NEXUS Arch: A Multicenter Study Evaluating the Initial Experience With a Novel Aortic Arch Stent Graft System

David Planer, MD,✉ Gabby Elbaz-Greener, MD,* Nicola Mangialardi, MD,†‡ Thomas Lindsay, MD,§ Augusto D'Onofrio, MD,¶ Hubert Schelzig, MD,‖ Lyubov Chaykovska, MD,**†† Andrew Hill, MD,‡‡ Andrew Holden, MD,‡‡ Michele Antonello, MD,¶ Kong T. Tan, MD,§ Matteo Orrico, MD,†‡ Sonia Ronchey, MD,‡ Yaniv Marmur, BSc,§§ Felice Pecoraro, MD,¶¶ and Mario Lachat, MD**††*

Objective: To assess the initial clinical experience with a novel endograft system (NEXUS Aortic Arch Stent Graft System) designed to treat aortic arch pathologies and address the morphology and hemodynamic challenges of the aortic arch.

Summary Background Data: The aortic arch remains the most challenging part of the aorta for both open and endovascular repair. Transcatheter aortic arch repair has the potential to significantly reduce surgical risks.

Methods: Patients underwent transcatheter aortic arch repair with a single branch, 2 stent graft system, implanted over a through-and-through guidewire from the brachiocephalic trunk, to the descending aorta with an ascending aorta stent graft. The ascending aorta stent graft is deployed into a designated docking sleeve to connect the 2 stent grafts and isolate the aortic arch pathology. Proximal landing zone in all cases was in Zone 0. Anatomical inclusion criteria included adequate landing zone in the ascending aorta, brachiocephalic trunk, and descending thoracic aorta. Preparatory debranching procedure was performed in all patients with carotid–carotid crossover bypass and left carotid to left subclavian bypass, or parallel graft from descending aorta to left subclavian artery. Safety and performance were evaluated through 1 year. Survival analysis used the Kaplan–Meier method.

Results: Twenty-eight patients, 79% males, with a mean age of 72.2 ± 6.2 years were treated with 100% procedural success. Isolated aortic arch aneurysm was the principle pathology in 17 (60.7%) of patients, while chronic aortic dissection was the principle pathology in 6 (21.4%) of patients. The remaining 5 (17.8%) had combined or other pathologies. At 1 month, the vascular pathology was excluded in 25 of 26 alive patients (96.1%). The 30 days mortality rate was 7.1%, stroke rate was 3.6% (all nondisabling), and combined mortality/stroke rate was 10.7%. One-year mortality was 10.7%, without device or aneurysm-related death. Two patients (7.1%) reported stroke or transient ischemic attack at 1 year that recovered completely. One year combined mortality/stroke rate was 17.8%. There were 3 patients (10.7%) that had device-related unplanned reinterventions through 1 year.

Conclusions: The NEXUS Aortic Arch Stent Graft System, a novel single branch, 2 stent graft system used for endovascular aortic arch repair that

From the *Heart Institute, Hadassah - Hebrew University Medical Center, Jerusalem, Israel; †Ospedale San Camillo-Forlanini, Roma, Italy; ‡Ospedale San Filippo Neri, Roma, Italy; §Peter Munk Cardiac Centre, Toronto General Hospital, Toronto, Canada; ¶Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padua, Padua, Italy; ‖Universitätsklinik für Gefäß- und Endovaskularchirurgie, Düsseldorf, Germany; **Aortic and Vascular Center, Clinic Hirslanden, Zürich, Switzerland; ††Clinic for Cardiac and Vascular Surgery, University Hospital Zürich, Zürich, Switzerland; ‡‡Auckland Hospital, Auckland, New Zealand; §§Endospan Ltd., Herzlia, Israel; and ¶¶Vascular Surgery Unit, University of Palermo, AOUP "P. Giaccone", Palermo, Italy.

✉planer@hadassah.org.il

D.P. contributed to the conception and design of the study, participated in acquisition of data, analysis and interpretation of data; drafted the manuscript, and gave final approval of the manuscript. G.E.G. contributed to the conception and design of the study, participated in analysis and interpretation of data; drafted the manuscript and gave final approval of the manuscript. N.M. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript, and gave final approval of the manuscript. T.L. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript, and gave final approval of the manuscript. A.D. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript and gave final approval of the manuscript. H.S. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript, and gave final approval of the manuscript. L.C. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript and gave final approval of the manuscript. A.H. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript and gave final approval of the manuscript. A.H. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript and gave final approval of the manuscript. M.A. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript and gave final approval of the manuscript. K.T.T. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript, and gave final approval of the manuscript. M.O. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript and gave final approval of the manuscript. S.R. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript and gave final approval of the manuscript. Y.M. contributed to the conception and design of the study, participated in analysis and interpretation of data; critically revised the manuscript and gave final approval of the manuscript. F.P. contributed to the conception and design of the study, participated in acquisition of data; critically revised the manuscript and gave final approval of the manuscript. M.L. contributed to the conception and design of the study, participated in acquisition of data, analysis and interpretation of data; drafted the manuscript and gave final approval of the manuscript.

M.L. reports being a Principal Investigator for the clinical studies reported in this manuscript, receiving fees as a consultant and proctor for Endospan since 2014 and CryoLife since 2019, as well as being a medical director for Endospan and holder of stock options since 2019. D.P. reports being a consultant and a proctor for Endospan since 2012 and CryoLife since 2019, as well as being a medical director for Endospan and holder of stock options since 2019. Y.M. was an employee of Endospan Ltd.

Funding for this study was provided by Endospan Ltd.

The other authors declare no conflict of interests.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website, www.annalsofsurgery.com.

ISSN: 0003-4932/23/27702-e460

DOI: 10.1097/SLA.0000000000004843

requires landing in the ascending aorta, demonstrates a high success rate with excellent 1 year safety and performance.

Keywords: aortic stent graft, endovascular aortic arch repair, NEXUS

(*Ann Surg* 2023;277:e460–e466)

The aortic arch remains the most challenging part of the aorta for both open and endovascular repair.[1] Conventional surgical arch replacement, although considered the gold standard, with either direct surgical repair or with "Frozen Elephant Trunk" grafts are high-risk and complex surgeries, requiring cardiopulmonary bypass and deep hypothermic circulatory arrest and brain protection.[2,3] According to the current European Association for Cardio-Thoracic surgery (EACTS) and the European Society for Vascular Surgery (ESVS) guidelines, endovascular repair of the aortic arch should be considered in patients unfit for open surgery.[3] Therefore, for patients with high surgical risk, the need for less invasive alternatives is pertinent.

Even if endovascular aortic repair has become standard of care for many patients with pathologies of the descending thoracic and/or abdominal aorta, there are few reports about aortic arch stent grafting. Most of the reports available are with off-label use of endovascular devices,[4] or custom made devices that are not widely available.[1,5,6]

The NEXUS Aortic Arch Stent Graft System (NEXUS) is a CE-certified off-the-shelf double stent graft system, developed specifically to address the morphology and hemodynamic challenges of the aortic arch and to mitigate the risk of stroke. This report presents the initial multicenter experience with the safety and performance of the NEXUS device.

METHODS

Cohort Definition

This prospective cohort includes patients treated with the NEXUS stent graft system either under the first-in-man (FIM) study (NCT02365454) or as compassionate use with systematic data collection (NCT03420066) in 5 centers in Europe, Canada, and New Zealand (Supplemental Table 1, http://links.lww.com/SLA/D27). All compassionate patients were individually approved by the local Ethical Committee and/or national Ministry of Health, as required by local authorities. The study protocol was approved by the each site Ethical Committee and national Ministry of Health, as required by regulations. All patients signed an informed consent prior to inclusion.

Inclusion and Exclusion Criteria

The NEXUS is intended for use in patients with aortic arch pathology. Inclusion criteria included patients with aortic arch aneurysms, dissections, residual aneurysm, or dissection following ascending aorta open or endovascular repair, pseudoaneurysms, and penetrating aortic ulcers, deemed to be at high risk for surgery.

Anatomical inclusion criteria are primarily adequate landing zone at the ascending aorta, descending aorta and brachiocephalic trunk (BCT) (Fig. 1A) and peripheral arteries that can accommodate the NEXUS delivery system (6.7 mm of the iliac/femoral arteries and 2.7 mm of the right axillary artery). Major exclusion criteria include: acute dissection or rupture; suspected infected etiology; significant intra-luminal plaques; untreated aneurysm or dissection of the ascending aorta or the BCT, connective tissue disease (eg, Marfan and Ehler-Danlos syndromes); contraindications to contrast media or allergy to device materials (Supplemental Table 2, http://links.lww.com/SLA/D27).

NEXUS Aortic Stent Graft System

The NEXUS Aortic Arch Stent Graft System is an off-the-shelf double stent graft system (Fig. 1B): the arch stent graft is implanted from the BCT, to the descending thoracic aorta, with a docking sleeve facing the ascending aorta. The ascending stent graft has a curved configuration and is implanted into the arch stent graft's docking sleeve. The connection between the stent grafts incorporates an active locking mechanism designed to ensure fixation and sealing between the 2 stent grafts. The self-expandable stent grafts are composed of nitinol stents, polyester fabric, and tantalum radiopaque markers for correct rotational and longitudinal deployment. The delivery systems of both stent grafts contain hydrophilic coating and are preshaped to reduce manipulation and friction at the arch. The delivery systems are 20 French introducer compatible.

Preparatory Procedures

The NEXUS device enables feeding of a single supra-aortic branch delivered into the BCT. The other supra-aortic branches, namely, the left common carotid (LCC) artery and the left subclavian artery (LSA), were revascularized according to the operator's discretion with extra anatomic bypass from the right common carotid (RCC) artery to the LCC and LCC to LSA arteries (RCC-LCC-LSA), or parallel graft technique. The bypass procedures were performed generally a few days prior to NEXUS. The parallel graft procedures were performed simultaneously with the NEXUS implantation.

Procedure

NEXUS implantation was performed under general anesthesia with fluoroscopy guidance. Arterial access of the femoral artery and right axillary artery were obtained and a through & through axillary-femoral artery guidewire (0.035″ Stiff Glide wire, Terumo) was placed. A contra-lateral femoral arterial access was obtained for angiographic catheters placement. A temporary trans-venous pacemaker lead was placed in the right ventricle. Systemic heparinization to an ACT of > 350 seconds was given and monitored throughout the procedure. The NEXUS arch stent graft was introduced and advanced over the through & through guidewire to its position with the cranial struts of the BCT branch located just proximal to the right carotid artery origin. After correct longitudinal and rotational orientations were verified, the arch stent graft was deployed from the BCT branch to the descending thoracic aorta with attention to achieve correct apposition of the docking sleeve in the ascending aorta. The arch stent graft delivery system was then withdrawn. Safety threads connected to the cranial end of the BCT branch were fixated outside the axillary artery introducer sheath to assure fixation of the device during the procedure. For ascending stent graft implantation, a stiff guidewire was placed in the left ventricle, the ascending stent graft was advanced over the wire, and positioned with the proximal struts located distal to the sino-tubular junction and the distal locking latches covering the docking sleeve to achieve adequate fixation and sealing between the stent grafts. The ascending stent graft was deployed under rapid cardiac pacing and the delivery system was withdrawn. Simultaneous inflation of 2 molding balloons—one at the needs to be docking sleeve section and the second at the BCT branch protruding to the arch, was performed under rapid pacing. Completion angiography was performed to assess

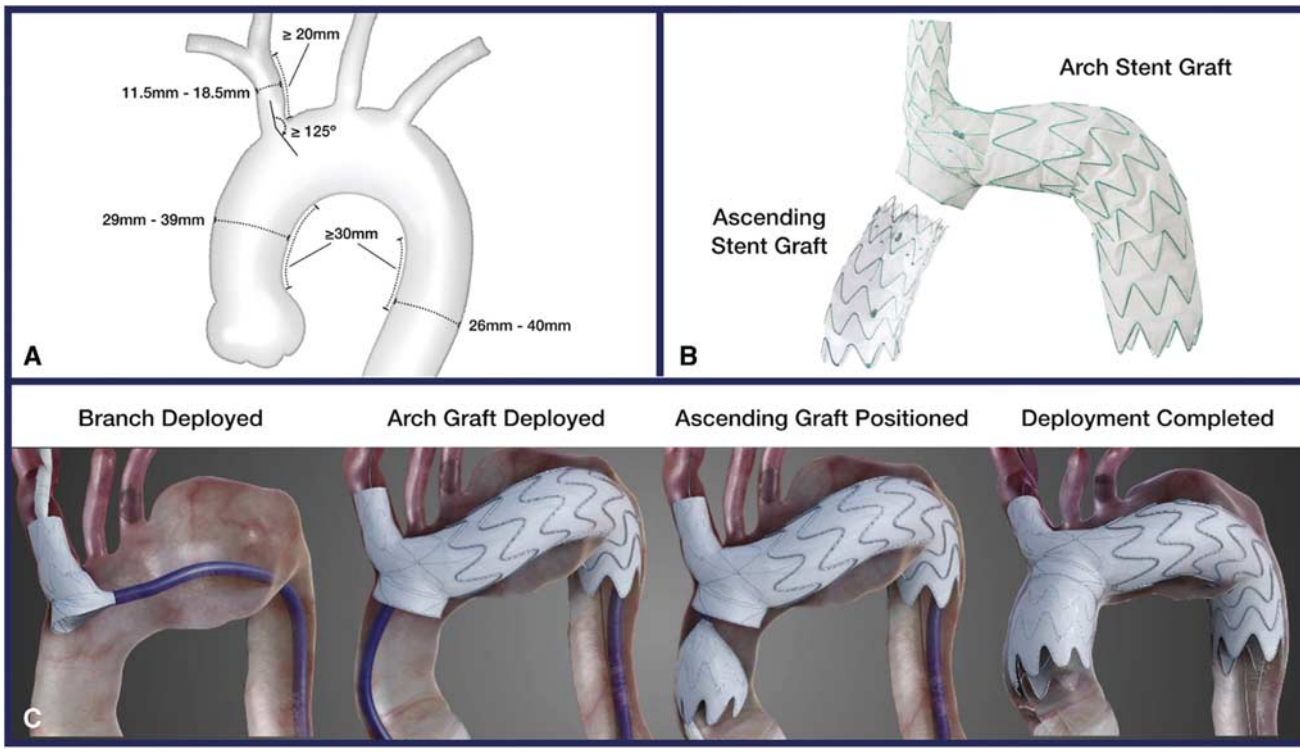

FIGURE 1. NEXUS Aortic Stent Graft System. A, Anatomical parameters required for NEXUS implantation. B, Arch and ascending grafts of NEXUS. C, Principle deployment steps.

correct apposition of the graft, exclusion of the pathology, and patency of supra-aortic vessels (for principle deployment steps, see Fig. 1C).

Study Objectives and Analysis

The objectives of the study were to evaluate the performance and safety of the NEXUS. The primary performance outcome was successful disease treatment at 30-days post-implantation, defined as stent graft positioned in the aortic arch isolating the diseased lesion.

The primary safety endpoint was freedom from device-related mortality within 30 days.

Secondary safety endpoint was defined as freedom from device-related unplanned reinterventions. In addition, exclusion of the primary aortic pathology and freedom from Major Adverse Events (MAE) through 30 days and 1 year were also assessed.

MAE was defined as: all-cause mortality, myocardial infarction, new onset renal failure requiring dialysis, paraplegia, disabling stroke, and new onset aortic valve insufficiency.

All serious adverse events were recorded and adjudicated by an independent Clinical Events Committee (CEC) according to the DEFINE group and the VARC-2 definitions.[7,8] Computer tomography angiography (CTA) interpretation performed in the follow-up visits included the recording of the following parameters: apposition, migration, patency, occlusion of visceral vessels, stent fracture or deformity, aneurysm rupture, aneurysm growth, endoleak type Ia, Ib, II, III, IV, V, and gutters endoleak[9] (for endoleak definition see Supplemental Table 3, http://links.lww.com/SLA/D27). Scheduled CTAs were performed at 30 days, 6 months, 1 year and were assessed by an independent radiologist.

Statistical Analysis

Data are presented as means and standard deviations or median and interquartile range (IQR) for continuous variables and proportions for categorical variables. Survival analysis used the Kaplan–Meier method. Comparisons were made with Student t test, Mann–Whitney U test of the Fisher exact test, as appropriate. P value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 24 (SPSS, Chicago, IL).

RESULTS

Patient Characteristics

A total of 28 patients were treated with the NEXUS as part of the investigational study (n = 18) and compassionate use pathway (n = 10). Mean age was 72 + 6.2 (years) and 22 (79%) were males. Baseline clinical characteristics of the study population are listed in Table 1. There was no significant statistical difference between the FIM study and compassionate use pathway in baseline patients' characteristics.

Aortic Pathology

Isolated aortic arch aneurysm was the principle pathology in 17 patients (60.7%) while chronic aortic dissection was the principle pathology in 6 patients (21.4%). Of them 3 had Stanford type A dissection, postsurgical ascending aortic replacement, 3 had chronic Stanford type B dissection without adequate endovascular landing at zones 1 or 2. There was 1 patient (3.6%) with penetrating aortic ulcer, and 4 patients (14.2%) with combined pathologies.

TABLE 1. Baseline Characteristics

Variable	First in Man Cohort (n = 18)	Compassionate Cohort (n = 10)	Entire Cohort (n = 28)	P Value
Age (years), mean ± SD	71.7 ± 5.9	73.2 ± 6.9	72.2 ± 6.2	0.55
Male	16 /18 (88.9%)	6/10 (60%)	22/28 (78.6%)	0.15
BMI kg/m^2, mean ± SD	28.6 ± 5.4	27.2 ± 7.2	28.1 ± 6.0	0.57
DM	2/18 (11.1%)	0/10	2/28 (7.1%)	0.52
HTN	18/18 (100%)	9/10 (90%)	27/28 (96.4%)	0.36
DLP	6 /18 (33.3%)	5/9 (55.5%)	11/27 (40.7%)	0.41
Current smoker	3/18 (16.7%)	1/10 (10%)	4/28 (14.3%)	1.00
COPD	5/18 (27.8%)	4/10 (40%)	9/28 (32.1%)	0.68
CAD	7/18 (38.9%)	2/10 (20%)	9/28 (32.1%)	0.42
Arrhythmia	6/18 (33.3%)	1/10 (10%)	7/28 (25%)	0.36
Previous sternotomy	12/18 (66.7%)	3/10 (30%)	15/28 (53.6%)	0.11
CVA/TIA	1/18 (5.6%)	1/10 (10%)	2/28 (7.1%)	1.00
CHF (NYHA III/IV)	0	2/10 (20%)	2/28 (7.1%)	0.12
PVD	2/18 (11.1%)	1/10 (10%)	3/28 (10.7%)	1.00
CKD (creatinine > 2.0)	2/18 (11.1%)	0	2/28 (7.1%)	0.52
Anemia	7/18 (38.9%)	2/10 (20%)	9/18 (32.1%)	0.42
ASA risk score ≥ 3	16/17 (94.1%)	9/10 (90%)	25/27 (92.5%)	0.70

ASA indicates American Society of Anesthesiology; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive lung disease; CVA, cerebrovascular accident; DLP, dyslipidemia; DM, diabetes mellitus; HTN, hypertension; IQR, interquartile range; NYHA, New York Heart Association; PVD, peripheral vascular disease; TIA, transient ischemic attack.

Location of the treated pathology (aneurysm/proximal entry tear) was in zone 0B (7.1%), zone 0C (32.1%), 1 (28.6%), zone 2 (25.0%), and zone 3 (7.1%).[10] In all patients, proximal landing was at zone 0 (ascending aorta distal from sino-tubular junction to the brachiocephalic branch) (Fig. 2).

Preparatory Procedure

Twelve patients (42.8%) received a double bypass (RCC-LCC-LSA) and 12 (42.8%) patients had a single bypass (RCC-LCC) mostly in combination with a parallel graft. Three (10.7%) patients had aortic debranching from zone 0, and 1 patient did not undergo a preparatory procedure just prior to the NEXUS procedure, as he had already undergone wrapping and debranching from the ascending aorta 1 year prior to NEXUS procedure. Five (17.8%) patients underwent wrapping of the ascending aorta[11] due to enlarged ascending aorta (maximal diameter > 39 mm). All surgical grafts were patent at the index procedure.

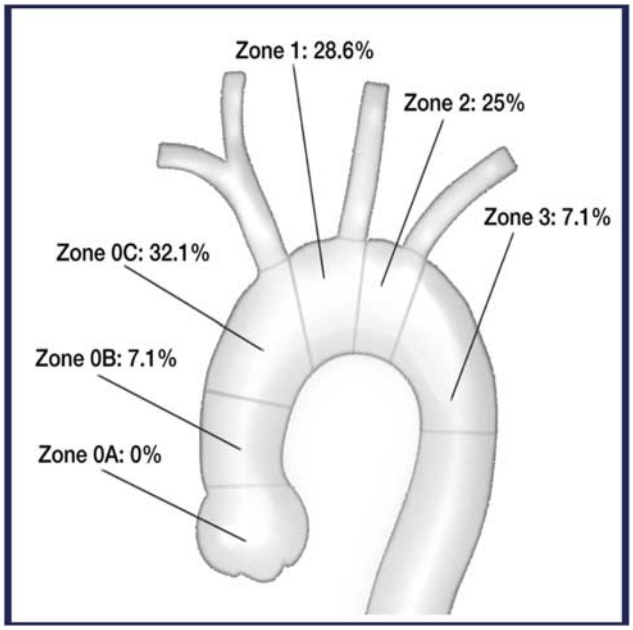

FIGURE 2. Modified classification of aortic arch according to Roselli et al[10] with percentage of most proximal pathology treated.

NEXUS Implantation

Table 2 summarizes procedural characteristics. All procedures were completed successfully with the NEXUS device implanted from zone 0 to zone 4 and BCT branch in the intended position. In 10 patients, a planned parallel stent graft was implanted to supply the LSA in a "periscope" configuration. In 14 (50%) patients a planned distal extension stent graft was implanted in the distal thoracic aorta. Median total procedure time was 185 minutes [IQR 148−254] and NEXUS procedure time (arch stent graft delivery system insertion to ascending stent graft delivery system retrieval) was 80 minutes [IQR 46.5−113].

Outcomes

All patients alive completed the 1-year follow-up. Detailed outcomes are present in Supplemental Table 4, http://links.lww.

TABLE 2. Procedural Characteristics

Variable	Median [IQR]
Total procedure time (min)*	185 [148-254]
NEXUS procedure time (min)†	80 [46.5-113]
Fluoroscopy time (min)‡	48 [37.5-54]
Contrast volume (mL)§	122.5 [102.5-187.5]
Length of hospitalization following procedure (d)	8.5 [7.0-14.7]
Number of patients admitted to ICU	16/28 (57.1%)
Length of ICU stay (d)	1.0 [1.0-3.0]
Complete percutaneous access	19/28 (67.9%)

*Total procedure time: skin-to-skin; data was collected for 26 patients.
†NEXUS procedure time: time from access with the arch stent graft delivery system until retrieval of the ascending stent graft delivery system; data was collected for 17 patients.
‡Fluoroscopy time data was collected for 25 patients.
§Contrast volume data was collected for 24 patients.
ICU indicates intensive care unit.

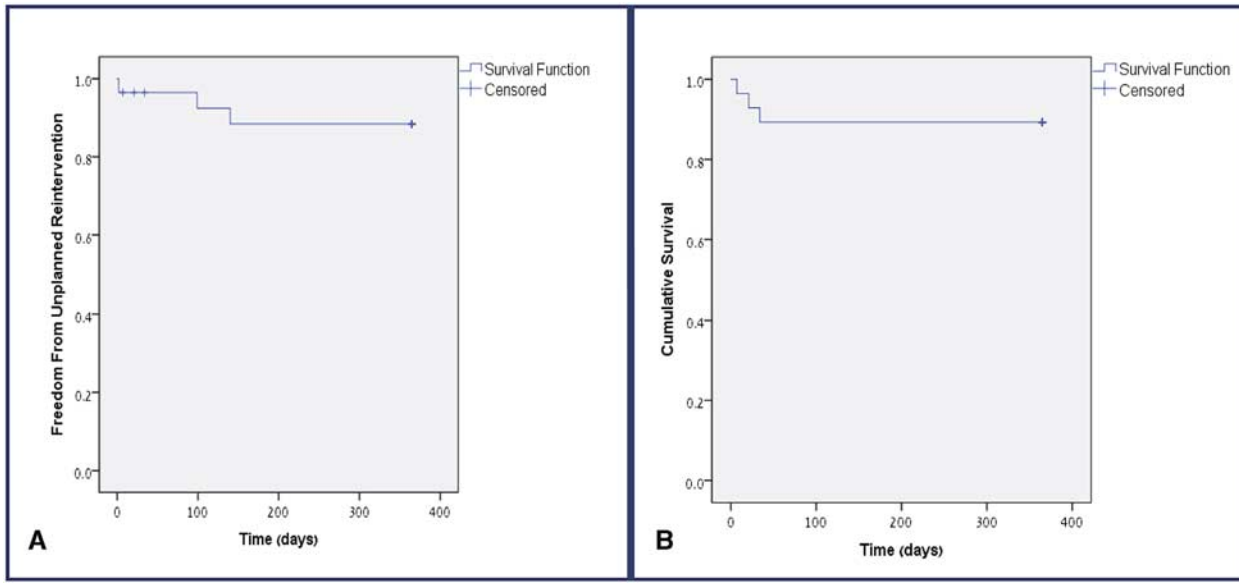

FIGURE 3. Kaplan-Meier survival curves. A, Freedom from device-related unplanned reinterventions. B, Overall survival.

com/SLA/D27. The primary performance endpoint of successful disease treatment at 30 days was achieved in 25 of 26 alive patients (96.1%).

The primary safety endpoint; freedom from device-related mortality through 30-days was achieved in all patients. Two patients (7.1%) had procedure-related mortality through 30 days. One patient died suddenly, with no evidence of device failure, bleeding, CVA, and myocardial infarction at autopsy. The second patient had multiple brain infarcts at autopsy, without evidence of device failure. The presumed cause of death was multiple brain infarcts. There were no instances of intraoperative mortality or emergent conversion to open surgery.

Freedom from MAE at 30 days was achieved in 89.2% of the patients. In addition to the 2 mortality patients there was 1 patient with new onset renal failure requiring dialysis. The patient's renal function returned to baseline after 2 weeks. There were no reports of paraplegia, disabling stroke, aneurysm rupture, myocardial infarction, and new onset aortic valve insufficiency.

Freedom from device-related unplanned reinterventions was achieved in 25 patients (89.3%) through 1 year (Fig. 3A). One patient had perforation of the left ventricle during NEXUS implantation. This patient underwent percutaneous repair of left ventricle perforation with Amplatzer VSD closure device and coil embolization. This patient required also permanent pacemaker implantation. One patient had a hematoma in the ascending aorta noted early postoperatively that was not associated with a dissection flap on serial echo and CT imaging. At 3-months post NEXUS implantation, the patient was asymptomatic; however, CT demonstrated that the hematoma had evolved into a type A dissection with a flap noted at the proximal end of the ascending module. It was repaired under circulatory arrest by ascending graft removal and replacement with a surgical graft. The same patient underwent also additional thoracic endograft deployment (TEVAR) at the descending thoracic aorta to treat a type III endoleak between the NEXUS arch stent graft and a distal extension. The third patient underwent coil embolization of gutters endoleak.

There were no reports of type Ia, IV, and type V endoleaks. There was 1 report of expected type Ib endoleak (preplanned as a 2-stage procedure with distal thoracic stent graft extension). Expected Type II endoleaks were seen in 4 patients presenting retrograde flow from a nonoccluded LSA. Planned embolization of the LSA was successfully performed.

Overall, there were 2 patients with type III endoleaks between NEXUS arch and ascending grafts. One patient (3.6%) with late filling type III endoleak demonstrated at 30 days CTA and resolved spontaneously at follow-up. Another patient developed type III endoleak demonstrated at 6 months follow-up and remained stable at 1 year, without evidence of aneurysm growth. In patients treated with parallel graft from the descending aorta to the LSA, gutters endoleak was seen at 30 days in 4 patients (14.3%) and in 2 patients (7.1%) at 1 year. Outcome analysis of subgroup of patients treated with parallel grafts is provided in Supplemental Table 5, http://links.lww.com/SLA/D27.

A 1-year follow-up CTA demonstrated no graft migration, stent graft separation, branch occlusion, stent fracture, graft infolding or collapse. There was 1 report of asymptomatic surgical graft occlusion(LCCarterytoLS A)and no reports of periscope occlusion (Fig. 4 demonstrate representative preprocedural and follow-up CTA images). Through 1 year mortality occurred in 1 additional patient bringing the total of all-cause mortality to 3 patients (10.7%) (Fig. 3B). The mortality was adjudicated by the CEC as possibly procedure related. There was 1 additional patient (3.6%) of TIA through 1 year. There were no additional reports of new onset renal failure, paraplegia, myocardial infarction, or aortic insufficiency.

DISCUSSION

The NEXUS Aortic Arch Stent Graft System is a novel transcatheter off-the-shelf single branch, 2-stent graft system, specifically designed to address aortic pathologies involving or extending to the aortic arch. This paper describes the initial evaluation of this stent graft system in 28 patients having high or prohibitive risk for conventional open arch repair. All patients underwent successful implantation of the device, with 100% technical success, and achieved 96.1% of the primary

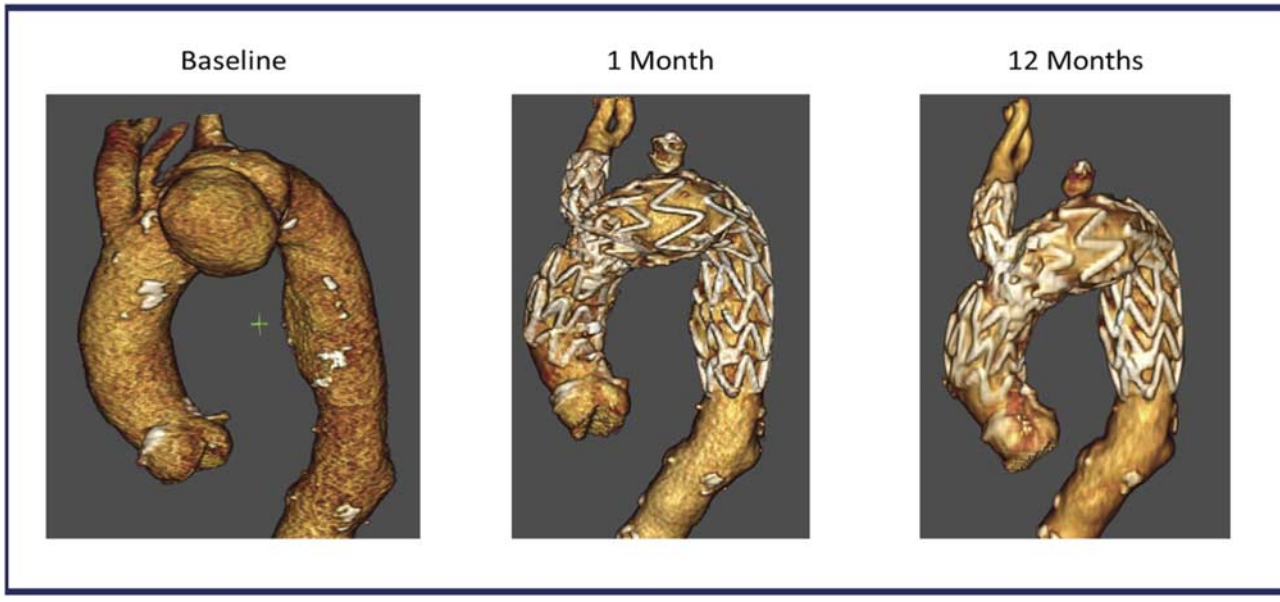

FIGURE 4. CTA of a patient treated with NEXUS for aortic arch aneurysm showing preprocedural, 1 month and 12 months follow-up. Images courtesy of Dr Andrew Hill, Auckland New Zealand.

performance endpoint of successful deployment and exclusion of the pathology. There were no reports of device-related mortality with freedom from procedure-related mortality of 92.8% at 30 days. There was no aneurysm-related mortality or device failure through 1 year follow-up. There was 1 report of endoleak between NEXUS stent grafts (type III) at 1 year.

Aortic arch pathologies remain a complex clinical challenge.[1,12] While open surgery is still considered the gold standard for treatment of aortic arch pathologies, the associated morbidity and mortality as well as high-risk patients' characteristics makes this approach nonrelevant to the majority of the patients, driving current developments toward less invasive procedures in patients with significant comorbidities. Hybrid procedures with debranching of the supra-aortic arteries from the ascending aorta with complementary endovascular stent graft implantation across the arch are considered lower risk procedures, but nevertheless require sternotomy with overall mortality and morbidity not significantly different from open surgery.[13,14] A complete endovascular approach with parallel graft technique (chimneys and periscopes) was proven safe and effective, with reasonable rate of reinterventions but is off-label in the instructions for use of the devices.[4,15]

Branched devices are a recently evolving technique that allows endovascular solution for supplying the supra-aortic arteries.[16] A recent study of a single-center experience with the custom-made inner branched arch endograft (Cook Medical, Bloomington, IN) of 54 patients reported a technical success rate of 98% and a 30-day mortality and major stroke incidence of 5.5% and 5.5%, respectively. One-year survival was 83% and there were 17% of reinterventions.[17] The experience with the Bolton Relay Plus branched arch endograft (Terumo Aortic, Sunrise, FL) by Czerny et al reported 15 patients treated with double-branched stent graft with 100% technical success. Type I and III endoleaks occurred in 6.7%, in-hospital mortality was 6.7%, disabling and nondisabling strokes occurred in 6.7% and 13.3%, respectively. Over a median follow-up of 263 days all cause death was 27% without any aorta-related death.[18]

Although these preliminary studies show promising results, the clinical experience is still limited, and thus, endovascular aortic arch repair in Zone 0 is recommended by the current European Association for Cardio-Thoracic surgery (EACTS) and the European Society for Vascular Surgery (ESVS) for patients with a suitable anatomy, who are unfit for open surgery.[3] Of note, currently there is no off-the-shelf approved branched device for treating aortic arch pathologies that require landing at zone 0.[16]

Reported rate of early mortality and stroke rate in open and hybrid surgery varies widely.[1,13,14,19] In a systematic review of 46 studies reporting outcome of hybrid aortic arch repair techniques, the pooled estimate for 30-day in-hospital mortality was around 10%, the estimate for cerebrovascular events was around 7%, and irreversible spinal cord ischemia around 4%. In total endovascular aortic arch repair, technical success rate was 84.2%, reported mortality rate was 13.2%, and early cerebrovascular events rate was 15.8%.[19] The relatively low rate of major adverse events and 100% technical success rate in the current series was facilitated by several features of the NEXUS. The device is implanted from the BCT branch and deployed through the aortic arch to the descending aorta, over a femoral-axillary, through and through wire. There are several potential advantages of this configuration. First, it saves the need to cannulate the supra-aortic trunks branches and to connect them to a stent graft in the arch. This significantly reduces endovascular manipulation in the arch, and may consequently reduce the risk of embolic stroke. Second, this configuration improves stability of the stent graft, both during the procedure as the arch stent graft is continuously connected and secured via the axillary access with temporary stitches, as well as long-term stability derived from the unique geometrical structure. And third, it allows, except for the very short branch deployment time, continuous blood flow to the brain throughout the procedure. The preshaped delivery system enables self-orientation of the device and further minimizes device manipulation at the arch and ascending aorta. In addition, the curved ascending stent graft

naturally tracks the curvature of the ascending aorta, to improve sealing, and prevent "bird beaking" and traumatic erosion of the aortic wall.[20,21]

Management of supra-aortic vessels with the single-branch configuration device dictates a preparatory procedure to redirect blood to cranial and upper extremities' vessels. In this series, the branch stent graft was deployed in the BCT with cervical bypass, mostly RCC-LCC-LSA performed few days before NEXUS deployment. Other configurations included a single RCC-LCC bypass with parallel graft in a "periscope" configuration to the LSA. Although shown effective without any report of failure of the parallel graft, the parallel graft technique had a relatively high rate of reinterventions to treat gutters endoleaks. Due to the small number of patients, it is difficult to draw conclusions regarding the preferred method of supra-aortic vessels management. In this cohort, this was left to the discretion of the operator.

The study should be interpreted in the contexts of several limitations. First, the major limitation of the current study is the relatively small number of patients. It represents early experience in which the majority of study sites treated up to 3 patients. Consequently, the learning curve is still ongoing. Second, the study was nonrandomized. No formal comparison was made to other available devices or surgical alternatives; however, comparison to published data shows promising results of the NEXUS system. Finally, the short-term nature of this study does not allow for conclusions regarding long-term durability of the NEXUS system. Long-term follow-up is ongoing.

In conclusion, in patients with aortic arch pathologies that require landing in the ascending aorta, endovascular repair with the NEXUS Aortic Arch Stent Graft System can be performed with high success rate and promising results at 1 year. Further follow-up is required to establish the long-term safety and effectiveness of this device.

ACKNOWLEDGMENTS

The authors thank Vittorio Alberti, Michael Hofmann, Thomas Pfammatter, Gilbert Puippe, for their contributions to the study and patient treatment.

REFERENCES

1. Rommens KL, Estrera AL. Contemporary management of aortic arch aneurysm. *Semin Thorac Cardiovasc Surg*. 2019;31:697–702.
2. Gupta P, Harky A, Jahangeer S, et al. Varying evidence on deep hypothermic circulatory arrest in thoracic aortic aneurysm surgery. *Tex Heart Inst J*. 2018;45:70–75.
3. Czerny M, Schmidli J, Adler S, et al. Current options and recommendations for the treatment of thoracic aortic pathologies involving the aortic arch: an expert consensus document of the European Association for Cardio-Thoracic surgery (EACTS) and the European Society for Vascular Surgery (ESVS). *Eur J Cardiothorac Surg*. 2019;55:133–162.
4. Pecoraro F, Lachat M, Cayne NS, et al. Mid-term results of chimney and periscope grafts in supra-aortic branches in high risk patients. *Eur J Vasc Endovasc Surg*. 2017;54:295–302.
5. Haulon S, Greenberg RK, Spear R, et al. Global experience with an inner branched arch endograft. *J Thorac Cardiovasc Surg*. 2014;148:1709–1716.
6. van Bakel TM, de Beaufort HW, Trimarchi S, et al. Status of branched endovascular aortic arch repair. *Ann Cardiothorac Surg*. 2018;7:406–413.
7. Diehm N, Vermassen F, van Sambeek MR, et al. Standardized definitions and clinical endpoints in trials investigating endovascular repair of aortic dissections. *Eur J Vasc Endovasc Surg*. 2013;46:645–650.
8. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Thorac Cardiovasc Surg*. 2013;145:6–23.
9. Chaikof EL, Blankensteijn JD, Harris PL, et al. Reporting standards for endovascular aortic aneurysm repair. *J Vasc Surg*. 2002;35:1048–1060.
10. Roselli EE, Idrees JJ, Johnston DR, et al. Zone zero thoracic endovascular aortic repair: a proposed modification to the classification of landing zones. *J Thorac Cardiovasc Surg*. 2018;155:1381–1389.
11. Pecoraro F, Shingaki M, Steuer J, et al. Treatment of isolated ascending aortic aneurysm by off-pump epiaortic wrapping is safe and durable. *Interact Cardiovasc Thorac Surg*. 2016;23:286–291.
12. Sood V, Patel HJ, Williams DM, et al. Open and endovascular repair of the nontraumatic isolated aortic arch aneurysm. *J Vasc Surg*. 2014;60:57–63.
13. Chakos A, Jbara D, Yan TD, et al. Long-term survival and related outcomes for hybrid versus traditional arch repair-a meta-analysis. *Ann Cardiothorac Surg*. 2018;7:319–327.
14. Milewski RK, Szeto WY, Pochettino A, et al. Have hybrid procedures replaced open aortic arch reconstruction in high-risk patients? A comparative study of elective open arch debranching with endovascular stent graft placement and conventional elective open total and distal aortic arch reconstruction. *J Thorac Cardiovasc Surg*. 2010;140:590–597.
15. Bosiers MJ, Donas KP, Mangialardi N, et al. European multicenter registry for the performance of the chimney/snorkel technique in the treatment of aortic arch pathologic conditions. *Ann Thorac Surg*. 2016;101:2224–2230.
16. Anwar MA, Hamady M. Various endoluminal approaches available for treating pathologies of the aortic arch. *Cardiovasc Intervent Radiol*. 2020;43:1756–1769.
17. Tsilimparis N, Detter C, Law Y, et al. Single-center experience with an inner branched arch endograft. *J Vasc Surg*. 2019;69:977–985.e1.
18. Czerny M, Rylski B, Morlock J, et al. Orthotopic branched endovascular aortic arch repair in patients who cannot undergo classical surgery. *Eur J Cardiothorac Surg*. 2018;53:1007–1012.
19. Moulakakis KG, Mylonas SN, Markatis F, et al. A systematic review and meta-analysis of hybrid aortic arch replacement. *Ann Cardiothorac Surg*. 2013;2:247–260.
20. Kudo T, Kuratani T, Shimamura K, et al. Determining the optimal proximal landing zone for TEVAR in the aortic arch: comparing the occurrence of the bird-beak phenomenon in Zone 0 vs Zones 1 and 2. *J Endovasc Ther*. 2020;27:368–376.
21. Lee WA. Failure modes of thoracic endografts: prevention and management. *J Vasc Surg*. 2009;49:792–799.