From the Society for Vascular Surgery

# Endovascular repair for blunt thoracic aortic injury using the Zenith Alpha low-profile device

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***Objective:*** **The objective of this study was to report 30-day results from a prospective, nonrandomized, multicenter trial that evaluated the safety and effectiveness of the Zenith Alpha thoracic endovascular graft (Cook Medical, Bloomington, Ind) for treatment of blunt thoracic aortic injuries (BTAIs).**

***Methods:*** **Eligible patients with BTAIs (grade II to grade IV) in the descending thoracic aorta were treated with the Zenith Alpha device, which is available in smaller graft diameters (starting at 18 mm) and lower profile delivery systems (starting at 16F) than currently available thoracic endografts. The device (nitinol stents and polyester graft material) accommodates a tighter aortic curvature (radius of 20 mm) than the predicate Zenith TX2 Pro-Form. Follow-up clinical and imaging evaluations were performed at 30 days, at 6 and 12 months, and annually thereafter through 5 years. The primary end point was 30-day mortality.**

***Results:*** **Between January 2013 and May 2014, 50 patients (44 men; mean age, 43 ± 19 years; range, 18-89 years) were treated with the Zenith Alpha device at 17 U.S. sites. The mean Injury Severity Score was 31 ± 14 (range, 3-66). Technical success was achieved in 100% of patients, with 0% intraoperative mortality. Device access was entirely percutaneous in 22 patients (44%). Smaller size grafts (18-24 mm) were used in 15 patients (30%). The mean procedure time was 85 ± 44 minutes (range, 34-278 minutes), and mean blood loss was 103 ± 145 mL (range, 0-1000 mL). The 30-day mortality rate was 2%; one patient died 24 days after the procedure of respiratory failure related to associated injuries and not to the device or procedure as adjudicated by an independent Clinical Events Committee (CEC). One patient experienced a stroke 7 days after the procedure (cause undetermined by the CEC), and one patient underwent reintervention for a site-reported proximal type I endoleak (core laboratory reported unknown endoleak type) at 30 days after the procedure. There have been no conversions to open surgical repair, paraplegia, or aortic rupture within 30 days.**

***Conclusions:*** **Short-term results indicate that the Zenith Alpha thoracic endovascular graft appears safe and effective for the treatment of BTAIs. This low-profile device enables complete percutaneous repair in a large percentage of patients and can achieve high rates of technical success and very low rates of aortic injury-related mortality within 30 days. (J Vasc Surg 2015;62:1495-503.)**

During the past two decades, endovascular treatment has emerged as the standard of care for blunt thoracic aortic injury (BTAI) repair, demonstrating lower mortality and paraplegia rates than open repair.[1,2] The 2011 Society for Vascular Surgery Clinical Practice Guidelines[3] recommend endovascular repair of grade II to grade IV injuries and conservative nonoperative management for grade I minimal aortic injury. BTAI is most commonly the result of deceleration injuries, such as motor vehicle collisions or falls from extreme heights. As a result, patients presenting with BTAI on average are much younger than the typical patient undergoing thoracic aortic endograft repair for aneurysmal disease. As such, patients with BTAI often have smaller iliac access vessels, smaller thoracic aortas, and narrower aortic arch curvatures, which present challenges for thoracic endovascular aortic repair using currently available thoracic aortic endografts.

For this reason, in 2008, the American Association for the Surgery of Trauma (AAST) called for a "major and urgent need for improvement of the available endovascular devices" for the treatment of BTAI.[4] The Zenith Alpha thoracic endovascular graft (Cook Medical, Bloomington, Ind; referred to as Zenith Alpha in this manuscript) was designed to meet these needs with smaller introducer sheaths, smaller diameter devices, and a nitinol-based stent frame with thinner, more tightly woven Dacron graft material. The device also conforms

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better to narrow aortic arches. The purpose of this study was to report the 30-day results from a prospective, nonrandomized, multicenter trial that evaluated the safety and effectiveness of the Zenith Alpha device for treatment of BTAIs.

## METHODS

**Study design.** The TRANSFIX trial is a prospective, nonrandomized, noncomparative, single-arm, multicenter clinical trial that was conducted under an investigational device exemption to assess the safety and effectiveness of the Zenith Alpha thoracic endovascular graft for the treatment of patients with BTAI. This study was designed to enroll a total of 50 patients from U.S. or global institutions. The primary safety end point was all-cause mortality and aortic injury-related mortality at 30 days. The primary effectiveness end point was device success at 30 days, which was defined as technical success (ie, successful access of the injury site and deployment of the device in the intended location and endovascular graft patency on completion of deployment), with the absence of device collapse, type I or type III endoleak requiring intervention, or conversion to open surgical repair at 30 days.

The TRANSFIX clinical trial was performed according to the Declaration of Helsinki II and monitored by an independent Data and Safety Monitoring Board. Ethical approval was obtained from the relevant Institutional Review Board at each institution, and informed consent was obtained for all procedures.

**Patient eligibility.** Patients were eligible for this study if they were 16 years and older and had a BTAI (grade II to grade IV) in the descending thoracic aorta. Patients with only intimal injuries (grade I) to the aorta were excluded from the study. For this study, grade II injury was defined as intramural hematoma or large intimal flap, including a change in external contour, according to Azizzadeh et al[5] and Starnes et al.[6] All patients were required to have proximal and distal fixation sites with a length ≥20 mm and a diameter ≥15 mm and ≤42 mm. Detailed inclusion and exclusion criteria are summarized in Table I.

Preoperative computed tomography angiography (CTA) images were assessed by each investigative site to determine a patient's eligibility and to plan for the endovascular repair, including selection of appropriate fixation sites and device sizes (sizing guidelines were provided in the instructions for use). On occasion, data obtained intraoperatively or postoperatively (such as core laboratory analysis of preoperative imaging) may differ from the preoperative assessment by site, but this was not considered a protocol violation or evidence of inappropriate enrollment. Because patients with traumatic aortic injury most often have other serious concomitant nonaortic injuries, endovascular repair of the aortic injury may have been postponed until other injuries were treated; however, according to the protocol, all patients were to be treated within 14 days of occurrence of the injury. On procedure initiation (ie, cutdown or percutaneous access started), the patient was included in the intent-to-treat population.

**Device description and implantation procedure.** The study device used in TRANSFIX is the same proximal component of the Zenith Alpha thoracic endovascular graft that is also currently under clinical investigation in the United States for the treatment of patients with descending thoracic aortic aneurysms or ulcers. Whereas the endovascular system for the treatment of aneurysms or ulcers also includes an overlapping distal component, the system for the treatment of BTAI includes only the proximal component because the aortic segment requiring coverage is expected to be much more focal than that for an aneurysm or ulcer.

The stent graft is constructed with self-expanding nitinol stents sewn onto a polyester graft material (Fig 1). The proximal component of the Zenith Alpha device can be straight or tapered and incorporates a bare alignment proximal stent and an internal sealing stent with fixation barbs. Compared with the predicate Zenith TX2 thoracic aortic aneurysm endovascular graft (stainless steel stents, a thicker polyester material, and a covered proximal stent), the Zenith Alpha device enables a lower profile introduction system (16F to 20F compared with 20F to 24F), is available in a wider range of diameters (18 to 46 mm compared with 22 to 42 mm), and accommodates an aortic arch with a smaller radius of curvature (20 mm compared with 35 mm). In addition, the use of the bare alignment stent in combination with a precurved cannula on the delivery system is designed to assist in adequate proximal arch conformability.

Standard endovascular techniques were used for the deployment of the Zenith Alpha device. Coverage of the left subclavian artery was acceptable; however, revascularization of the left subclavian artery was selectively considered. Fluoroscopic guidance and angiography were used throughout the procedure to verify positioning of the device with respect to the patient's anatomy.

**Patient follow-up.** The results of the endovascular repair were assessed by angiography intraoperatively. The study follow-up consisted of clinical examinations and blood tests performed within 7 days after the procedure, and clinical examinations and CTA were performed at 30 days, at 6 and 12 months, and yearly thereafter through 5 years. All CTA images were evaluated at each investigative site and by a centralized core laboratory. Results reported in the manuscript reflect analysis by the core laboratory unless indicated otherwise. Clinical events were adjudicated by an independent Clinical Events Committee (CEC) according to standard operating procedures to assess whether the events were due to a pre-existing or unrelated condition or were procedure related, technique related, or device related. Aortic injury-related mortality was defined as any death determined by an independent CEC to be causally related to the initial implant procedure, secondary intervention, or rupture of the transected aorta.

**Data analysis.** Data were managed by a centralized data-coordinating center, Cook Research Incorporated (West Lafayette, Ind). Statistical analyses were performed by using Statistical Analysis Software (SAS) for Windows (release 9.3; SAS Institute, Cary, NC). Continuous

**Table I.** Inclusion and exclusion criteria

| *Inclusion criteria* | *Exclusion criteria* |
|---|---|
| General | General |
| BTAI of the descending thoracic aorta | ISS at the time of initial hospital admission is 75 |
| Age ≥16 years | Aortic injuries are classified as grade I |
| Informed consent given by the patient or a legally authorized representative | |
| Willing and able to comply with the follow-up schedule | |
| Medical | Medical |
| No previous placement of a thoracic endovascular graft | Pregnancy |
| No prior open surgical repair involving the descending thoracic aorta including suprarenal aorta and arch | Known allergy to polyester, polypropylene, nitinol, or gold |
| Treatment with the Zenith Alpha thoracic endovascular graft can be performed within 14 days of the BTAI | Allergic reaction to contrast material |
| | Aortic dissection |
| | Systemic infection (eg, sepsis) |
| | Degenerative connective tissue disorder (eg, Marfan disease) |
| | Bleeding diathesis, uncorrectable coagulopathy, or refusal of blood transfusion |
| | Simultaneously participating in another investigative device or drug study (The patient must have completed the primary end point of any previous study at least 30 days before enrollment in this study and not enroll in another study until 30 days after BTAI repair in this study.) |
| Anatomic | Anatomic |
| Suitable for treatment with the Zenith Alpha endovascular graft and 16F, 18F, or 20F Z-Trak Plus introduction system | Treatment length (ie, length of aortic injury including proximal and distal fixation sites) along greater curvature: |
| Proximal fixation site length measuring ≥20 mm between the left common carotid artery and most proximal extent of the injury site (covering left subclavian artery is acceptable) | >105 mm for 18- to 26-mm-diameter grafts |
| Distal fixation site length measuring ≥20 mm between the most distal aspect of aortic injury and most distal extent of graft | >109 mm for 28- to 32-mm-diameter grafts |
| Proximal neck diameter, measured outer wall to outer wall on a sectional image or multiplanar reconstruction (CT), ≥15 mm and ≤42 mm | >113 mm for 34- to 36-mm-diameter grafts |
| Distal neck diameter, measured outer wall to outer wall on a sectional image or multiplanar reconstruction (CT), ≥15 mm and ≤42 mm | >117 mm for 38- to 40-mm-diameter grafts |
| Ability to preserve the left common carotid artery and celiac artery | >121 mm for 42-mm-diameter grafts |
| | >125 mm for 44- to 46-mm-diameter grafts |
| | Aortic arch radius of curvature <20 mm (only if the device is intended to be deployed in the aortic arch) |
| | Tortuosity, calcification, occlusive disease, or arterial diameter of the intended access vessels (eg, iliac and femoral arteries), measured inner wall to inner wall on a sectional image, that are not conducive to placement of the introducer sheath (16F, 18F, or 20F); use of an access conduit is acceptable |
| | Prohibitive calcification, occlusive disease, or tortuosity of intended fixation sites |
| | Circumferential thrombus in region of intended fixation sites |
| | Aneurysm or angulation in the distal thoracic aorta that would preclude advancement of the introduction system |

*BTAI,* Blunt thoracic aortic injury; *CT,* computed tomography; *ISS,* Injury Severity Score.

variables are reported as means and standard deviations unless otherwise noted, and categorical variables are reported as percentages. In this study, the primary end points were reported by using descriptive statistics and 95% confidence intervals (CIs).[7]

## RESULTS

Seventeen institutions in the United States enrolled 50 patients with BTAI between January 2013 and May 2014 (Appendix, online only). This manuscript reports 30-day results for all patients and additional events beyond 30 days, reflecting data received as of July 10, 2014, which are subject to regulatory authority review for a determination of safety and effectiveness. Within 30 days, one patient died and one patient was lost to follow-up; clinical evaluation at 30 days was available in 45 of 50 patients (90%). Follow-up core laboratory analysis of the CT imaging was available for 42 of 50 patients (84%) at 30 days. Longer term follow-up is ongoing.

### Preprocedural patient characteristics

Patient demographics and preoperative comorbid medical conditions are presented in Table II. A majority of the patients were male (88%; 44 of 50). The mean age of the patients was 43 ± 19 years (range, 18-89 years), with a large subgroup of young patients between 16 and 35 years old (42%; 21 of 50). Injury characteristics are presented in Table III. Motor vehicle accidents were the most common cause of presenting injuries (72%; 36 of 50). The mean Injury Severity Score (ISS) was 31 ± 14 (3-66, on a scale of 1 to 75), and 34% of patients (17 of 50) presented with severe coma (Glasgow Coma Scale [GCS] score ≤ 8).

Aortic injury characteristics, specifically, injury grade and core laboratory assessment of anatomic aortic injury,

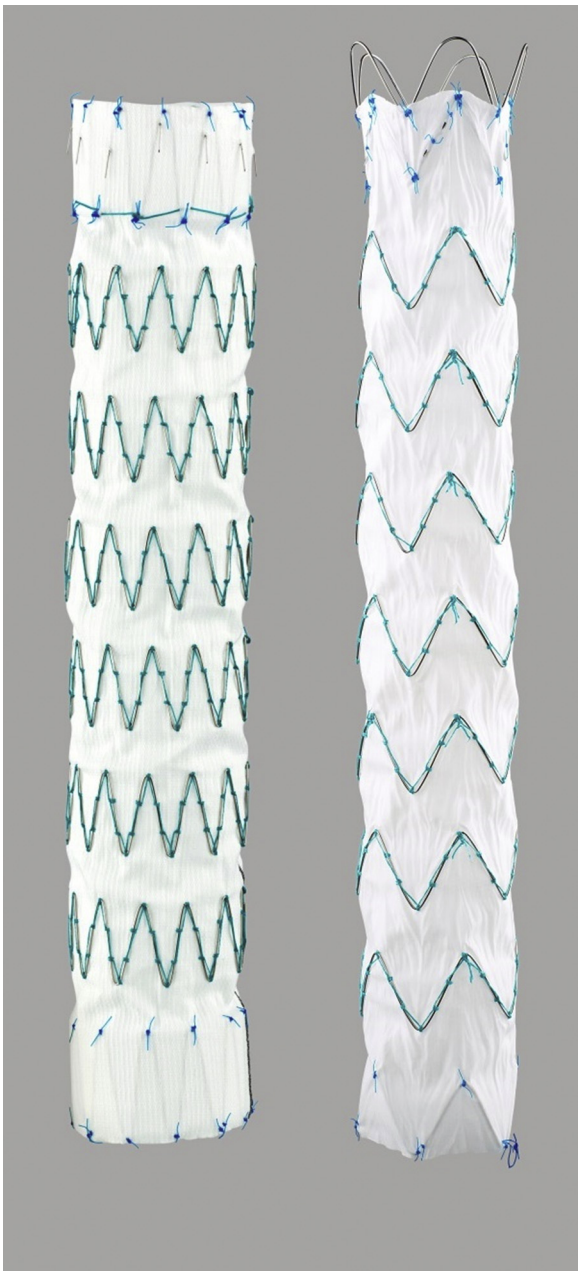

**Fig 1.** Images of the Zenith TX2 endovascular graft and Zenith Alpha thoracic endovascular graft (proximal component, available as either straight or tapered). The Zenith Alpha thoracic endovascular graft is an investigational device in the United States and is limited by U.S. law to investigational use. It is CE Mark approved only for the indication of endovascular treatment of patients with aneurysms and ulcers in the descending thoracic aorta having vascular morphology suitable for endovascular repair.

are presented in Table IV. No patients presented with grade I aortic injury (an exclusion criterion in this study), and three patients presented with grade IV injury (rupture). The mean aortic arch radius was 22 mm. The access vessels and proximal and distal seal zones were largely disease free (the majority of patients presented with no or only mild tortuosity, occlusive disease, calcification, or thrombus).

**Table II.** Demographic and pre-existing comorbid medical conditions (n = 50)

| *Characteristic* | *% (n/N)*[a] |
|---|---|
| Age, years | |
| Mean ± standard deviation (N, range) | 43 ± 19 (50, 18-89) |
| 16-35 | 42 (21/50) |
| ≥36 | 58 (29/50) |
| Gender | |
| Male | 88 (44/50) |
| Female | 12 (6/50) |
| Race | |
| White | 76 (38/50) |
| Hispanic or Latino | 10 (5/50) |
| Black or African American | 8 (4/50) |
| Asian | 6 (3/50) |
| American Indian or Alaska Native | 0 (0/50) |
| Medical history[a] | |
| Cardiovascular | |
| Cardiac arrhythmia | 2 (1/49) |
| Congestive heart failure | 0 (0/49) |
| Coronary artery disease | 6 (3/49) |
| Myocardial infarction | 4 (2/49) |
| Surgical or percutaneous treatment | 6 (3/50) |
| Vascular | |
| Thromboembolic event | 0 (0/49) |
| Aneurysm (patient history) | 0 (0/49) |
| Dissection | 0 (0/50) |
| Bleeding diathesis or coagulopathy | 0 (0/49) |
| Carotid endarterectomy | 0 (0/50) |
| Hypertension | 26 (13/50) |
| Pulmonary | |
| Chronic obstructive pulmonary disease | 2 (1/49) |
| Renal | |
| Chronic renal insufficiency | 0 (0/49) |
| Dialysis | 0 (0/49) |
| Endocrine | |
| Diabetes | 8 (4/49) |
| Infectious disease | |
| Sepsis | 0 (0/49) |
| Hepatobiliary | |
| Liver disease | 4 (2/49) |
| Neoplasms | |
| Cancer | 4 (2/49) |
| Neurologic | |
| Paralysis | 0 (0/49) |
| Paraparesis | 0 (0/49) |
| Stroke | 0 (0/49) |
| TIA or reversible ischemic deficit | 0 (0/49) |
| Connective tissue | |
| Marfan syndrome | 0 (0/49) |
| Ehlers-Danlos syndrome | 0 (0/49) |
| Substance use | |
| Past or current smoker | 46 (23/50) |

*TIA*, Transient ischemic attack.
[a]Several comorbid conditions were not reported for one patient as very little information about the medical history for this patient was available.

## Procedural results

Procedural results are described in Table V. All but one patient received general anesthesia (98%; 49 of 50) during the procedure. Device access was entirely percutaneous

**Table III.** Injury characteristics

| *Measure* | *% (n/N)* |
|---|---|
| Cause of injury | |
| Motor vehicle accident | 72 (36/50) |
| Motorcycle accident | 14 (7/50) |
| Pedestrian hit by a motor vehicle | 6 (3/50) |
| Fall | 4 (2/50) |
| Other[a] | 4 (2/50) |
| GCS score | |
| Minor (≥13) | 48 (24/50) |
| Moderate (9-12) | 18 (9/50) |
| Severe (≤8) | 34 (17/50) |
| ISS (scale of 0-75)[b] | |
| Mean ± SD | 31 ± 14 (50/50) |
| Median (range) | 29 (3-66) |
| ASA class | |
| Class 1 | 0 (0/50) |
| Class 2 | 8 (4/50) |
| Class 3 | 24 (12/50) |
| Class 4 | 52 (26/50) |
| Class 5 | 16 (8/50) |
| Associated traumatic injuries | |
| Abdominal injuries (solid organ, bowel, bladder) | 62 (31/50) |
| Head injury | 38 (19/50) |
| Long bone fracture | 58 (29/50) |
| Lung injury | 58 (29/50) |
| Neurologic deficits | 20 (10/50) |
| Pelvis fracture | 30 (15/50) |
| Rib fractures | 68 (34/50) |
| Scapula fracture | 10 (5/50) |
| Unstable fractures (cervical, thoracic, or lumbar spine) | 14 (7/50) |
| Other[c] | 32 (16/50) |

*ASA,* American Society of Anesthesiologists; *GCS,* Glasgow Coma Scale; *ISS,* Injury Severity Score; *SD,* standard deviation.

[a]One patient operating a moped and another patient while riding a bicycle were both hit by motor vehicles.

[b]The ISS is an anatomic scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned an Abbreviated Injury Scale (AIS) score, 0 being the best and 6 being the worst, and is allocated to one of six body regions: (1) head, (2) face, (3) chest, (4) abdomen, (5) extremities (including pelvis), and (6) external. Only the highest AIS score in each body region is used. The three most severely injured body regions have their scores squared and added together to produce the ISS.

[c]Other associated traumatic injuries generally comprise a combination of fractures, including the extremities.

in 22 patients (44%). No iliac conduits or iliac ruptures were reported. Forty-nine patients received a single Zenith Alpha component, and one patient received two components. In one patient who received a single Zenith Alpha component (28 mm in diameter), two commercially available TX2 components (28 mm and 32 mm in diameter) were placed during the index procedure because of undersizing of the Zenith Alpha component; per the site, device sizing was performed on the basis of a CT scan obtained before complete resuscitation of the patient. Smaller size grafts (18 to 24 mm) were used in 15 patients (30%); detailed device diameters and configurations are illustrated in Fig 2.

Technical success was achieved in 100% of patients, with no intraoperative mortality. The left subclavian artery was covered in 21 patients (47%), with no revascularization of the left subclavian artery performed for any of these patients and no adverse outcomes on follow-up. Hypotension was induced during device deployment in five patients (10%), and cerebrovascular fluid drainage was performed in two patients (4%).

**Table IV.** Anatomic characteristics (core laboratory reported)

| *Characteristic* | *% (n/N)* |
|---|---|
| Aortic injury grade[a] | |
| Grade I: intimal tear | 0 (0/49) |
| Grade II: Intramural hematoma or large intimal flap | 8 (4/49) |
| Grade III: Pseudoaneurysm | 86 (42/49) |
| Grade IV: Free rupture | 6 (3/49) |
| Aortic injury | Mean ± SD (N, range) |
| Length of aortic injury, mm | 32 ± 18 (48, 10-119) |
| Maximum diameter over the extent of injury, mm | 32 ± 6 (46, 21-48) |
| Aortic arch radius, mm | 22 ± 5 (49, 12-35) |
| Length of LCC to proximal extent of aortic injury, mm | 28 ± 13 (47, 0.1-73) |
| Length of celiac artery to distal aortic injury, mm | 186 ± 29 (40, 104-253) |

*LCC,* Left common carotid artery; *SD,* standard deviation.

[a]The preprocedure computed tomography (CT) scan for one patient (1200059) was not reviewed by the core laboratory at the time of the data lock.

### Thirty-day results

**Mortality, rupture, and conversion to open repair.** One patient died within 30 days, resulting in a 30-day all-cause mortality rate of 2%. This patient, a 72-year-old man, presented with a grade III traumatic aortic injury after a motor vehicle accident, with concomitant injuries of fractured ribs (≥8), fractured lumbar vertebra, fractured pubis, open dislocation of the ankle, and fractured thumb. The patient's American Society of Anesthesiologists (ASA) class was 4, the ISS was 38, and the GCS score was 15. During hospitalization after the endovascular repair, the patient developed a series of respiratory complications and died 24 days after the index procedure of respiratory failure. The death was adjudicated by an independent CEC as related to concomitant injuries and not related to the aortic injury, the procedure, or the device.

No aortic ruptures or conversions to open surgical repair were observed within 30 days.

**Major adverse events.** Major adverse events occurring within 30 days (Table VI) included one death as described earlier, one case of stroke (2%), one case of renal failure requiring dialysis (2%), and one case of wound complication requiring return to the operating room (2%). There were no occurrences of paraplegia or any other major adverse events reported within 30 days.

A 62-year-old man experienced a stroke within 30 days. This patient presented with multiple injuries (ASA class was 4, ISS was 34, and GCS score was 12) and a grade III aortic injury after a motor vehicle accident.

**Table V.** Procedural and clinical utility results

| *Intraoperative data* | *% (n/N)* |
|---|---|
| Type of anesthesia | |
| General | 98 (49/50) |
| Local | 2 (1/50) |
| Regional | 0 (0/50) |
| Access type | |
| Surgical cutdown | 56 (28/50) |
| Percutaneous | 44 (20/50) |
| Conduit | 0 (0/50) |
| No. of Zenith Alpha stent grafts deployed | |
| 1 component | 98 (49/50) |
| 2 components | 2 (1/50) |
| LSA coverage[a] | |
| Yes | 47 (21/45) |
| No | 53 (24/45) |

| *Clinical utility results* | *Median or mean ± SD (N, range)* |
|---|---|
| Median time from injury to procedure, days[b] | 1 (50, 0-20) |
| Procedure time, minutes | 85 ± 44 (50, 34-278) |
| Estimated blood loss, mL | 103 ± 145 (50, 0-1000) |
| Fluoroscopy time, minutes | 9 ± 8 (48, 3-57) |
| Clinical utility measures | |
| Duration of ICU stay, days | 16 ± 13 (49, 1-51) |
| Duration of mechanical ventilation, days | 11 ± 13 (49, 0-51) |
| Days to resumption of oral fluid intake | 10 ± 15 (45, 0-78) |
| Days to resumption of regular diet | 14 ± 19 (44, 0-99) |
| Days to resumption of bowel function | 6 ± 5 (46, 0-24) |
| Days to hospital discharge | 23 ± 20 (49, 2-120) |

*ICU,* Intensive care unit; *LSA,* left subclavian artery; *SD,* standard deviation.
[a]Core laboratory reported.
[b]One patient was treated 20 days after the original injury, which was considered a protocol deviation; however, the patient was included in the intent-to-treat analysis. Because of this deviation, the median was reported rather than the mean.

A single study device was placed distal to the left subclavian artery. The patient was diagnosed with deep venous thrombosis 5 days after the procedure, and an inferior vena cava filter was placed on the following day. Seven days after the procedure, the patient experienced an ischemic hemispheric stroke, embolic in nature (scored 5 on modified Rankin scale). The patient was discharged from the hospital 24 days after the procedure to a long-term care facility. The patient completed his 12-month follow-up and was alive as of 346 days after the procedure.

A 25-year-old man experienced renal failure requiring hemodialysis 6 days after the procedure. This patient presented with intra-abdominal perirenal hemorrhage, multiple left kidney infarcts, increased creatinine concentration, and hypotension before the endovascular repair, which could be factors that led to renal failure, and the CEC adjudicated this event as unrelated to the procedure, the device, or the aortic injury. This patient was diagnosed with multisystem organ failure on the same day and expired 33 days after the procedure.

On the day of the index procedure, one patient experienced a wound complication, specifically a left iliac dissection requiring surgical intervention (left external iliac to common femoral artery bypass) after being treated with a closure device. Subsequently, the same patient returned 30 days after the index procedure for a stenosis of the right common femoral artery, which was treated with a right iliofemoral bypass.

**Secondary interventions.** One patient underwent a secondary intervention 30 days after the procedure for a site-reported proximal type I endoleak; the core laboratory assessed the endoleak to be of an unknown type. Significant device undersizing was noted by the core laboratory (18-mm-diameter device placed in a 19.7-mm-diameter aorta, per core laboratory review); the site also indicated that the patient was not fully resuscitated during the preprocedural CT scan. The patient underwent placement of six Heli-FX screws (Aptus Endosystems, Sunnyvale, Calif) at the proximal zone of the graft, which was later deemed unsuccessful by the site. The patient was subsequently converted to open surgical repair 181 days after the original implant procedure. The patient exited the study 30 days after the conversion according to the protocol, with no additional adverse events reported.

**Device performance.** Core laboratory assessment of imaging studies at 30 days demonstrated patent devices in all patients (100%; 41 of 41), with no type I or type III endoleaks (Table VII). One instance of device compression was reported at 30 days. This patient received two Zenith Alpha proximal components, and the compression was observed in the proximal section of the second component, which was placed to provide additional coverage at the distal end of the injury. Retrospective analysis suggested that the second component may have been deployed through a distal suture loop of the first component, resulting in a focal compression. The device compression was not associated with any clinical sequelae and was resolved by balloon angioplasty performed 335 days after the index procedure (device compression was no longer observed on the angiogram by the core laboratory). No barb separation, stent fracture, or other device integrity issues were observed.

Per study protocol, the 30-day examination is the baseline examination for evaluation of device migration (>10 mm). In 10 patients, an additional CT examination was performed before the 30-day follow-up time point, and no migration was noted in these patients at 30 days.

**Aortic injury healing.** Injury healing (defined as the absence of visible aortic injury; an example is shown in Fig 3) was observed in 32 of 42 patients (76%) with available core laboratory analysis of 30-day CT imaging (Table VII). Of 10 patients with residual aortic injury, 8 patients were available for diameter assessment, and none had an increase >5 mm in the aortic injury diameter compared with the preprocedure measurements.

**Primary study end points.** The primary safety and effectiveness end points are reported in Table VIII. At 30 days, the all-cause mortality rate was 2% (1 of 50; 95%

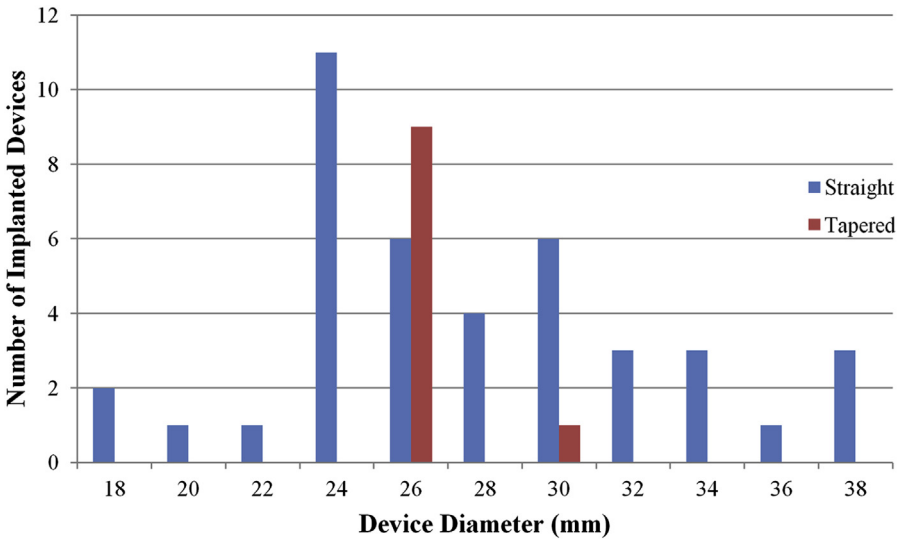


**Fig 2.** Distribution of deployed proximal Zenith Alpha thoracic components.

**Table VI.** Thirty-day major adverse events

| *Event* | *% (n/N)* |
|---|---|
| All-cause death | 2 (1/50) |
| Stroke | 2 (1/50) |
| Paraplegia | 0 (0/50) |
| Q-wave myocardial infarction | 0 (0/50) |
| Cardiac event defined as involving arrest or resuscitation | 0 (0/50) |
| Renal failure requiring permanent dialysis, hemofiltration, or kidney transplantation[a] | 2 (1/50) |
| Pulmonary embolism involving hemodynamic instability or surgery | 0 (0/50) |
| Graft infection | 0 (0/50) |
| Conversion to open repair | 0 (0/50) |
| Wound complication requiring a return to the operating room | 2 (1/50) |

[a]In patients with a normal preprocedure serum creatinine level.

**Table VII.** Thirty-day core laboratory imaging analysis

| *Measure* | *% (n/N)* |
|---|---|
| Injury healing | |
| Aortic injury no longer visible | 76 (32/42) |
| Injury diameter increase >5 mm compared with before the procedure | 0 (0/8)[a] |
| Endoleak | |
| Type I[b] | 0 (0/41) |
| Type II | 2.4 (1/41) |
| Type III | 0 (0/41) |
| Type IV | 0 (0/41) |
| Unknown | 4.9 (2/41) |
| Patency | 100 (41/41) |
| Device integrity | |
| Graft kink | 0 (0/42) |
| Device compression[c] | 2.5 (1/42) |
| Device infolding | 0 (0/42) |
| Barb separation | 0 (0/42) |
| Stent fracture | 0 (0/42) |

[a]Result based on eight patients with residual injury, and maximum diameter was not assessed in two patients.
[b]One patient was diagnosed from the site as having a proximal type I endoleak; alternatively, the core laboratory evaluated the endoleak as unknown type.
[c]Compression observed in the proximal section of a second main body stent graft.

CI, 0%-5.88%), and the aortic injury-related mortality rate was 0% (0 of 50; 95% CI, 0%-7.1%). The device success rate at 30 days was 96% (48 of 50; 95% CI, 90.6%-100%). As described earlier, two patients did not meet the device success criteria at 30 days; one patient experienced device compression and one patient underwent a secondary intervention to treat a site-reported proximal type I endoleak.

### Additional safety results beyond 30 days

Four late deaths were observed beyond 30 days. The causes of these four late deaths were multisystem organ failure (on day 33), respiratory failure and multisystem organ failure (on day 36), respiratory failure (on day 73), and exsanguination due to an esophageal-aortic fistula (on day 116). The first three deaths were adjudicated by the CEC as not aortic injury related.

The fourth death was adjudicated by the CEC as aortic injury related (specifically procedure related). This patient, a 28-year-old woman who was involved in a motor vehicle accident, presented with a grade III traumatic aortic injury and subarachnoid and subdural hemorrhage with multiple fractures in the head and torso (ASA class was 4, the ISS was 50, and the GCS score was 4). The patient experienced multiple infections (cerebrospinal fluid infection, pneumonia, bacteremia, and ventriculitis) during hospitalization and on follow-up developed a pseudoaneurysm at the

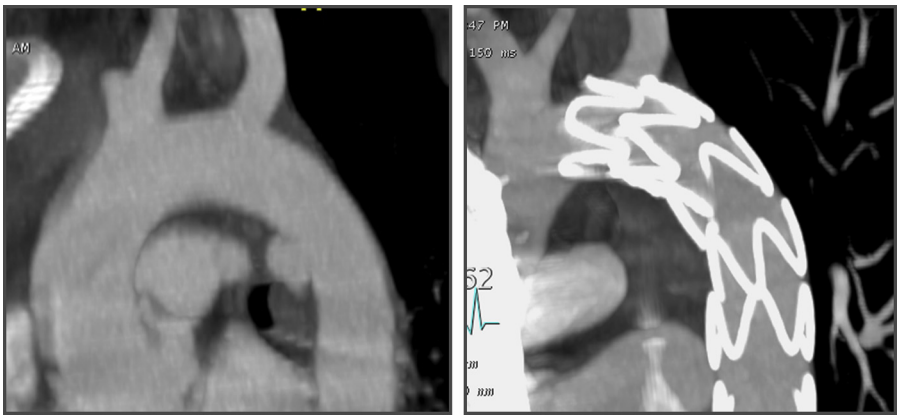


**Fig 3.** Preassessment aortic injury (*left*) and postprocedure injury healing (*right*).

**Table VIII.** Study end points (30 days)

| *End point* | *% (n/N)* | *95% CI* |
|---|---|---|
| Safety | | |
| All-cause mortality | 2 (1/50) | 0-5.88 |
| Aortic injury-related mortality[a] | 0 (0/50) | 0-7.1 |
| Effectiveness | | |
| Device success | 96 (48/50) | 90.6-100 |

*CI*, Confidence interval.
[a]The 95% CI was computed using the exact method.

proximal end of the study device, which may have been related to the infection. The patient underwent two unsuccessful secondary interventions on days 73 (stent graft placement) and 78 (ministernotomy, arch debranching, aortic bypass of the innominate and left carotid arteries, endograft placement, and bilateral chest tube placement) to treat the pseudoaneurysm. On day 116, the patient experienced a cardiac arrest and did not respond to resuscitation; the cause of death was exsanguination due to an esophageal-aortic fistula. The national principal investigator for the study (B.W.S.) believes this was due to occult stent graft infection as a result of repeated bacteremia.

Other notable events beyond 30 days include one case of incomplete quadriplegia that was adjudicated by the CEC as not aortic injury related, one secondary intervention (placement of additional stent grafts and left subclavian artery bypass) performed on day 219 for the treatment of a possible endoleak or area of residual injury (it was determined by the site that the initial injury was incompletely covered during the initial procedure), and one surgical conversion performed on day 181 in a patient who previously underwent unsuccessful secondary interventions for a site-reported type I endoleak, as described earlier.

## DISCUSSION

The management of patients presenting with BTAI has essentially become a semielective procedure in most modern trauma centers. It was once associated with significant adverse outcomes including stroke and paraplegia with open repair, but endovascular methods of repair with newer devices have virtually extinguished the occurrence of these adverse outcomes.[1] Further refinements of this technology are needed that are based on long-term outcome and durability data, which, however, are extremely difficult if not impossible to obtain in this population of young patients.

In the 2006 meta-analysis evaluating stent graft repair for BTAI performed by Tang et al,[1] technical success was achieved in 96.5% of patients with no instances of paraplegia and a 0.85% stroke rate. The most common procedure-related complication at that time was iliac artery injury as a result of large device delivery systems. In the AAST2 trial, there was an astonishing 20% device-related complication rate.[4] It was clear almost a decade ago that there was an urgent need for improved device design with smaller delivery systems.

Lessons we have definitely learned in managing patients with BTAI in the last decade include the following: (1) intentional coverage of the left subclavian artery can be done, and this has been associated with a low risk of an ischemic complication[8-10]; (2) the risk of paraplegia is low[1]; (3) minimal, grade I aortic injuries do not require intervention and can be observed until healing is confirmed with imaging[6,11]; and (4) patients should be adequately resuscitated and reimaged before definitive repair to avoid the risk of device undersizing.[12]

The current study is the fourth investigational device exemption clinical trial to prospectively evaluate a device specifically designed to treat BTAI.[8-10] Technical success in the current study, as in the three prior device trials, was 100%. In the current study, there was only one access-related major complication, suggesting that the small delivery system is adequate in a majority of patients.

In the current study, there were two adverse events as a result of significant device undersizing, including one patient who required a second larger device at the index procedure and one patient who required delayed open

conversion. Device undersizing generally results when preoperative CT scans are performed on hypotensive, underresuscitated patients. To avoid this complication, the CT scan can be repeated before the procedure when the patient is well resuscitated, or the aortic diameter measurements can be confirmed with intravascular ultrasound at the time of the procedure.

The Zenith Alpha device currently has the smallest diameter delivery system for any thoracic device. This allows a completely percutaneous procedure in a large percentage of patients and the treatment of younger patients and female patients with smaller diameter access vessels. Smaller diameter devices (18-24 mm) were used in 30% of patients, enabling BTAI treatment of smaller thoracic aortas in this cohort of younger patients. Another feature of the device is the nitinol-based stent frame, which allows improved magnetic resonance compatibility. This is critical because advanced imaging is often required for successful diagnosis and management of stroke and paraplegia, two most worrisome complications for thoracic stent grafting. Also, the introduction system of the Zenith Alpha device includes a precurved inner cannula that can better accommodate the aortic arch anatomy. This feature, in combination with a more conformable stent graft design, enables the use of the Zenith Alpha device in tight aortic arches with a radius of curvature as small as 20 mm.

## CONCLUSIONS

Short-term results indicate that the Zenith Alpha device appears safe and effective for the treatment of BTAIs. Completely percutaneous repair is possible in a large percentage of patients. This device, when it is used to repair BTAI, can be expected to have high rates of technical success and very low rates of aortic injury-related mortality within 30 days. The Zenith Alpha has the smallest delivery system profile of any thoracic device and improved compatibility with magnetic resonance imaging. This device represents a significant advancement for the management of patients with BTAI.

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## AUTHOR CONTRIBUTIONS

Conception and design: BS, CY
Analysis and interpretation: BS, CY
Data collection: BS, AD, JG, KW, CY
Writing the article: BS, AD, JG, KW, CY
Critical revision of the article: BS, AD, JG, KW, CY
Final approval of the article: BS, AD, JG, KW, CY
Statistical analysis: CY
Obtained funding: Not applicable
Overall responsibility: BS

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*Additional material for this article may be found online at www.jvascsurg.org.*

**APPENDIX (online only).** TRANSFIX investigators

| *Investigator* | *Site* | *Location* | *Patients enrolled, % (n/N)* |
|---|---|---|---|
| Amit Dwivedi, MD | University of Louisville | Louisville, Ky | 18 (9/50) |
| Benjamin Starnes, MD[a] | University of Washington, Harborview Medical Center | Seattle, Wash | 12 (6/50) |
| Joseph S. Giglia, MD | University Hospital, University of Cincinnati | Cincinnati, Ohio | 8 (4/50) |
| Karen Woo, MD | University of Southern California Medical Center | Los Angeles, Calif | 8 (4/50) |
| John F. Angle, MD | University of Virginia | Charlottesville, Va | 6 (3/50) |
| Arash Bornak, MD | University of Miami | Miami, Fla | 6 (3/50) |
| Francis Caputo, MD | Cooper University Hospital | Camden, NJ | 6 (3/50) |
| Jeffrey Slaiby, MD | Rhode Island Hospital | Providence, RI | 6 (3/50) |
| Carlos Timaran, MD | University of Texas Southwestern Medical Center | Dallas, Tex | 6 (3/50) |
| Brajesh K. Lal, MD | University of Maryland Medical Center | Baltimore, MD | 4 (2/50) |
| Vito Mantese, MD | Mercy Hospital St. Louis | St. Louis, Mo | 4 (2/50) |
| Ravi Rajani, MD | Emory University Hospital | Atlanta, Ga | 4 (2/50) |
| Michael J. Wilderman, MD | Hackensack University Medical Center | Hackensack, NJ | 4 (2/50) |
| Zachary Baldwin, MD | University of Mississippi Medical Center | Jackson, Miss | 2 (1/50) |
| Nimesh Desai, MD, PhD | Pennsylvania Hospital | Philadelphia, Pa | 2 (1/50) |
| Ali Khoynezhad, MD | Cedars Sinai Medical Center | Los Angeles, Calif | 2 (1/50) |
| Mohammed Moursi, MD | University of Arkansas for Medical Sciences | Little Rock, Ark | 2 (1/50) |
| Total patients | | | 50 |

[a]National principal investigator.