Thoracic endovascular aortic repair (TEVAR) has supplanted open surgical repair for all of the various pathologies of the descending thoracic aorta, including thoracic aneurysms, transections, dissections, and penetrating aortic ulcers (PAUs). The perioperative and 30-day morbidity, mortality, and rates of paraplegia all compare favorably to historical series of open surgical repair. The mid- and long-term durability of TEVAR devices must be examined rigorously and compared to the historical gold standard of open repair to ensure that patients undergo the treatment not only with the lowest perioperative risk, but also with the greatest long-term durability and benefit. We know from the endovascular treatment of abdominal aortic aneurysms that the long-term durability of endografts has been called into question 3 to 5 years after device implantation due to issues of migration, untreated endoleaks, and subsequent aneurysm sac expansion and delayed rupture.¹

Multiple thoracic aortic stent graft technologies have emerged to treat the various pathologies of the descending thoracic aorta. Continued refinements of the stent grafts themselves, as well as their delivery systems, have shown improved results over earlier device iterations. As surgeons continue to gain experience with TEVAR techniques, the risks associated with such therapy have decreased. The Relay Thoracic Stent Graft with Plus Delivery System (Bolton Medical) (Figures 1 and 2) is one such device that has undergone refinement of its original delivery system. The midterm (5-year) results of the United States Pivotal Trial were recently reported, showing favorable outcomes compared to historical surgical controls. The device delivery system was redesigned during this period, and a subset analysis was performed to analyze differences between the two cohorts. This article presents the results of this subcohort of patients, highlighting the clinical and technical benefits of device delivery improvements.

PIVOTAL TRIAL RESULTS

The Relay Thoracic Stent Graft with Plus Delivery System received US Food and Drug Administration approval in September 2012, but it has been used in Europe and other international markets since 2005. The Bolton Relay Thoracic Aortic Endovascular Pivotal Trial was a prospective, nonrandomized, multicenter, United States investigational device exemption study conducted at 27 United States sites. Between January 2007 and May 2010, 120 TEVAR patients were treated with the Relay device. Thirteen additional patients were enrolled during the continued access phase of the study through September 2012. Ninety-five patients were treated with the original Relay transport delivery system, and 38 patients were treated with the RelayPlus delivery system. The initial and midterm results of the device were recently published.² TEVAR outcomes were compared to a retrospectively and prospectively captured cohort of 60 open surgical controls. Patients were followed clinically and underwent imaging yearly for 5 years after TEVAR.

Stent grafts were successfully delivered in 129 of 133 (97%) patients. Access failures were noted early in the
study and were associated with the use of the original transport delivery system. Perioperative outcomes revealed a lower mortality rate with TEVAR compared to open surgical controls (5.3% vs 10%; \( P = .23 \)). TEVAR was associated with a significantly lower rate of major adverse events (MAEs), defined as stroke, paralysis/paraplegia, myocardial infarction, procedural bleeding, respiratory failure, renal failure, wound healing complications, and aneurysm-related mortality. (20.3% vs 48.3%; \( P < .001 \)). This was mostly due to a lower frequency of adverse respiratory complications (5.5% vs 21.6%; \( P = .007 \)), and periprocedural bleeding (transfusion was required in 10 [7.5%] vs 50 [84.7%] patients; \( P < .001 \)). Midterm (5-year) outcomes of freedom from aneurysm-related mortality were similar between groups (91.3% for TEVAR vs 89.4% for open surgery; \( P = .406 \)). Freedom from MAEs at 5 years favored the TEVAR cohort (65.7% vs 44.7%; \( P = .001 \)). Ten (7.5%) patients required secondary procedures after TEVAR. Aneurysm sac size decreased or remained stable in 113 (85%) patients through 5-year follow-up. Endograft migration occurred in three (2.3%) patients, and wireform fractures were seen in two (1.5%) patients. There were no instances of aneurysm rupture or endograft occlusion in the TEVAR cohort.

**SUBSET ANALYSIS**

In September 2009, two major changes were implemented concurrently to the study design confounding the aforementioned results. The first major change to the study design was the introduction of the Plus delivery system. Of the 133 patients enrolled in the pivotal study, 38 were treated with the newer RelayPlus device.

The following modifications were made to the original transport delivery system with the new Plus delivery system: (1) hydrophilic coating was placed on the sheath tip as well as higher radiopacity, (2) the delivery sheath was lengthened, and (3) the inner stainless steel catheter was replaced with a precurved nitinol inner catheter to improve tracking to the natural curvature of the aorta; the precurved design self-aligns the S-bar. The S-bar is a curved nitinol torsion bar that provides longitudinal support to the Stent Graft and is ideally placed on the outer curvature of the distal aortic arch. The Plus delivery system uses a two-stage device deployment technique, consisting of an outer delivery sheath followed by an inner sheath containing the device. The outer sheath provides support during delivery and protects access vessels by acting as a conduit for the inner sheath. The flexible inner sheath allows for atraumatic advancement and staged graft expansion for precise deployment. The new design not only improves the steerability and tractability of the device, but also the precision of deployment in tough angulated arches.

The second major change to the study design was the inclusion of patients with PAUs. Saccular aneurysms and PAUs accounted for 41 of 133 (30.8%) patients in the study. PAUs are an ideal pathology to treat with TEVAR, as the pathology is typically isolated with relatively normal seal zones proximally and distally. PAU is defined as an ulceration of an aortic atherosclerotic plaque penetrating the internal elastic lamina into the media, often associated with a variable degree of intramural hematoma formation. PAUs are often multiple and vary greatly in size and can be up to 5 mm in diameter and 4 to 30 mm in depth. They can occur at any point throughout the aorta, most commonly in the middle and lower descending aorta, less frequently in the aortic arch and abdominal aorta, and rarely in the ascending aorta.

In a recent literature review and meta-analysis by D’Annoville et al of TEVAR in patients presenting with PAUs, > 80% of patients were treated with a single device, there was a very low stroke rate of 2.4% (7 of 287), and the paraplegia rate was low at 2.9% (9 of 308). Only one patient had permanent paraplegia, and neurologic deficits completely resolved in the other eight patients. Based on the pivotal trials of the other commercially available TEVAR devices used solely in the setting of aneurysmal disease, patients typically have an average 5% risk of stroke and 5% risk of paraplegia/paraparesis.

Although confounded by selection bias in the published literature, the risk of stroke and paraplegia associated with TEVAR in the setting of PAU appears lower compared to pivotal device trials of TEVAR involving aneurysmal disease alone. The lower risks associated with PAUs may be related to the use of single, short-piece thoracic endografts involving less aortic coverage. Quicker procedures are also likely associated with less wire manipulation and catheter exchanges. The pathology is also most likely in the mid to lower portions of the descending thoracic aorta, and as such, the risk of stroke is lower. The addition

**Figure 2. The Relay Thoracic Stent Graft with Plus Delivery System.**

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of patients presenting with PAU to the study design confounds the results of the Bolton Relay Thoracic Aortic Endovascular Pivotal Trial when making direct comparisons to the results of studies evaluating other available thoracic endografts.

Outcomes

A subset analysis of outcomes was performed comparing patients treated with the original transport delivery system with those treated with the updated Plus delivery system. The RelayPlus group had 100% device delivery and no device alignment issues, as the precurved nitinol inner cannula allowed for self-alignment of the S-bar to the greater curvature. There were no type I or III endoleaks, device migrations, or stent strut fractures. Follow-up was similar between the two groups (3.2 years for the RelayTransport delivery system vs 3 years for RelayPlus). In the original RelayTransport device cohort, there were five type I endoleaks (5.1%) and one type III endoleak (1.1%). Migration was seen in three patients (3.2%), and there was evidence of two wireform fractures of the stent struts (2.1%). In terms of MAEs, there was a significant difference between the two cohorts, with six (15.8%) MAEs seen in the RelayPlus group versus 34 (35%) MAEs in the original RelayTransport group.

There are several factors that could explain the improved results associated with the RelayPlus system other than device delivery design improvements alone. As the trial progressed, the investigators gained greater experience with the delivery and deployment of the device, as well as improved patient selection. In the RelayTransport system, 24 of 95 (25.3%) patients required an iliac conduit versus two of 38 (5.3%) using the RelayPlus delivery system (P = .017).

There was a noticeable improvement in the rate of stroke in RelayPlus group. One (1 of 38, 2.6%) patient experienced a stroke in the RelayPlus cohort versus 12 (12 of 95, 12.6%) patients in the original RelayTransport cohort (P = .108). This single patient had a stroke beyond the 30-day perioperative period but was noted at a 6-month evaluation. The lower stroke rate could be attributed to design improvement vis-à-vis self-alignment of the S-bar and less torque and manipulation required to position the device. An addition of patients with PAUs later in the trial could also have affected stroke rates. Less wire manipulation as well as catheter and device exchanges could explain the lower stroke rate seen in the RelayPlus cohort. Because the RelayPlus cohort was small, it may be impossible to perform further subset analyses to assess for other meaningful significant differences.

CONCLUSION

The Bolton Relay Thoracic Aortic Pivotal Trial supports the use of the Relay Thoracic Stent Graft with Plus Delivery System as an effective, safe, durable treatment option for patients with descending thoracic aortic aneurysms and PAUs. The RelayPlus delivery system appears to confer improved results over the first-generation delivery system design, making the procedure even safer for patients. Results from Bolton Relay Thoracic Aortic Pivotal Trial compare favorably to the midterm results of studies evaluating other commercially available thoracic stent grafts. Further follow-up of the patients enrolled in the pivotal trial, as well as those enrolled postapproval, is needed to ensure long-term durability of the device.