

# The MOTHER Multicenter Registry

An overview and discussion of a registry that may help us understand how and to what degree various factors influence the risk of complications after TEVAR.

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Endovascular repair of the thoracic aorta (TEVAR) has broadened the therapeutic options available for conditions affecting the aortic arch and descending thoracic aorta. The number of thoracic endovascular procedures performed has risen steadily over recent years, whereas the number of open surgical operations has remained stable (Figure 1).<sup>1</sup> This suggests that rather than replacing traditional techniques, TEVAR complements open surgery and allows more patients to be definitively managed than was previously possible.<sup>2</sup> Some patients are deemed unfit for open surgery due to poor physiological reserve, and although the risk of aortic-related death is abolished, they are subject to an increased risk of death from all other causes in comparison with matched controls.

Understanding which patients will gain maximum benefit from TEVAR requires additional well-validated clinical evidence that describes perioperative events and midterm follow-up. Unfortunately, many series fail to discriminate between different aortic pathologies when reporting outcomes, making the results hard to assess and pooled analysis difficult. This is partly due to a lack of globally accepted reporting standards. One potential way to improve this situation could be by combining data obtained from high-quality trials at a raw data level.

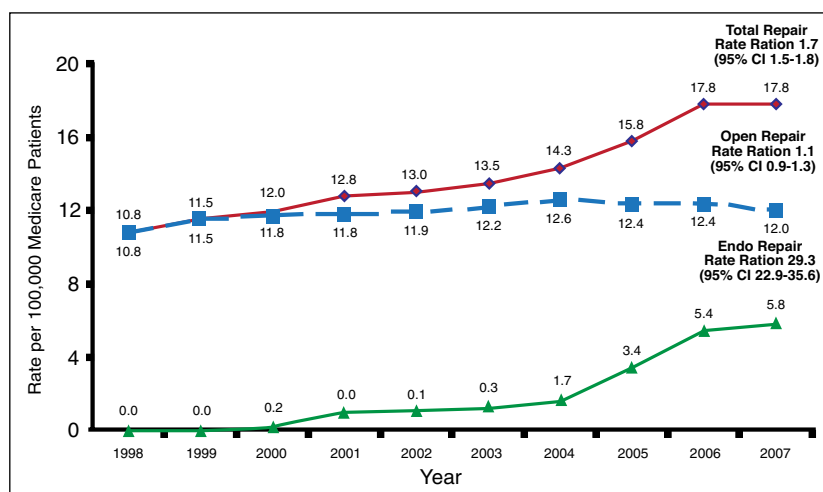


Figure 1. The rates of thoracic and thoracoabdominal repair (triangles), open repair (squares), and endovascular repair in the Medicare population from 1998 to 2007. Note the increase in total repairs but the stability of the open figures. Reprinted from the *Journal of Vascular Surgery*, Vol. 53/6, Scali S, et al. National trends and regional variation of open and endovascular repair of thoracic and thoracoabdominal aneurysms in contemporary practice. 1499–1505, Copyright (2011), with permission from Elsevier.

## THE MEDTRONIC OUTCOMES OF THORACIC ENDOVASCULAR REPAIR (MOTHER) REGISTRY

The Medtronic Outcomes of Thoracic Endovascular Repair (MOTHER) registry comprises five prospective trials conducted by Medtronic, Inc. (Minneapolis, MN) with the addition of institutional data from a single UK center, St. George's Vascular Institute. The sponsored trials include pre-market investigational trials (52% of patients, all arms of VALOR<sup>3</sup> and VALOR II) and post-market registries (27% of patients, INSTEAD,<sup>4</sup> Valiant Captivia registry, and the VIRTUE registry<sup>5</sup>). The institutional data series was a prospectively collected dataset

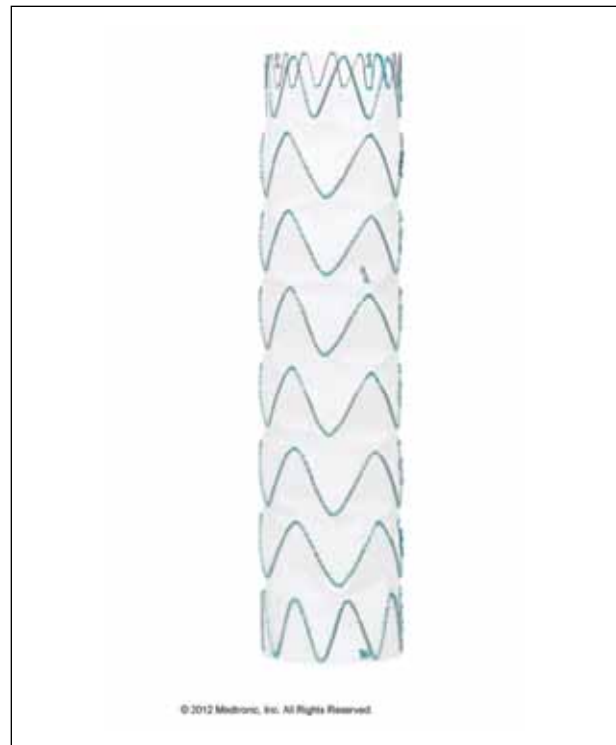


**Figure 2.** The improved conformability of the Valiant® thoracic device afforded by the sinusoidal springs located on the outside of the graft fabric. The eight-peaked FreeFlo springs are also displayed.

that included all thoracic endovascular aortic repairs performed over a period of 8 years that used either the Talent® thoracic or Valiant® thoracic stent graft systems (Medtronic, Inc.) that were not entered into any of the aforementioned trials (Table 1).

There were stringent protocols for collection and validation of data, and for more than half of the patients, independent adjudication was used for any adverse events that occurred. The institutional series was prospectively maintained, and follow-up was assessed by computed tomography according to local protocol. The patient cohort was stratified into three groups determined by presenting pathology: thoracic aortic aneurysm (TAA), acute type B aortic dissection (A-BD) (< 2 weeks after symptom onset), and chronic type B aortic dissection (C-BD) (> 2 weeks after symptom onset). There was an insufficient number of patients with other pathologies (eg, transection, mycotic aneurysm) for individual subgroup analysis.

TAA diameter > 5.5 cm, rapid expansion, symptoms attributable to the aneurysm, and aneurysm rupture were considered indications to treat TAA patients. All patients with acute type B dissection were treated if they presented with malperfusion of an arterial territory, rupture



**Figure 3.** The distal component of the Valiant® thoracic graft.

or impending rupture of the false lumen, uncontrollable blood pressure, unremitting pain, a rapidly expanding aorta, or a diameter of > 4.5 cm. In the chronic type B dissection group, there were some patients with stable type B dissections that were treated as part of the INSTEAD trial. Indications for reintervention in all cases were assessed on an individual case-by-case basis at each center.

The primary outcomes of interest were death, stroke (including transient ischemic attack), acute spinal cord injury (paraplegia and paraparesis combined), and endograft-related events, specifically those that required aortic reintervention. Deaths were classified as aortic- or nonaortic-related and were classified as specifically as possible. Aortic-related deaths were defined as any death occurring that was directly attributable to the index procedure, any subsequent reintervention, aortic rupture, or other aortic complication.

All patients in the MOTHER registry had either the Medtronic Talent® thoracic or Valiant® thoracic stent graft systems implanted. Both are modular stent graft systems that feature sinusoidal nitinol rings and springs for radial force and increased conformability, with a woven polyester fabric covering to exclude the diseased section of aorta. Developments from the Talent® design in the Valiant® thoracic stent graft include an eight-peaked proximal bare-spring (FreeFlo) configuration

that distributes radial force evenly. The relocation of the springs to the outside of the graft improves graft apposition and provides enhanced graft stability (Figures 2 and 3). In order to enhance the three-dimensional conformability of the graft, the longitudinal connecting bar that was present in the Talent® model has been removed.

The Captivia® delivery system has been designed to facilitate simple, accurate deployment. The ergonomic delivery system provides an option to deliver the graft gradually, using a gradual “unscrewing” action or, alternatively, by depressing a button and using one smooth withdrawing action (Figure 4). The tip capture mechanism is then recaptured to complete the process, and the delivery system can then be safely removed.

### SPECIFIC AIMS OF THE MOTHER REGISTRY

TEVAR has demonstrated an early mortality advantage over open surgical treatment of the thoracic aorta, which appears greater comparatively than that observed in the abdominal aorta.<sup>6,7</sup> Serious morbidity and other adverse events are also less common, and many clinicians now consider TEVAR as a first-line therapy for most conditions affecting the thoracic aorta. The applicability of endovascular and hybrid techniques continues to expand with emerging device technology and refined indications for use.<sup>1,5</sup>

Despite the obvious benefits, TEVAR is not altogether without risk. Neurological complications have been dreaded by surgeons since the early days of open aortic operations, and recent cohort studies report a 5% to 7% risk of stroke and a 2% to 3% risk of paraplegia following TEVAR.<sup>8,9</sup> These are serious complications and can cause long-term disability. The optimum strategy for preventing these events has not yet been defined but is likely to be multifactorial, making use of a tailored combination of measures.

The length of aortic coverage necessary to seal an aneurysm or exclude a dissection has been shown by some to increase the risk of paraplegia and stroke, as has coverage of the left subclavian artery.<sup>10</sup> The MOTHER registry represents an exciting opportunity to try to understand how—and to what degree—these factors influence the risk of neurological complications. Regression analysis will allow quantification of this risk and the construction of risk-prediction models that may eventually help to protect patients from serious complications.

Mid- to long-term follow-up of the patients enrolled in the EVAR trial suggested that the early mortality benefit derived from endovascular repair of abdominal aortic aneurysms may be lost eventually due to an excess of aortic-related deaths,<sup>11</sup> although important limitations to this study exist, such as the failure to include incisional

The MOTHER registry will not resolve all contentious areas of practice, but it will certainly contribute in several important ways to the existing literature.

hernias as a related reintervention after open repair. The observation regarding aortic-related deaths may have overshadowed the importance of the high nonaortic death rate observed in aneurysm patients, which is potentially an opportunity for increasing life expectancy. Some large administrative datasets have confirmed a high rate of all-cause mortality in TAA patients at follow-up, but there is a lack of good-quality data available at the individual patient level. The MOTHER database will make use of the rigorous follow-up of patients in the component trials to allow analysis of many factors that may influence midterm follow-up. Defining the cause and frequency of deaths in a large series of patients will help to determine if TEVAR is being offered appropriately to high-risk patients, as there have been concerns that

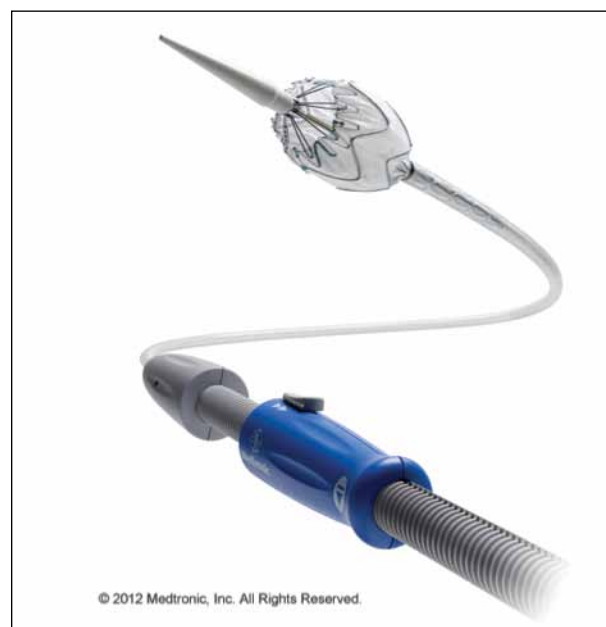


Figure 4. The Captivia® delivery system. The graft is shown mid-deployment with the first few springs emerging from the sheath. The blue handle is either turned for maximum control during delivery or can be withdrawn quickly if the gray lever is depressed. Until the operator is satisfied with the position of the graft, the proximal bare stents remain constrained.

the all-cause death rate is higher than in open surgical patients, despite risk adjustment.<sup>2</sup>

The frequency of aortic reintervention is considered to be the Achilles' heel of endovascular aortic repair in all anatomical locations.<sup>11</sup> To prevent late aortic death, resource-

intensive surveillance programs and secondary procedures are necessary. Predicting those patients who are most at risk for these problems would be of great utility and could help with surgical planning and gauging the intensity of subsequent surveillance. Gaining a greater understanding of

**TABLE 1. THE MOTHER REGISTRY**

Registry	No.	NCT Identifier	Stent	Indication	Purpose/ Endpoint	Duration
VALOR <sup>3</sup>	359	00604799	Talent®	Test: TAA with low/moderate risk (comparator with OSR); registry: as for test but not for comparison; high-risk: not suitable for OSR or high risk (TAA = 333, C-BD = 13, A-BD = 8)	Phase II/III study to determine success of aneurysm treatment at 1 year	5-year follow-up (2003–2011)
VALOR II	160	00413231	Valiant®	TAA only in patients who are a candidates for OSR with low/moderate risk	Phase II/III study to determine success of aneurysm treatment at 1 year	5-year follow-up (2006–2014)
CAPTIVIA	68	01181947	Valiant® Captivia®	All indications (included TAA = 49, C-BD = 23, A-BD = 19, other = 8)	Postmarket surveillance to evaluate mid-term clinical performance	3-year follow-up (2010–2013)
VIRTUE <sup>4</sup>	100	01213589	Valiant® Xcelerant®	Acute (50) and chronic type B dissection (50)	Collection of safety, performance, and health economic data	3-year follow-up (2006–2012)
INSTEAD <sup>5</sup>	100	00525356	Talent®	Chronic type B dissection	Phase III comparison of stent vs medical therapy in chronic dissection	5-year follow-up (2002–2007)
St. George's Vascular Institute	223	N/A	Talent®/Valiant®	All indications (included TAA = 128, A-BD = 37, C-BD = 41, other = 17)	Institutional series of TEVAR with Medtronic stent grafts	Variable follow-up (2002–2010)
Abbreviations: OSR, open surgical repair.						

the effect of individual preoperative aneurysm morphology will almost certainly play a part in achieving this goal. There is emerging evidence that morphology affects the outcome of infrarenal aneurysm repair,<sup>12</sup> but unfortunately, there is no protocol for assessing the thoracic aorta as there is for infrarenal abdominal aortic aneurysms.<sup>13,14</sup> The MOTHER registry contains anatomical information from many of the patients entered into individual registries, measured by an independent core lab. This will allow detailed analysis of the morphological risk factors for midterm technical failure of TEVAR and may help allow the formulation of some guidelines for endograft planning.

TEVAR successfully prevents aortic death in TAA patients, but there is less quality prospective data that confirm these findings in those with dissection. The MOTHER registry will enable comparison of mid- to long-term survival in all groups of patients and allow an indirect comparison with equivalent open surgical series. This will be especially valuable in the chronic dissection group. The treatment of aortic dissection has different indications and objectives from that of aneurysmal disease, and some experts feel that endovascular procedures may not provide a robust long-term solution, despite reports of excellent early results for acute, subacute, and chronic presentations.<sup>4,5,15</sup>

Despite this, a contemporary series detailing midterm results of open surgical procedures demonstrated a high incidence of complications.<sup>16</sup> Although stent graft placement is associated with favorable aortic remodeling and false lumen thrombosis, the place of TEVAR in the treatment of chronic dissection will require demonstration of an ability to prevent aortic death in the medium-term. The MOTHER registry will help to determine the midterm death rate in dissection patients and the cause of these deaths in comparison to TAA. It is also possible that more complex morphological analysis may be undertaken to determine the effect of stenting on the false lumen in the midterm and to correlate this with clinical outcomes.

## CONCLUSION

As more evidence supporting the practice of TEVAR emerges, there will be a greater understanding of which patients are most likely to benefit from this approach. A barrier to this has been the relative few number of procedures that are performed, meaning that randomized control trials on the scale of those performed for infrarenal aortic aneurysm have not yet been feasible. The existing literature has aided expert consensus, but even guidelines commissioned by bodies such as the North American Society for Vascular Surgery can often only base recommendations on weak evidence. To develop a more usable core of literature, it is vital that universally acceptable reporting standards are defined and adhered to.

The MOTHER registry will not resolve all contentious areas of practice, but it will certainly contribute in several important ways to the existing literature. Specific aims include determining the influence of presenting pathology on short- and midterm outcomes, identifying risk factors for neurological complications, and describing the influence of aortic morphology on patient survival and endograft durability. The ultimate goal will be a fully validated risk stratification system for use in clinical practice, which will help to improve the safety of TEVAR. ■

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