Lessons From the TVT Registry

An assessment of the TVT registry, which is studying the real-world outcomes of patients undergoing new valvular therapies.

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Regulatory approval of new therapeutic strategies carries with it multiple challenges. If there are predicate devices with established track records, the postapproval process, while still essential, may not be as complex and may carry with it a smaller chance for unattended risks and consequences.

CHALLENGES IN DEVICE APPROVAL

In the setting of transcatheter aortic valve replacement (TAVR), which was approved in 2011, there was no established predicate device approved in the United States, and accordingly, there were multiple challenges. These included, among others:

1. An unmet clinical need in that up to 30% of patients with severe aortic stenosis were not able to be treated with the standard of care.
2. There was already an existent gold standard of care (ie, surgical aortic valve replacement), which had a long track record during the previous 25 years. The risks and outcomes of this surgical procedure and the devices used had been well studied, and objective performance criteria were available and used in regulatory considerations.
3. Although there was considerable global experience with TAVR, only one randomized clinical trial had been performed. This lack of randomized clinical trial data resulted in delays in consideration of regulatory approval in the United States.
4. Risks associated with introducing this new procedure into more routine clinical practice were not inconsequential, and a learning curve was expected by virtue of the nature of aortic stenosis and the patient population considered for the procedure being characterized by advanced age, multiple comorbidities, and either inoperable or high risk for traditional surgery. Also important was the fact that the available technology was large and inflexible and was associated with peripheral vascular complications.
5. At the time, the approach used for postmarket surveillance studies typically involved small numbers of patients and were industry sponsored. Accordingly, it was difficult to gauge the incidence of complications, as well as the outcomes of the larger group of patients.

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TVT REGISTRY DESIGN

Given these issues at the time of the initial US Food and Drug Administration (FDA) panel, the Society of Thoracic Surgeons and the American College of Cardiology, in consultation with the FDA, recommended the development of a national registry that would have several functions, including (1) the collection of data on all patients undergoing TAVR with a commercially approved device, so that the numerator and denominator of events/patients/procedures could be captured; (2) the use of standardized definitions for baseline characteristics, procedural performance, and complications; (3) the development of a series of processes for site and physician selection, adjudication of events, reporting processes, steps to ensure confidentially of data, as well as informed patient consent; (4) the development of an infrastructure for protocol design

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and scientific data query; and (5) the development of processes to involve all relevant stakeholders, including industry, regulatory agencies, patient care advocates, and continued professional society involvement. These processes resulted in the eventual development of a Centers for Medicaid & Medicare Services National Coverage Determination (CMS-NCD), which mandated a generic registry for TAVR but did not mandate any specific sponsors and administrative structure for that registry. However, included in this mandate was the provision that all approved TAVR devices would be included regardless of the device manufacturer. Based on this mandate and the experience with multiple other registries (eg, INTERMACS and Cath PCI among others), the Society of Thoracic Surgeons and the American College of Cardiology worked with a variety of stakeholders (including industry, coordinating centers, patient care groups, regulatory agencies, and others) to develop the TVT registry.

The TVT registry has now accumulated records of approximately 30,000 patients undergoing commercial TAVR device implantation at almost all approved centers in the United States. Multiple accomplishments include standardized definitions, development of scientific data on the field and outcomes in general, late-breaking clinical trials on overall performance of TAVR (both 30-day and 1-year data), as well as important subsets of patients such as those with end-stage renal disease and chronic obstructive airway disease. The TVT registry also includes testing of risk prediction models, incorporation of new devices, FDA expansion of the instructions for use (which expanded coverage to include alternative access approaches), and most recently, a new structural heart disease target—mitral regurgitation with the MitraClip device (Abbott Vascular).

Future plans include an expanded role for registries such as TVT for both premarket approval studies as well as postmarket surveillance. Such registries will be an essential component of comparative effectiveness research that will allow for the optimization of patient selection criteria and the optimization of patient care outcomes. They will also facilitate the development of new technologies and shorten regulatory approval processes, as well as serve as a vehicle for public reporting of hospital performance. Such analyses will facilitate identification and the promulgation of best practices.

FUTURE DIRECTIONS AND CHALLENGES

Although the TVT registry has functioned extremely well to date, it is still confronted by challenges. Sustainability is an important issue. The registry has been funded from several sources, but the most predominant source has been hospital fees. As mentioned, TVT was based on the CMS-NCD, which mandated participation in such a registry for procedural reimbursement. Industry grants and funding from the professional societies have also been extremely important. An important future consideration is that NCDs often have a finite time frame. At the present time, based on continuous evidence development with new scientific data on patient selection criteria, outcomes, and particularly quality of life, it is hoped that the CMS-NCD will continue. Interactions with industry are central for other sources of funding. If the TVT registry can continue to receive grants for the development and management of postapproval studies, or eventually design premarket studies that will make the device approval process more efficient, then with value-added accomplishments, industry funding will be more likely. The potential role of the National Institutes of Health in funding comparative effectiveness grants on data from this registry is another possibility. Finally, changes in health policy with implementation of outcome-based payment strategies will depend on data such as that able to be gathered from registries such as TVT. An essential component of sustainability is continued development and documentation of the value of the TVT registry to each stakeholder. ■

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