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VIEWPOINT

Insights From the Early Experience of the Society of Thoracic Surgeons/ American College of Cardiology Transcatheter Valve Therapy Registry

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ABSTRACT

The current system for postmarket surveillance of medical devices in the United States is limited. To help change this paradigm for transcatheter valve therapies (TVTs), starting with transcatheter aortic valve replacement, the Society of Thoracic Surgeons and the American College of Cardiology partnered to form the TVT Registry program in close collaboration with the U.S. Food and Drug Administration and the Center for Medicare and Medicaid Services. The goal of the TVT Registry is to measure and improve quality of care and patient outcomes in clinical practice and to have a pivotal role in the scientific evidence and surveillance for medical devices. Challenges were faced in the early experience of the registry included developing multistakeholder partnerships, data collection requirements, and the use of the registry for pre- and post-market device evaluations. In addressing these challenges, the TVT Registry demonstrates that it is feasible for professional societies to assume a pivotal role in pre- and/or post-market studies, leveraging a clinical registry infrastructure. Sharing the TVT Registry experience may help other professional societies and stakeholders better anticipate and plan for these challenges. (J Am Coll Cardiol Intv 2015;8:377–81) © 2015 by the American College of Cardiology Foundation.

To help address the limitations of medical device surveillance in the United States and to assess quality of care and patient outcomes in current clinical practice, the Society of Thoracic Surgeons (STS) and American College of Cardiology (ACC) partnered to form the Transcatheter Valve Therapy (TVT) Registry (1). Initially focused on transcatheter aortic valve replacement (TAVR), the program was developed in collaboration with the U.S. Food and Drug Administration (FDA) and the Centers for Medicare and Medicaid Services (CMS). The TVT Registry was specifically designed to both measure care delivery and patient outcomes and to support medical device surveillance and research, including the needs of FDA and CMS.

Both the STS and the ACC have long-standing experience with national clinical registry programs, namely, the STS National Database and the National Cardiovascular Data Registry (NCDR) (2,3). The TVT Registry has the features of the other STS and NCDR

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ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

CMS = Centers for Medicare and Medicaid Services

FDA = U.S. Food and Drug Administration

IDE = Investigational Device Exemption

NCDR = National Cardiovascular Data Registry

PAS = post-approval study

STS = Society of Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

TVT = transcatheter valve therapy

programs, yet was specifically designed to enable the professional societies to work with other stakeholders to enhance the evaluation, approval, and post-market surveillance of new device strategies in the United States. As with any new program, a number of challenges have been faced since the TVT Registry's inception.

The goal of this paper is to briefly summarize the early experience of the TVT Registry, focusing on key issues including multistakeholder partnerships, data collection requirements, and the role of the clinical registry program with regard to both pre- and post-market research and device surveillance. It is hoped that the insights gained from the early experience of the TVT registry may help inform other professional societies and stakeholders interested in developing similar programs. In addition, this paper serves as a prelude to regular reports of TVT Registry data to be published in the *Journal of the American College of Cardiology* and *JACC: Cardiovascular Interventions*.

TIMELINE AND SELECTED ACCOMPLISHMENTS

The design, core functions, and overall goals of the TVT Registry have been previously described (1). The program has had a number of key events and accomplishments to date, which are summarized in **Table 1** (1,4-7). The TVT Registry plans to publish regular reports summarizing key data and trends from the program in future issues of the *Journal of the American College of Cardiology*. As a prelude to these regular data reports, this paper relates insights from the early experience of the TVT Registry to help other professional societies or organizations interested in developing similar programs. The TVT Registry has faced significant challenges in attempting to have a pivotal role in pre- and post-market device evaluations and surveillance. The remainder of this paper is therefore focused on key aspects of these challenges, including multistakeholder partnerships, data requirements and sustained participation, post-market data and device surveillance, post-approval studies, and Investigational Device Exemption (IDE) and premarket studies.

MULTISTAKEHOLDER PARTNERSHIPS

One key action for the TVT Registry was the inclusion of representatives from the FDA and CMS on the Steering Committee. Furthermore, it was quickly realized that it is critical to work jointly with both pre- and post-market personnel at the FDA to effectively address the medical device life cycle. Moreover, the TVT Registry has a Stakeholder Advisory Committee with representation from industry, consumer and patient organizations, hospitals and health systems, professional societies, the National Institutes of Health, the FDA, and the CMS. Although it is challenging to balance the perspectives and input from various stakeholders, we believe that the commitment to multistakeholder partnerships in the governance of the registry program is a critical component for long-term success. Stakeholders must be able to see that their input helps shape the strategic vision and goals of the registry program, such as the execution of collaborative projects including post-approval studies, device surveillance, publications with TVT Registry data, and plans for public reporting. **Figure 1** depicts the various stakeholders and primary programmatic output goals of the TVT Registry.

DATA REQUIREMENTS AND SUSTAINED PARTICIPATION

The scope of data collection is a key challenge for the TVT Registry. The initial dataset resulted from collaboration between the professional societies, the FDA, and the CMS, including harmonization with the Valve Academic Research Consortium data elements. The dataset needed to meet the requirements of multiple stakeholders, including assessment of patient characteristics, procedure indications and results, complications, and longitudinal outcomes. The desire to use the registry for pre- and post-market studies was also considered.

It is difficult to balance data collection sufficient to support the various goals of the TVT Registry stakeholders yet not impose undue burden on sites. Minimizing unnecessary or redundant data collection is a top priority; the TVT Registry has initiated a dedicated effort to reduce the data elements collected. In the future, the increased availability of electronic data (e.g., from electronic health records) may support data capture for programs like the TVT Registry and further reduce, or in some cases obviate, the need for data collection.

In addition, there must be sustained site participation to fulfill the goals of the TVT Registry as a clinical quality program, device surveillance network, and infrastructure for pre- and post-market studies. The TVT Registry satisfies the requirements of the CMS national coverage determination, which directly supports site participation. Anticipating that the

coverage with evidence requirement may be removed at some point, there will need to be adequate value delivered for sites to continue participation. This may include the value of quality of care measurement and national benchmarking reports, meeting payer and/or state quality reporting needs, the use of the registry data for documenting performance improvement for sites and clinicians, the desire for ongoing participation in device surveillance efforts in collaboration with the FDA, and the ability for sites to participate in pre- and/or post-market studies that are conducted using the TVT Registry infrastructure.

POST-MARKET DATA AND DEVICE SURVEILLANCE

Over the past decade, registry programs including the NCDR have conducted individual studies on device safety, and the FDA has collaborated with investigators for post-market research studies. The TVT Registry extends this competency by being designed to serve as a device surveillance system to inform regulators, clinicians, sponsors, and the public about device performance. Although the vision of the registry as a device surveillance network is clear, a number of challenges must be met. For example, the system must be responsive to the needs and timelines of regulatory and industry partners. Currently, the TVT Registry, like most clinical registry programs, receives data submitted by trained site personnel. This process enhances data completeness and accuracy but does not constitute real-time surveillance. The TVT Registry will need to enhance device surveillance capabilities to optimally support the FDA's strategic plan for device surveillance (8).

POST-APPROVAL STUDIES

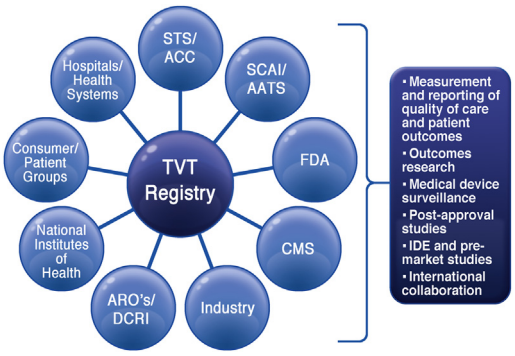
It is more challenging to operationalize clinical registries to conduct the formal post-approval studies (PASs) that are mandated by the FDA as a condition of device approval and have been traditionally executed by industry. An explicit goal of the TVT Registry was to use the registry infrastructure to conduct PASs. The hope is to demonstrate efficiencies by using existing registry program sites, contracts, and data collection, augmented by any additional requirements for a specific PAS. Moreover, the TVT Registry data could serve as a de facto PAS by virtue of the capture of virtually all patients receiving a device. In the first year of the TVT Registry, a PAS for the Edwards Sapien valve was successfully designed and approved. Whether clinical registry programs like TVT may be used for a given PAS will be determined by the FDA on a case-by-case basis. The burden is on the TVT Registry to be designed to provide the data that the FDA requires and to ensure that the benefits

TABLE 1 Timeline and Selected Events/Accomplishments for the TVT Registry

Year (Month Where Applicable)	Event/Accomplishment
2011 (July)	TVT Registry proposed at the FDA Advisory Panel for Edwards Sapien Valve.
2011 (July–September)	Development of standard data elements and definitions for the TVT Registry in collaboration with the FDA and CMS and consistent with the Valve Academic Research Consortium, STS, and NCDR program data elements (1).
2011 (December)	Launch of the TVT Registry (Version 1).
2011–2012	Professional society collaboration on the development of standards for patient selection and procedural performance to help support anticipated CMS National Coverage Determination, which was released in May 2012.
2011 to present	Data are submitted by trained data managers using a web application with data quality checks, following the data quality programs established by STS and NCDR (4). The data quality program for the STS and NCDR registry programs include training of site data managers, technical support for data submission (e.g., range checks and data quality reporting), data analytics (e.g., missingness and validity of data entries), and auditing.
2011 to present	Relationship with the Duke Clinical Research Institute to serve as an analytic center for the TVT Registry, including data analytics, reporting, and event adjudication.
2011 to present	Convening of 4 national committees: Steering, Research and Publications, Stakeholder Advisory, and Data Monitoring. These committees follow the established governance of the STS and NCDR registry programs and were developed with input from the FDA, the CMS, and 4 professional societies (STS, ACC, American Association for Thoracic Surgery, and Society for Cardiovascular Angiography and Interventions).
2012–2013	Development of PAS and IDE protocols.
2012–2014	Initial presentations and publication of data, including in-hospital outcomes for the initial 7,710 patients in the United States (5). Multiple abstracts were submitted to national meetings in the first 2 years of the registry, including one selected for the Richard E. Clark Award at the 2014 STS Annual Meeting, and another presented as a late-breaking clinical trial at the 2014 ACC Scientific Sessions.
2012–2014	In the first year of the TVT Registry (i.e., through 2012), 156 U.S. centers joined, and 2,400 commercial TAVR records were entered in the registry. As of June 2014, the TVT Registry has 319 participating centers, and there are more than 18,500 TAVR cases in the registry.
2013 (August)	Demonstration of rapid data analytics to help inform a policy recommendation with regard to TAVR alternative access, at the behest of the FDA (6).
2013	Initiation of working groups for TAVR risk models and a mitral procedure module; first TVT risk model (for in-hospital risk-adjusted mortality) completed May 2014, for implementation in the hospital quality benchmark reports.
2013	Joining the International Consortium of Cardiovascular Device Registries to begin global harmonization of medical device registries (7).
2014	Eleven research proposal applications approved for manuscript development, funded by the TVT Registry.
2014 (June)	TVT Registry version 2, including reduction of TAVR data elements and modification of some data elements on the basis of site feedback, and addition of the mitral module of the TVT Registry.

ACC = American College of Cardiology; CMS = Centers for Medicare and Medicaid Services; FDA = U.S. Food and Drug Administration; IDE = Investigational Device Exemption; NCDR = National Cardiovascular Data Registry; PAS = post-approval study; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement; TVT = transcatheter valve therapy.

FIGURE 1 Transcatheter Valve Therapy Registry Stakeholders and Primary Program Output Goals



ACC = American College of Cardiology; ARO = Academic Research Organization; AATS = American Association for Thoracic Surgery; CMS = Centers for Medicare and Medicaid Services; DCRI = Duke Clinical Research Institute; FDA = Food and Drug Administration; IDE = Investigational Device Exemption; STS = Society of Thoracic Surgeons; SCAI = Society for Cardiovascular Angiography and Interventions.

of conducting PASs using a clinical registry infrastructure are realized.

IDE AND PRE-MARKET STUDIES

Another goal of the TVT Registry is to evaluate all use of devices in clinical practice, which may extend beyond currently approved indications. The CMS National Coverage Determination distinguishes labeled from unlabeled uses and requires that unlabeled uses be furnished under coverage with evidence development as a condition of Medicare coverage. The TVT Registry provides an opportunity to evaluate the effectiveness of TAVR (and other new technology in the future) in broader indications under an IDE, in collaboration with the FDA and industry. However, the complex regulatory requirements involved in IDE studies are a significant challenge.

Although the FDA has the authority to waive certain IDE requirements, waivers are granted under rare circumstances, and this process requires legal consultation and extensive documentation to justify them.

An additional aspiration of the TVT Registry is to support pre-market studies. The TVT Registry could serve as a hospital network from which to recruit sites, and existing TVT Registry data could be used to inform trial planning (e.g., targeting sites that do a certain volume of specific procedures). The routinely collected data for the TVT Registry could serve as a core dataset for a given clinical trial, with additional data elements collected for a specific study as needed. Ongoing TVT Registry data collection after study completion could be used for post-trial surveillance. It is also recognized that clinical trials may involve both U.S. and international sites. Hence, with support of the FDA, the TVT Registry has joined the International Consortium of Cardiovascular Device Registries (7). Goals of this collaboration is harmonization of data elements and pursuit of collaborative research. Therefore, it holds potential for the use of the TVT Registry and collaborating international programs with regard to the conduct of clinical trials, although this potential has not been realized to date.

In addition, the device industry has expressed reasonable concerns about the ability of clinical registry programs to meet pre-market study requirements for data integrity, monitoring, and timeliness. However, the FDA is supportive of the concept of potential efficiencies offered by clinical registry programs like the TVT Registry. In sum, the role of clinical registry programs for IDE and pre-market studies is appealing in concept and will be pursued, but remains uncertain.

CONCLUSIONS

Extending the capabilities of traditional clinical registry programs, the TVT Registry was designed with multistakeholder collaboration to support device safety and effectiveness monitoring in clinical practice. An a priori goal was to try to bridge the pre- to post-market device life cycle and be a "living platform" for safety, efficacy, and effectiveness data that can accommodate new technologies/devices. The TVT Registry helps professional societies be more involved in aspects of pre- and post-market studies. Despite the challenges of launching a national registry program with these goals, the early years of the TVT Registry have included successful national implementation of the program, data reporting to stakeholders on the initial U.S. TAVR experience, and approval for both a PAS and an IDE study. It is hoped that the early TVT Registry experience will be helpful to other professional societies and stakeholders in developing similar programs.

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