proximal aortic surgery | 31 (48) | 2 (22) |

Values are presented as n (%) or as the median (quartile 1-quartile 3). *Includes 1 patient with a large pseudoaneurysm in the rupture group. The pseudoaneurysm was thought to be either related to a penetrating aortic ulcer or from trauma. †Renal insufficiency was defined as a creatinine level ≥1.5 mg/dL. ‡History of renal failure was defined as having a serum creatinine value ≥2.5 mg/dL or previous renal dialysis. §Due to gunshot wound.

point included permanent stroke, permanent paraplegia/paraparesis, unanticipated aortic-related reoperation (excluding reoperation for bleeding), and all-cause mortality.

Secondary end points included the individual components of the composite primary end point, aortic disease-related mortality, myocardial infarction, respiratory failure, renal failure, thromboembolic adverse events, bowel ischemia, failed device patency, extension procedures within the downstream aorta, and end points specifically related to the extension procedures. Paraplegia/paraparesis was defined as complete or partial loss of lower limb motor function related to spinal cord ischemia and not related to stroke. If stroke or paraplegia/paraparesis were reported at discharge or within 30 days and persisted at 12 months or upon death before 12-month follow-up, the term was updated to permanent stroke or paraplegia/paraparesis. End points specifically related to extension procedures included failure of device extension integrity, type III endoleak, failed patency of the device extension overlap, MAE at 30 days after extension, and any secondary reinterventions related to the extension procedure.

Study assessments included the collection of data related to the primary end point (MAE) and its components and related to the secondary end points described previously, which were adjudicated by the Clinical Events Committee, which is an independent board of 5 external cardiothoracic surgeons. Data assessed for the secondary end points included computed tomography imaging, which was reviewed by the Core Laboratory (ERT, Inc) to determine the incidence of failed device patency, loss of device extension integrity, type III endoleak after the extension procedure, and failed patency of the device extension overlap. Site investigators augmented the data collected during the trial by reviewing medical records.

## RESULTS

### Primary Study Group

Early outcomes for the primary study group are presented in Table 3. At discharge or within 30 days, 10 patients (15%) had at least 1 of the MAE outcomes, including 2 deaths (3%). Causes of death are provided in Table E1. Persistent stroke occurred in 4 patients (6%). Persistent paraplegia/paraparesis occurred in 3 patients (5%), all of whom received a device with a 150-mm endovascular component. The most common early complication was respiratory failure (n = 15; 23%). Seven patients (11%) had renal failure at discharge or within 30 days; all 7 cases of renal failure occurred within 1 to 2 days from the index procedure and were treated with hemodialysis. Two patients had early thromboembolic adverse events. Of the 54 patients with adequate imaging at 30 days, all exhibited device patency.

At 1 year, 2 patients (3%) were lost to follow-up or withdrawal. Freedom from MAE—the study's primary outcome—was 81% (51/63). Twelve patients (19%) had at least 1 of the MAE (Table 4); this included 7 deaths (11%). Three deaths were considered aortic disease-related (Table E1). The first of these was a patient who

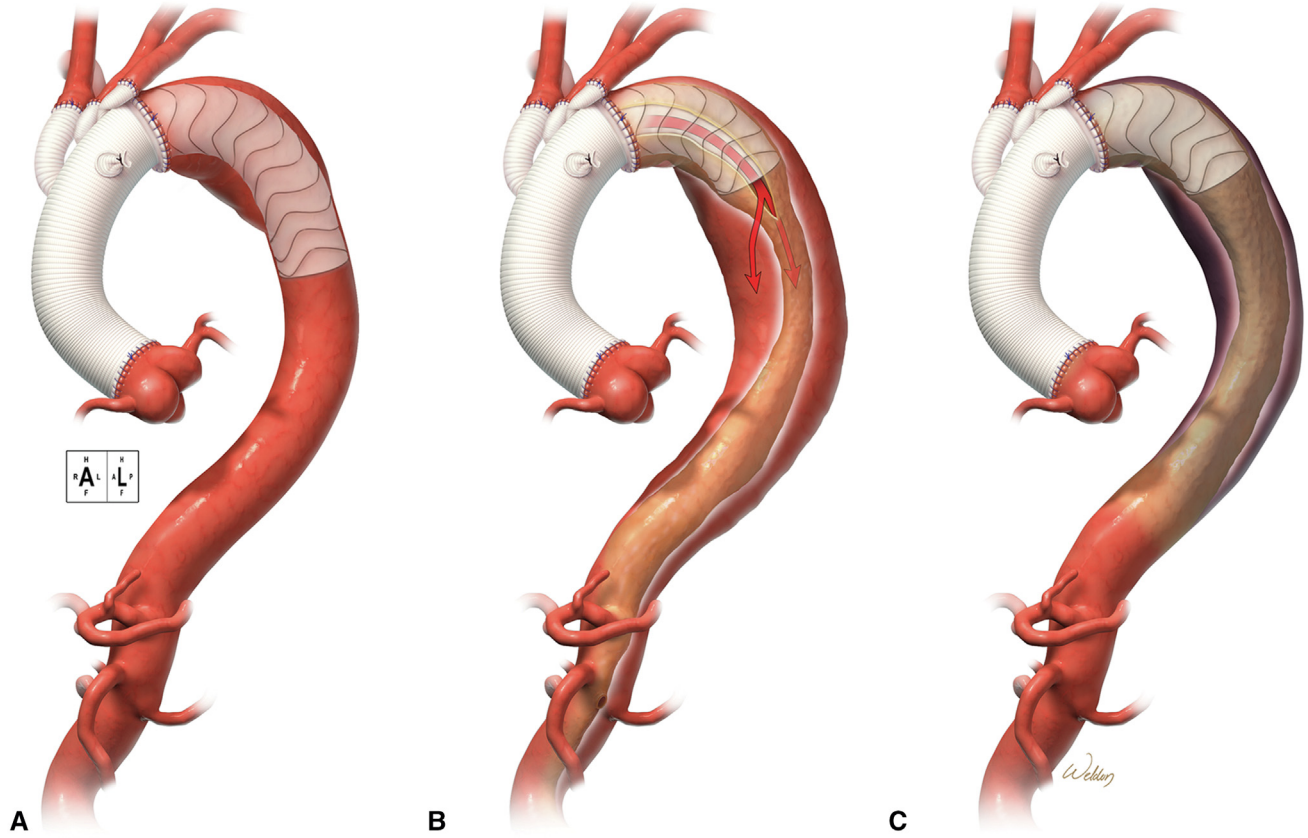


**FIGURE 2.** Illustrations of the Thoraflex Hybrid device (Terumo Aortic) as used in (A) a definitive repair of thoracic aortic aneurysm. Here, the distal aspect of the device lands in healthy aortic tissue where a secure seal may be achieved. B, Stage 1 repair of a chronic aortic dissection with fenestration of the true lumen wall to perfuse both lumens (including the avulsed left renal artery). Repair of extensive chronic aortic dissection often necessitates a planned extension procedure (stage 2) for definitive repair. C, Repair of acute aortic dissection. Here, the endograft portion of the device might help expand the true lumen. The distal aspect of the device lands in the residually dissected aorta. Used with permission from Baylor College of Medicine.

underwent an unanticipated aortic-related reoperation and unplanned endovascular extension on postoperative day (POD) 1 due to aortic rupture but died on POD 3 due to multisystem organ failure. The second patient required an unplanned endovascular repair of the descending thoracic aorta at 23 days because of rapid aneurysm growth and died of aortic rupture 69 days after implantation. The third death was due to sudden cardiac arrest on POD 147. Two cases of bowel ischemia were reported. The first occurred 22 days after the index procedure, and the second occurred 19 days after the endovascular extension had been performed on POD 74. Of the 51 patients with adequate imaging at 1 year, 50 (98%) had a patent device, and 1 had thrombosis of the left subclavian artery branch graft. No new thromboembolic events were reported.

Twenty-six of 63 patients (41%) received a planned extension procedure within 1 year of device implantation. One of the MAE occurred within 30 days of the extension procedure. That patient underwent an unanticipated aortic-related reoperation to repair a new-onset acute abdominal aortic dissection with rupture 11 days after extension repair. No instances were recorded of failed device extension integrity, failed patency of the device extension overlap, or death after the extension procedure. Two patients underwent additional open thoracoabdominal aortic repair after the extension procedures: 1 to treat acute dissection with rupture of the abdominal aorta 11 days after the extension procedure (the major adverse event described previously), and the other to treat enlargement of a residual aneurysm of the descending thoracic aorta (sans rupture) 58 days after the extension procedure. One patient had a type III endoleak after the extension procedure; this resolved within 12 months without treatment.

Two patients had unplanned extension repairs after the Thoraflex procedure. One patient had an unplanned endovascular extension (also counted as an unanticipated aortic-related reoperation) on POD 1 because of a ruptured descending thoracic aortic dissection. The other patient had an unplanned endovascular repair of the descending

**TABLE 2. Operative details of Thoraflex Hybrid (Terumo Aortic) study patients (N = 74) stratified according to study group**

| Variable | Primary group (n = 65) | Aortic rupture group (n = 9) |
|---|---|---|
| Emergency or urgent repair | 1 (2) | 9 (100) |
| Redo median sternotomy | 31 (48) | 3 (33) |
| Device used | | |
| Plexus | 48 (74) | 8 (89) |
| Ante-Flo | 17 (26) | 1 (11) |
| Length of endovascular component | | |
| 150-mm device | 37 (57) | 5 (56) |
| 100-mm device | 28 (43) | 4 (44) |
| Location of distal anastomosis (collar) | | |
| Between innominate and LCCA | 4 (6) | 0 |
| Between LCCA and LSCA | 30 (46) | 4 (44) |
| Distal to LSCA | 31 (48) | 5 (56) |
| Initial arterial cannulation site | | |
| LCCA | 1 (2) | 0 |
| Ascending aorta | 18 (28) | 2 (22) |
| Right axillary artery | 33 (51) | 7 (78) |
| Left axillary artery | 1 (2) | 0 |
| Innominate artery | 12 (18) | 0 |
| Brachiocephalic arterial reattachment approach | | |
| Innominate artery | | |
| Graft | 52 (80) | 8 (89) |
| Island | 13 (20) | 1 (11) |
| Left common carotid artery | | |
| Graft | 51 (78) | 8 (89) |
| Island | 13 (20) | 1 (11) |
| Ligated | 1 (2) | 0 |
| Left subclavian artery | | |
| Graft | 49 (75) | 8 (89) |
| Island | 11 (17) | 1 (11) |
| Ligated without replacement | 4 (6) | 0 |
| Native | 1 (2) | 0 |
| Cardiopulmonary bypass time, minutes | 195 (149-245) | 200 (155-228) |
| Hypothermic circulatory arrest time, minutes | 52 (35-64) | 44 (13-59) |
| Lowest core temperature, °C | 20 (18-23.8) | 22 (18-24) |
| Use of ACP | 60 (92) | 9 (100) |
| ACP time, minutes | 58 (46-73) | 54 (24-65) |
| Use of RCP | 11 (17) | 0 |
| RCP time, minutes | 26 (4.5-32.5) | 0 |
| Use of ACP and RCP | 6 (9) | 0 |
| Use of cerebrospinal fluid drainage* | 16 (25) | 0 |
| Any concomitant procedure | 36 (55) | 8 (89) |
| Nonroot aortic valve procedures | 14 (22) | 6 (67) |
| Aortic valve repair | 8 (12) | 5 (56) |
| Aortic valve replacement | 6 (9) | 1 (11) |
| Aortic root replacement | 13 (20) | 1 (11) |
| CVG: mechanical | 1 (2) | 0 |
| CVG: biological | 6 (9) | 1 (11) |
| Porcine bioroot | 3 (5) | 0 |
| Valve-sparing | 3 (5) | 0 |
| Aortic root repair† | 4 (6) | 1 (11) |
| Coronary artery bypass | 10 (15) | 2 (22) |
| Mitral valve repair | 3 (5) | 0 |
| Ablation for atrial fibrillation | 3 (5) | 0 |
| Left atrial appendage closure | 6 (9) | 0 |
| Other (not reported above)‡ | 4 (6) | 0 |

Values are presented as n (%) or as the median (quartile 1-quartile 3). The Thoraflex Hybrid Plexus and Ante-Flo devices are from Terumo Aortic. *LCCA*, Left common carotid artery; *LSCA*, left subclavian artery; *ACP*, antegrade cerebral perfusion; *RCP*, retrograde cerebral perfusion; *CVG*, composite valve graft. *Includes only intraoperative cerebrospinal fluid drainage, not postoperative drain placement as in use as a rescue measure. †For the primary group, these procedures included plication of the noncoronary and right coronary sinus, repair of pseudoaneurysm at the noncoronary sinus (closed with suture), repair of pseudoaneurysm at the proximal anastomosis of previous aortic root replacement at the sinotubular junction (closed with suture), and repair of periroot pseudoaneurysm under the noncoronary sinus (closed with suture). For the rupture group, repair involved remodeling the noncoronary sinus with a Dacron patch. ‡These procedures included septal myectomy, tricuspid valve repair, extraction of failed stent graft from descending thoracic aorta, and closure of atrial septal defect.

thoracic aorta because of rapid aneurysm growth at POD 23 and died 69 days after implantation.

### Aortic Rupture Group

Early outcomes for the aortic rupture study group are presented in Table 3. At discharge or within 30 days, 3 patients (33%) had at least 1 of the MAE outcomes, including 1 death caused by stroke (11%). Two patients (22%) suffered persistent stroke, 1 (11%) had persistent paraparesis, and 1 (11%) had renal failure. Of the 6 patients with adequate imaging at 30 days, all had maintained device patency.

At 1 year, 2 patients were lost to follow-up. Freedom from MAE—the study's primary outcome—was 71% (5/7). Two patients (29%) had at least 1 of the MAE (Table 4), including 1 death (14%) due to stroke, which was not considered aortic disease-related. Of the 4 patients with adequate imaging at 1 year, all maintained device patency, and none underwent an extension procedure.

## DISCUSSION

In this US-based multicenter trial, the treatment of extensive thoracic aortic disease with the Thoraflex Hybrid device showed encouraging results. In the primary group, we observed 81% freedom (51/63) from MAE at 1 year. Notably, the rates of early death and persistent stroke were 3% and 6%, respectively. These rates of early

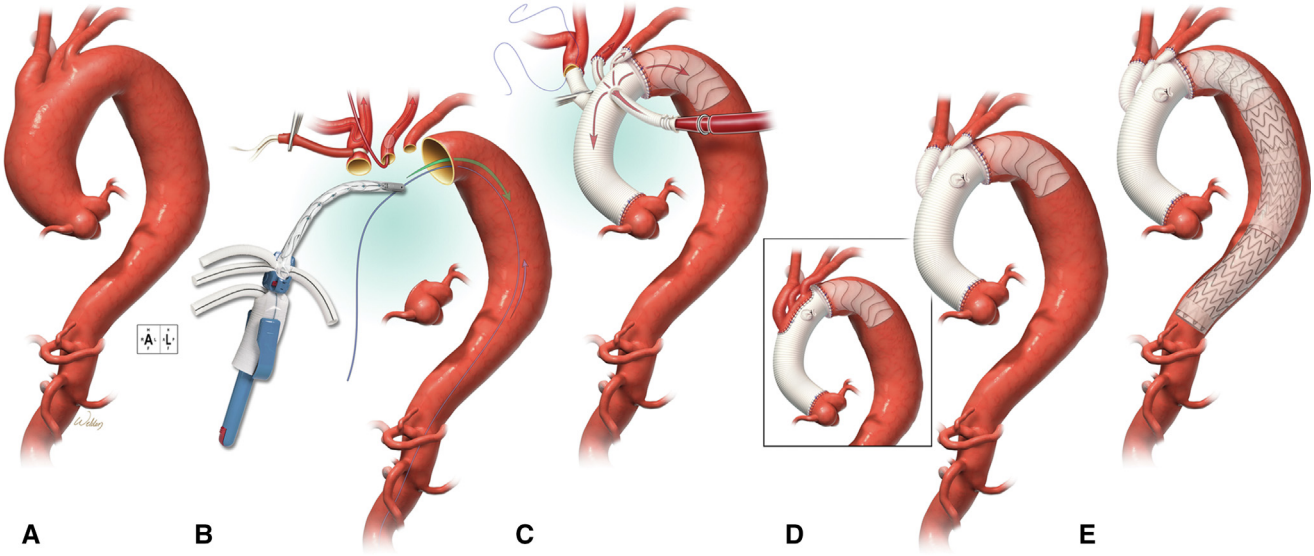


**FIGURE 3.** Illustration of repair using the Thoraflex Hybrid device (Terumo Aortic) in a patient with (A) extensive thoracic aortic disease that includes aneurysm of the ascending aorta, aortic arch, and descending thoracic aorta. B, After performing a median sternotomy and establishing cardiopulmonary bypass via right axillary artery cannulation, the aorta was transected proximally at the sinotubular junction and distally just beyond the left subclavian artery. A balloon catheter was inserted into the left common carotid artery to provide antegrade cerebral perfusion. A guide wire for the deployment procedure was inserted into the femoral artery and advanced retrograde with subsequent retrieval from the opening of the descending thoracic aorta. The tip of the device was threaded onto the guide wire and advanced into position in the descending thoracic aorta. C, The endograft portion of the device was deployed, and the delivery system was separated and removed from the graft. The device was secured by suturing the collar to the distal native aortic remnant. In this patient without aortic root disease, the proximal anastomosis was completed at the level of the sinotubular junction. Aortic perfusion was provided via a side branch. The brachiocephalic arteries were anastomosed. Reattachment of the innominate artery might necessitate ceasing perfusion through the right axillary artery as the tourniquet is removed. D, The completed stage 1 repair using the Thoraflex Hybrid Plexus device is shown. The brachiocephalic arteries were replaced with branch grafts. The Thoraflex Hybrid Ante-Flo device may be used to reattach the brachiocephalic arteries as an island patch (*inset*). E, Two weeks after the initial repair, a stage 2 extension procedure was performed via retrograde deployment of 2 stent grafts to provide definitive repair of the descending thoracic aorta. There is considerable overlap between the endograft portion of the hybrid device and the first stent-graft. Used with permission from Baylor College of Medicine.



complications are similar to or better than those for the traditional ET approach, with contemporary ET studies reporting rates of early death ranging from 7% to 17%, and rates of stroke ranging from 2% to 8%.[1-6] The risk of postoperative spinal cord deficit is where the traditional ET and FET approaches diverge. This risk is rare in traditional ET repair, but it remains a threat in FET repair. In our study, 4 of 74 patients (6%) developed paraplegia/paraparesis that persisted at the time of discharge. In contemporary meta-analyses of FET repair, the risk of paraplegia/paraparesis has ranged from 4% to 7%.[15-18]

The Achilles heel of the traditional ET approach is the delay between stages to repair the proximal and distal thoracic aorta. This delay not only increases the risk of death due to distal aortic rupture, but it keeps many patients from undergoing elective repair in a timely manner. An advantage of the FET technique over traditional ET repair includes the ability to perform complete repair in select patients within a single operation (Figure 2, *A*), thus avoiding the cumulative risk of 2 major procedures. The cumulative risk of early death from a 2-stage approach might be as great as 15% to 23%.[1,2,4-6,19] Estrera and colleagues[2] examined patients who did not undergo the second stage after traditional ET arch repair and showed that 18% died between 31 and 45 days. Svensson and colleagues[3] reported that the likelihood of completing a second-stage operation after traditional ET repair within 1 to 8 years of initial repair was 53% to 61%; further, without a second-stage repair, the likelihood of death was 16% to 27% within 1 to 8 years. In the traditional ET experience of Coselli and colleagues,[6] 56% of patients underwent a second-stage repair within a median interval of 3.2 months (IQR, 2.0-7.3 months); of these, most of the completion repairs were open procedures (185/203; 90%). In the current study, 41% (n = 26) of patients within the primary group underwent planned extension procedures of the downstream aorta within 1 year of having the Thoraflex Hybrid device implanted, and half of these procedures (13/26) were performed by 4 months (median, 122 [IQR, 73-157] days for the overall group) and were mostly endovascular completions (22/26; 85%). Thus, a possible advantage of the FET technique over the ET technique is the higher rate of endovascular completion.

**TABLE 3. Early outcomes (at discharge or within 30 days) of Thoraflex study patients (N = 74) stratified according to study group**

| Variable | Primary group (n = 65) | Aortic rupture group (n = 9) |
|---|---|---|
| Patients with at least 1 MAE | 10 (15) | 3 (33) |
| All-cause mortality | 2 (3) | 1 (11) |
| Aortic disease-related mortality | 1 (2) | 0 |
| Persistent stroke | 4 (6) | 2 (22) |
| Persistent paraplegia/paraparesis (n = 64)‡ | 3 (5)* | 1 (11)† |
| Unanticipated aortic-related reoperation | 2 (3) | 0 |
| Myocardial infarction | 0 | 0 |
| Respiratory failure§ | 15 (23) | 1 (11) |
| Renal failure‖ | 7 (11) | 1 (11) |
| Thromboembolic adverse events¶ | 2 (3) | 0 |
| Bowel ischemia | 1 (2) | 0 |
| Rescue use of cerebrospinal fluid drainage | 2 (3) | 2 (22) |
| Failed device patency | 0 | 0 |
| Postoperative lengths of stay, d | | |
| Intensive care unit stay | 4.5 (3-6) | 4 (3-9.8) |
| Hospital stay | 11 (7.3-17) | 9 (8.8-26) |

Values are presented as n (%) or as the median [quartile 1-quartile 3]. The Thoraflex device is from Terumo Aortic. *Two patients developed paraplegia, and one developed paraparesis (which was not considered an MAE when adjudicated by the Clinical Events Committee). †One patient developed paraparesis (which was not considered a MAE when adjudicated by the Clinical Events Committee). ‡Excludes 1 patient with preoperative paraplegia. §Respiratory failure was defined as ventilator dependence for greater than 48 hours before the time of discharge or 30 days. ‖Renal failure was defined as impaired kidney function necessitating dialysis before the time of discharge or 30 days. ¶Thromboembolic adverse events were defined as a blockage of a blood vessel by thromboemboli or a pulmonary embolism before discharge or within 30 days.

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Our results are comparable with those of other studies focused primarily on the Thoraflex Hybrid device (Table 5).[20,21,23,24,26,27] In series of nonemergency repair, early mortality rates ranged from 0% to 12%, with 1-year survival rates of at least 80%. Like any total aortic arch replacement procedure, FET repair has a substantial risk of postoperative stroke. In the primary group, the rates of persistent/permanent stroke at 30 days or discharge and at 1 year were 6% and 5%, respectively; in the rupture group, the rate was 22% at discharge or within 30 days and 29% at 1 year. Similarly, the rates of stroke from international studies of the Thoraflex Hybrid device have ranged from 6% to 18%, with the highest rates of stroke reported after emergency procedures to treat acute proximal aortic dissection.[20-27] In the current study, postoperative paraplegia/paraparesis that persisted at 1 year developed in 3 primary group patients (5%) who received devices with 150-mm endograft components. In the 8 international studies shown in Table 5, only 1 center observed no cases of spinal cord deficit; of those studies reporting a deficit, the rates of spinal cord deficit range from 2% to 8%.[20-27] Reflective of complex and extensive thoracic aortic disease, 41% of our primary group patients underwent planned stage 2 extension procedures (open and endovascular) within a year. This is comparable with the results of international studies reporting an extension rates ranging from 15% to 41% by approximately 2 years.[21-25,27] Despite efforts to hasten the second-stage repair, substantial life-threatening risks remained within the downstream untreated aorta. In our series, 3 patients had an aortic-related death that involved rapid growth or aortic rupture of the untreated, residually dissected aorta.

A limitation of this study includes the difficulty of evaluating a heterogeneous study population whose aortic disease frequently necessitated a patient-tailored operative approach. Another limitation is the substantial variation in surgical technique among participating centers with respect to mode of cerebral perfusion, the approach to recording procedural times, temperature targets during hypothermic circulatory arrest, the type of device selected, and other factors. Selection bias existed because surgeons recruited patients who were determined to be most likely to benefit from the device. Because there was not a concomitant, prospectively enrolled comparison group, we were able to present only descriptive statistics. Furthermore, regarding stage 2 extension repairs, there are nuanced distinctions in categorizing patients into planned and unplanned stage 2 repairs that cloud evaluation. For example, patients surviving with extensive residual aortic dissection might present with a relatively small-diameter distal aorta that subsequently expands to an aortic diameter that triggers reintervention. Although the second repair is considered unplanned, it is not entirely unexpected considering the natural history of aortic dissection.[28,29] Finally, several patients in our study had incomplete follow-up data at 1 year.

**TABLE 4. One-year outcomes of Thoraflex study patients (N = 70) stratified according to study group**

| Variable | Primary group (n = 63)* | Aortic rupture group (n = 7)† |
|---|---|---|
| Patients with at least 1 MAE | 12 (19) | 2 (29) |
| All-cause mortality | 7 (11) | 1 (14) |
| Aortic-disease related mortality | 3 (5) | 0 |
| Permanent stroke | 3 (5) | 2 (29) |
| Permanent paraplegia/paraparesis (n = 62)‡ | 3 (5)§ | 0 |
| Unanticipated aortic-related reoperation | 3 (5) | 0 |
| Myocardial infarction | 0 | 0 |
| Respiratory failure‖ | 15 (24) | 2 (29) |
| Renal failure¶ | 7 (11) | 1 (14) |
| Thromboembolic adverse events# | 2 (3) | 1 (14) |
| Bowel ischemia | 2 (3) | 0 |
| Failed device patency** | 1 (2) | 0 |
| Unplanned extension repairs within 1 y†† | 2 (3) | 0 |
| Planned extension procedure within 1 y | 26 (41) | 0 |
| Endovascular extension | 22 (35) | – |
| Time to extension, d | 122 (64-156) | – |
| 1 Stent graft | 6 (10) | – |
| 2 Stent grafts‡‡ | 13 (21) | – |
| 3 Stent grafts | 2 (3) | – |
| >3 Stent grafts | 1 (2) | – |
| Open extension | 4 (6) | – |
| Hybrid extent I thoracoabdominal repair§§ | 1 (2) | – |
| Extent II thoracoabdominal repair‖‖ | 3 (5) | – |
| MAE ≤30 d of extension procedure | 1 (2) | – |
| Complications of extension procedures within 1 y | | |
| Aortic rupture after extension procedure | 1 (2) | – |
| Loss of device-to-extension integrity | 0 | – |
| Type III endoleak¶¶ | 1 (2) | – |
| Failed patency of device-to-extension overlap | 0 | – |
| Secondary reintervention related to extension procedure## | 2 (3) | – |

Values are presented as n (%) or as the median [quartile 1-quartile 3]. The Thoraflex device is from Terumo Aortic. *MAE*, Major adverse events; *POD*, postoperative day. *One patient was lost to follow-up before 1 year, and 1 patient withdrew before 1 year. †Two patients were lost to follow-up before 1 year. ‡Excludes 1 patient with preoperative paraplegia. §Paraplegia developed in 2 patients, and paraparesis (which was not considered a MAE when adjudicated by the Clinical Events Committee) developed in 1 patient. ‖Respiratory failure was defined as ventilator dependence for >48 hours within 1 year after implantation. ¶Renal failure included any patient with impaired kidney function that necessitated dialysis within 1 year after implantation. #Thromboembolic adverse events were defined as a blockage of a blood vessel by thromboemboli or a pulmonary embolism within 1 year of implantation. **Occlusion of the left subclavian artery branch graft that did not necessitate treatment. ††Unplanned extension repairs were performed on PODs 1 and 23. ‡‡Repair in 1 patient involved stenting the superior mesenteric artery (snorkel approach) after impingement by endograft. §§Repair includes the deployment of a stent graft into the frozen elephant trunk to serve as a bridge to the open graft. This repair was done on POD 315. ‖‖These repairs were done on PODs 72, 95, and 240. ¶¶Imaging was assessed for type Ia (unanticipated), III, or IV endoleaks; a type III endoleak was detected during surveillance and spontaneously resolved without treatment. ##After the planned extension procedure, additional open repair of the distal aorta was needed in 1 patient to repair a new-onset acute abdominal aortic dissection with rupture 11 days after extension repair and in another patient without rupture but with aortic expansion 58 days after the extension procedure.

## CONCLUSIONS

Despite the limitations described, our study showed that total aortic arch replacement using the Thoraflex Hybrid device is an acceptable and versatile approach to repair in patients with complex thoracic aortic disease. In select patients, its use appears to facilitate extensive aortic repair of the proximal and distal aorta, including in the reoperative setting. Initial repair might be safely expanded to meet patient needs, including performing the simultaneous repair of the aortic root and aortic valve, and other procedures that would ordinarily push the limits of traditional total arch replacement. Because of its integrated design, the use of this hybrid device avoids complications that commonly plague the endovascular repair of the distal aortic arch and proximal descending thoracic aorta, namely device migration and type Ia endoleak. Furthermore, by providing a stable landing zone for subsequent downstream endovascular aortic repair, endovascular completion repair might be technically easier to perform than hybrid ET approaches. The Thoraflex Hybrid device seems particularly useful in treating patients with aortic dissection who often face multiple aortic repairs because of progressive aortic dilatation.

**TABLE 5. International experience with Thoraflex repairs**

| Reference | Patients, n | Early mortality, n (%) | Stroke, n (%) | Spinal cord deficit, n (%) | Survival | Extension of repair |
|---|---|---|---|---|---|---|
| Chabry et al[20] | 109 | 23 (21) | 17 (16)* | 9 (8)† | NR | NR |
| Kreibich et al[21] | 41 | 1 (2) | 4 (10)‡ | 0 | >90% at 20 mo | 39% at 7.7 mo |
| Berger et al[22] | 63 | 2 (3) | 4 (6)‡ | 1 (2)† | >90% at 1 y | 37% at 1.5 y |
| Beckman et al[23] | 211 | 25 (12) | 38 (18)‡ | 4 (2)† | 84% at 1 y | 15% at 2.2 y |
| Fiorentino et al[24] | 28 | 0 | 4 (14)‡ | 2 (7)§ | 92 ± 6% at 2 y | 41 ± 11% at 2 y |
| Berger et al[25] | 55 | 6 (11) | 9 (16)‡ | 3 (6)† | 85% at 1 y | 22% at 1 y |
| Chu et al[26] | 40 | 2 (5) | 3 (8)* | 2 (5)§ | 90% at 1 y | 1 (3%) |
| Shrestha et al[27] | 100 | 7 (7) | 9 (9)‡ | 7 (7)† | 81% at 2.7 y | 22% at 2.7 y |

The Thoraflex device is from Terumo Aortic. The report from Chabry and colleagues[20] reflects emergency procedures; the authors present paraplegia rates. In Kreibich and colleagues,[21] strokes were classified as nondisabling. In Berger and colleagues,[22] all repairs were performed in patients with previous aortic repair; most previous repairs (78%) were proximal aortic repair to treat acute type A aortic dissection. Regarding Fiorentino and colleagues,[24] spinal cord deficit was temporary, and stroke was disabling. In Berger and colleagues,[25] all repairs were to treat acute aortic dissection. The reports from Beckman and colleagues[23] and Shrestha and colleagues[27] present the experience of the Hannover Medical School. The former is from November 2012 to September 2018, and the latter is from April 2010 to October 2014; a brief period of overlap most likely includes duplicate repairs. The cases from Shrestha and colleagues[27] reflect paraparesis only. *NR*, Not reported. *Reported as stroke or transient ischemic attack. †Temporary or permanent paraplegia/paraparesis. ‡Reported as stroke. §Temporary, including those resolved with rescue measures such as the use of cerebrospinal fluid drainage.

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Notably, second-stage repair might be performed in an open fashion, which is thought to enhance repair durability and might thereby reduce the necessity for any subsequent aortic repair. Although 1-year results with this hybrid device are encouraging, further study is needed to better understand the selection of ideal surgical candidates and how to best plan for additional downstream aortic repair (Figure 4 and Video 1). Long-term data will be necessary to assess the durability of these repairs.

## STUDY INSTITUTIONS

Participating study sites (institution [site principal investigator(s), number of patients enrolled, site-specific institutional review board protocol number (IRB); date of approval])

- Cleveland Clinic (Eric E. Roselli, 15 patients, IRB 16-415; June 30, 2016)
- Baylor College of Medicine (Joseph S. Coselli, 14 patients, IRB H-38412; April 25, 2016)
- Northwestern University (S. Chris Malaisrie, 11 patients, IRB 2483; March 21, 2016)
- Mt Sinai Medical Center (Paul Stelzer and Allan Stewart, 8 patients, IRB 16-00308; May 4, 2016)
- Columbia University (Hiroo Takayama and Michael Borger, 6 patients, IRB AAAQ6906; February 7, 2017)

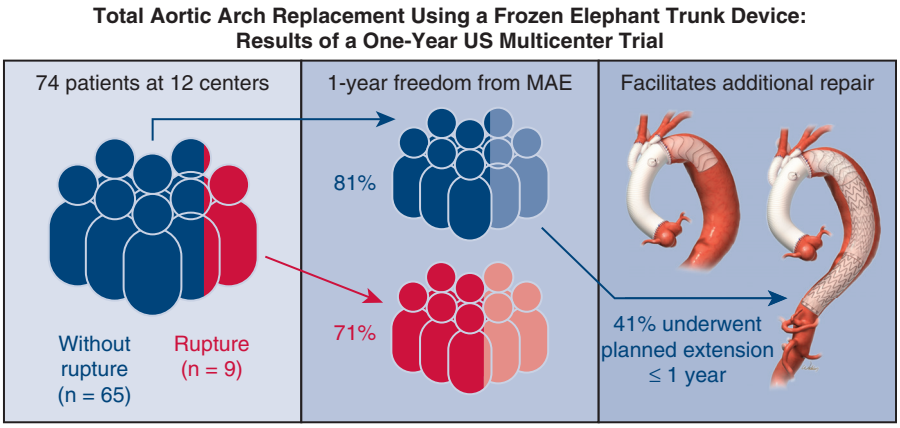
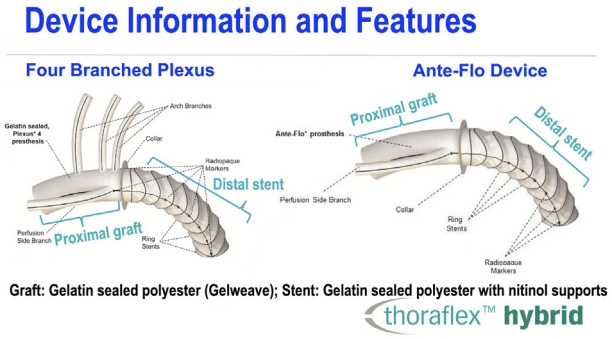



**FIGURE 4.** In a US multicenter investigation device trial, 74 patients with extensive thoracic aortic disease were recruited from 12 centers. Patients were recruited into a primary treatment group (n = 65) or secondary treatment group (n = 9; these patients were at risk of imminent rupture). All patients underwent total aortic arch replacement using a 1-piece hybrid device that facilitates the frozen elephant trunk technique. The primary end point was freedom from major adverse events (*MAE*), comprising all-cause mortality, permanent stroke, permanent paraplegia/paraparesis, and unanticipated aortic-related reoperation. A secondary area of study was the planned extension of repair. Two patients in each group were lost to follow-up or withdrawal by 1 year. Within the primary group, the freedom from MAE was 81% and 41% underwent planned extension of repair at 1 year. Within the rupture group, the freedom from MAE was 71% at 1 year.




**VIDEO 1.** Dr Joseph S. Coselli, National Principal Investigator, discusses key findings of the US pivotal trial for the Thoraflex Hybrid device (Terumo Aortic). The device facilitates a frozen elephant trunk approach to total aortic arch replacement by combining open and endovascular strategies into a 1-piece device. Video available at: https://www.jtcvs.org/article/S0022-5223(22)00921-7/fulltext.

- Emory Saint Joseph's Hospital (Edward P. Chen, 5 patients, IRB 86712; August 8, 2016)
- The University of Texas Health Science Center at Houston (Anthony L. Estrera, 4 patients, IRB HSC-MS-16-0308; May 20, 2016)
- University of Pittsburgh/UPMC Shadyside (Thomas G. Gleason and Forozan Navid, 4 patients, IRB 20160159; March 31, 2016)
- Stanford University (Michael P. Fischbein, 3 patients, IRB 38808; October 11, 2016)
- Weill Cornell Medicine (Leonard N. Girardi, 2 patients, IRB 1602016970; July 11, 2017)
- University of Michigan (Himanshu J. Patel, 1 patient, IRB HUM00110530; April 7, 2016)
- Hospital of the University of Pennsylvania (Joseph E. Bavaria, 1 patient, IRB 82468; May 11, 2016)

## Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/21%20AM/AM21_A43/AM21_A43_01%20-%20Joseph%20Coselli.mp4.


## Conflict of Interest Statement

All authors participate in clinical trials sponsored by Terumo Aortic. Dr Coselli consults for, receives royalties, and a departmental educational grant from Terumo Aortic; consults and participates in clinical trials for Medtronic, Inc, and W.L. Gore & Associates; and participates in clinical trials for Abbott Laboratories, Artivion, CytoSorbents, and Edwards Lifesciences. Dr Preventza consults for and participates in clinical trials for W.L. Gore & Associates, and Terumo Aortic. Dr LeMaire consults for Terumo Aortic and Cerus, and serves as a principal investigator for clinical studies sponsored by Terumo Aortic and CytoSorbents. Dr Bavaria reports relationships with Medtronic, Inc, and W.L. Gore & Associates, Edwards Lifesciences, Abbott/St Jude, and Cytosorbents. Dr Estrera consults for W.L. Gore & Associates. Dr Gleason serves on the advisory board for Abbott. Dr Malaisrie has received honoraria from Terumo Aortic, Cryolife, Medtronic, Inc, and Edwards Lifesciences. Dr Patel serves as a consultant for Terumo Aortic, Medtronic, Inc, and W.L. Gore & Associates. Dr Roselli consults, participates in clinical trials for, and receives research grants from Artivion, Cook, Medtronic, Inc, Terumo Aortic, and W.L. Gore & Associates. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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**Key Words:** aortic arch (total), aortic aneurysm, aortic dissection, hybrid repair, frozen elephant trunk

## Discussion

### Presenter: Dr Joseph Coselli

**Dr Axel Haverich** (*Hannover, Germany*). Thank you very much, Dr Coselli, for this excellent presentation. I'd also like to thank the organizing committee for the opportunity to discuss for this report, which deals with one of the most complicated topics in the specialty: aortic arch replacement. Dr Coselli and his distinguished group of thoracic and aortic surgeons are to be congratulated for their excellent 1-year results with the Thoraflex device for aortic arch repair.

The trial involved 12 US sites and recruited 65 patients without rupture into the primary study group and 9 patients into the rupture group. All patients underwent open surgical repair of the ascending aorta, aortic arch, and descending thoracic aorta for either aneurysm formation or aortic dissections. The primary end point was freedom from a composite measure of adverse events defined as permanent stroke, permanent paraplegia, unanticipated aortic-related reoperation, and all-cause mortality. In the primary study group, 2 patients were lost to follow-up. Freedom from major adverse events at 1 year was 79%. Seven patients died, including 2 of 65, within 30 days or before discharge. Seven patients developed renal failure. Twenty-six patients, for a remarkable 41%, underwent planned extension procedures, which included 22 endovascular procedures within the median of 122 days. In the aortic rupture group, 2 patients were lost to follow-up at 1 year, and freedom from major adverse events at this time was 71%. Two patients had strokes and 1 patient died. The authors concluded that the Thoraflex device facilitates aortic arch replacement and enables treatment of extensive thoracic aortic disease during a single procedure, or can facilitate a subsequent endovascular procedure. They also conclude that 1-year results with the Thoraflex Hybrid device are promising, but long-term data will be necessary to assess the durability of these repairs.

Taking this study together at this point, it provides excellent results in this truly difficult patient population, in the

elective and in the complicated group with rupture. It also has to be taken into consideration for these results for each of the 12 sites, it involves a learning curve with the use of this device. Our group in Hannover started the experience with Thoraflex in 2012 with the first-in-man study at this time. Two years later, we published our first case series. From then on, we published a number of substudies in certain subgroups of patients and also were involved in multicenter series. At our institution, a total of more than 300 patients have now been treated with a device of whom more than 50% were acute aortic dissections, and as a matter of fact, it has become our preferred choice in terms of devices in acute type A dissections, and we were very lucky to maintain a 100% follow-up of all patients with this device implanted. The complications we have seen in Hannover very much reflect the experience of the 12 US sites during the trial presented today, which includes qualitatively and quantitatively strokes, paraplegia, dialysis requirement, as well as mortality.

I'd like to ask 3 questions of Dr Coselli. Number 1, did the incidence or the occurrence of paraplegia correlate with the duration of circulatory arrest? And second, did the occurrence of paraplegia, as was influenced by the length of the stents being used (10 cm vs 15 cm)? And number 3: in terms of strokes, did the type of cerebral protection have any influence on the occurrence of stroke or the duration of the cerebral protection? Thank you very much for the opportunity to discuss this fine report.

**Dr Joseph Coselli** (*Houston, Tex*). I want to thank Dr Axel Haverich for his kind comments. I also want to congratulate him on his group's efforts following in the footsteps of the legendary Dr Hans Borst, who first conceived the elephant trunk approach to total aortic arch replacement, and also to Dr Malakh Shrestha, who has been instrumental in the development of this frozen elephant trunk device. Heartfelt thanks for his summary of his and our data.

To answer his question, we found no relationship between the length of circulatory arrest and the incidence of paraplegia. With regard to the device having either a 10- or 15-cm endograft portion, there was a trend toward having less risk for spinal cord issues using the shorter device. With regard to stroke, we had 4 in the primary group and 2 in the rupture group. And with regard to cerebral protection, there was no difference with regard to the time frame of the circulatory arrest. Of interest, all 6 of these patients had antegrade cerebral perfusion.

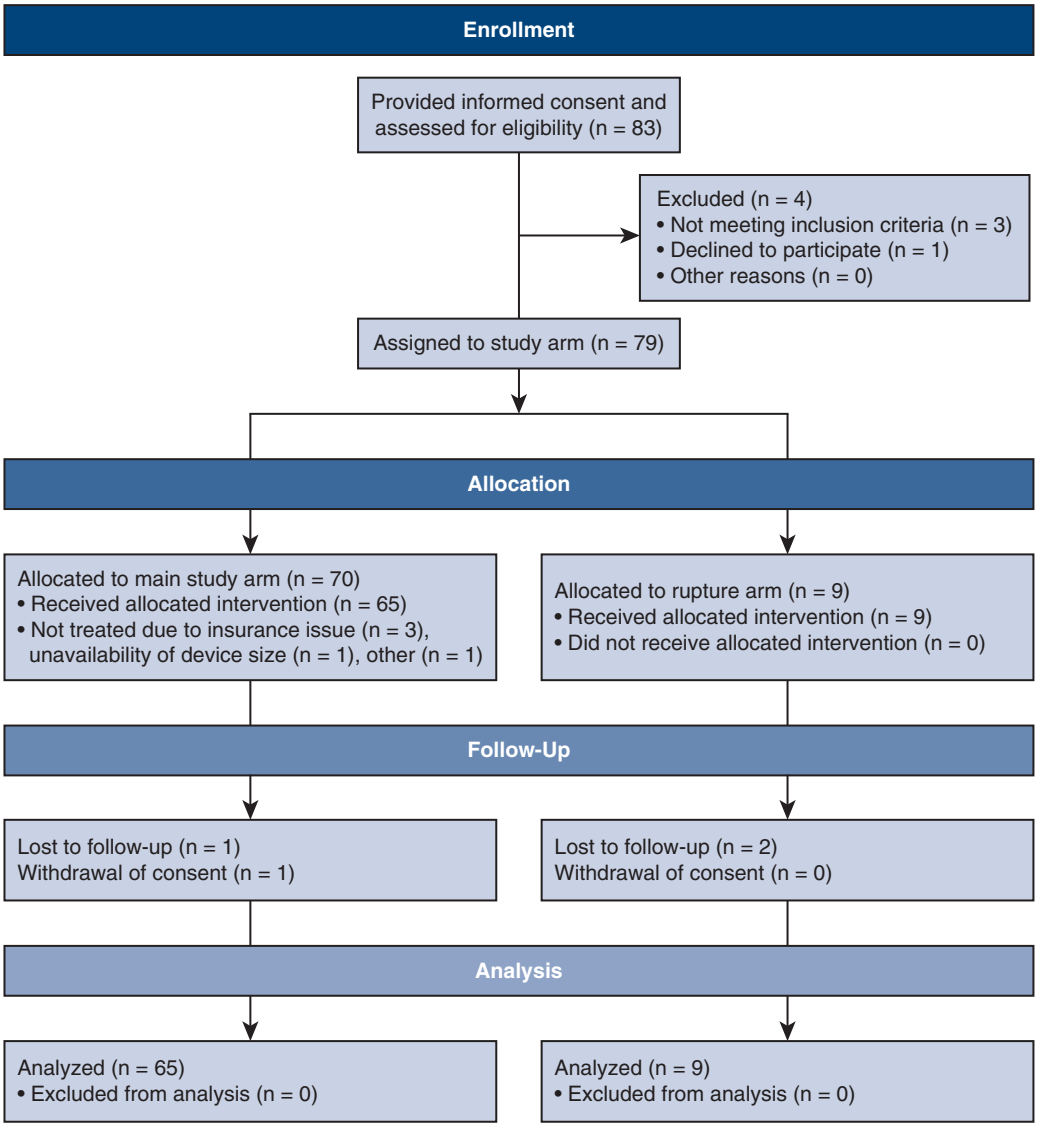


**FIGURE E1.** Consort flow diagram.

**TABLE E1. Causes of death**

| Patient | Days after procedure that death occurred | Cause of death |
|---|---|---|
| Primary study group | | |
| 1 | 2 | Shock |
| 2 | 3* | Unanticipated aortic-related reoperation† |
| 3 | 69* | Rupture‡ |
| 4 | 90 | Shock |
| 5 | 103 | Stroke |
| 6 | 130 | Unknown |
| 7 | 147* | Sudden cardiac arrest§ |
| Rupture group | | |
| 1 | 4 | Stroke |

*POD*, Postoperative day. *Aortic-related death. †This 55-year-old patient presented with a distal aortic arch/descending thoracic aortic diameter of 7.5 cm that was related to previously unrepaired chronic DeBakey type I aortic dissection. After initial repair, he developed an aortic rupture of the untreated segment on POD 1 and underwent an unplanned, emergency endovascular extension. He died on POD 3 due to multisystem organ failure. ‡This 39-year-old patient with a vascular Ehler–Danlos syndrome, DeBakey type I aortic dissection, and 3 previous median sternotomies underwent an unplanned endovascular extension to repair of the descending thoracic aorta because of rapid aneurysm growth at 23 days after frozen elephant trunk repair and died of aortic rupture 69 days after implantation. §This 54-year-old patient with DeBakey type I aortic dissection and previous median sternotomy had a >5-mm growth rate of the descending thoracic aorta after implantation and died due to sudden cardiac arrest on POD 147.