Year 1 of the TVT Registry

What have we learned, and where do we go from here?

BY ERIC L. SARIN, MD; MICHAEL J. MACK, MD; HANNA A. JENSEN, MD, PHD; AND VINOD H. THOURANI, MD

The Transcatheter Valve Therapy (TVT) registry represents a significant achievement in multiinstitutional and multiorganizational collaboration. Fostered by the awareness of an acute need for enhanced postmarket surveillance of cardiovascular devices in the United States,[1-3] it was born from the proactive measures of our two major professional organizations, the Society of Thoracic Surgeons (STS) and the American College of Cardiology (ACC), along with the US Food and Drug Administration (FDA), the Centers for Medicare and Medicaid Services (CMS), and the Duke Clinical Research Institute. Furthermore, there was coordination and intimate involvement with multiple stakeholders, including those from the medical device industry, hospitals, and patient and consumer interest groups.

BACKGROUND

Following the completion of the first PARTNER trial,[4,5] the leaders of these organizations were contacted by the FDA regarding the impending commercial approval of the first transcatheter aortic valve replacement (TAVR) device in the United States, which would represent a true technology disruption in the treatment of aortic stenosis. With the cooperation of the FDA and CMS, society leaders proposed a prospective national registry to capture real-world results for all of the anticipated new devices in the postapproval setting. In addition to providing a much-needed platform for ongoing postmarket surveillance, this database would also become an invaluable resource for quality assurance and serve as a stimulus for improvement initiatives. The first postapproval study using the TVT registry was initiated in collaboration with Edwards Lifesciences, the industry sponsor of the first FDA-approved TAVR device in the United States.

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REGISTRY DESIGN

The successful organization and coordination of the registry's many moving parts represents an ambitious effort. It necessitated linkage of the STS and ACC/National Cardiovascular Data Registry clinical databases with risk adjustment to CMS administrative claims data to assess longitudinal outcomes.[6] To maximize data capture, CMS linked participation to reimbursement through a national coverage determination, which requires institutional involvement and individual patient enrollment in the TVT registry to receive Medicare payment. The registry data elements have been carefully defined to harmonize with definitions from the STS, ACC, and Valve Academic Research Consortium (VARC and VARC 2).

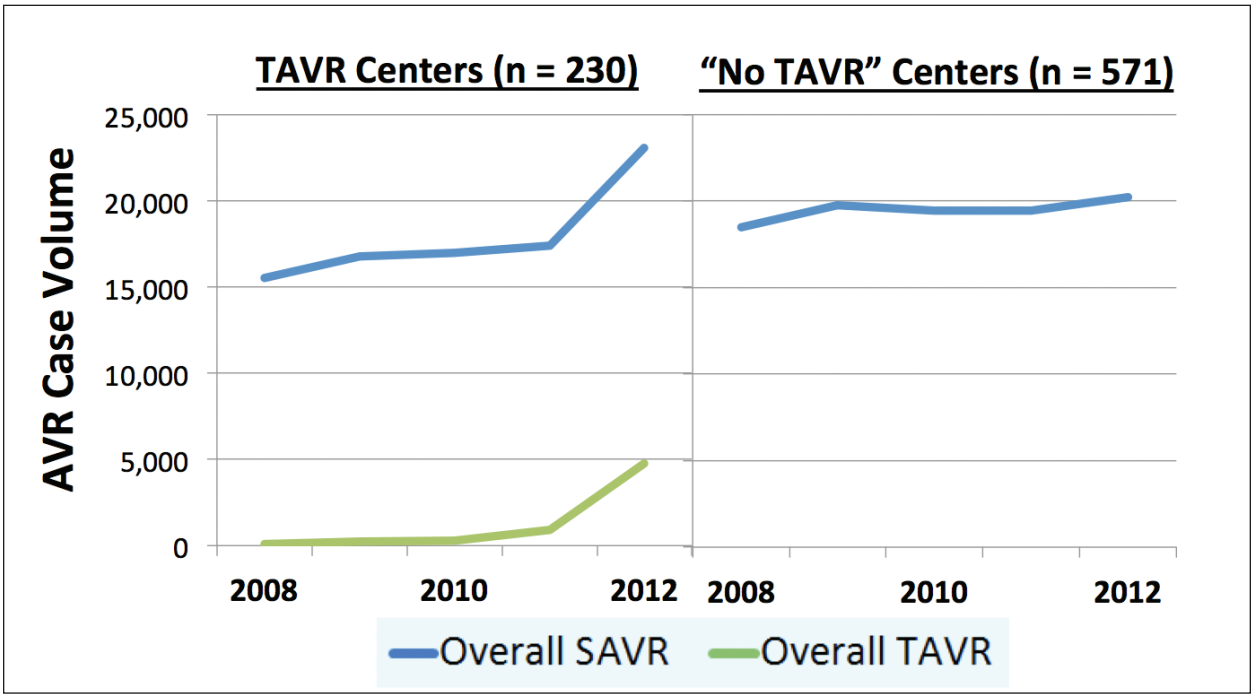


Figure 1. Aortic valve replacement volume in hospitals with or without TAVR centers. AVR = aortic valve replacement; SAVR = surgical aortic valve replacement.

As of June 2014, the TVT registry has collected over 17,000 individual patient records from more than 300 centers in the United States. This effort to develop, launch, and maintain this registry has recently started to bear fruit by providing multiple presentations during the last several months, which have allowed a first look at the collected data.

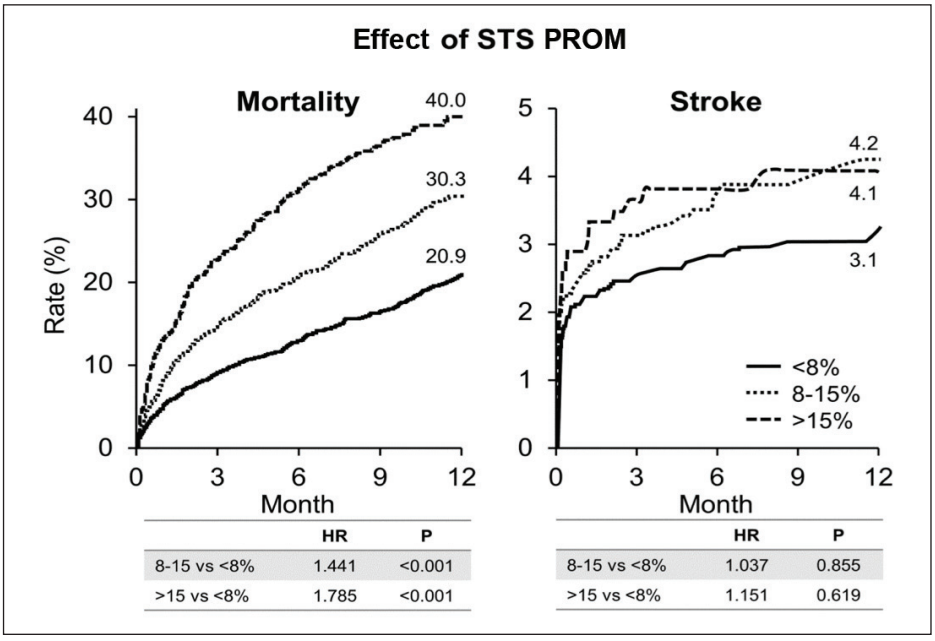
FINDINGS FROM INITIAL TVT REGISTRY ANALYSIS: NOVEMBER 2011 TO MAY 2013

The first outcomes published from the TVT registry by Mack and colleagues[7] included data collected from 224 participating hospitals for 7,710 procedures from November 2011 to May 2013 using the only commercially approved device during this period, the Sapien valve (Edwards Lifesciences). Primary outcomes included all-cause in-hospital mortality and stroke, and secondary analyses included procedural complications and outcomes assessed by clinical indication and access site. The median patient age for all patients was 84 years. The median calculated STS predicted risk of mortality (PROM) was 7%, with considerable variation from site to site (1.2%–17.4%). This is quite interesting, given that the STS PROM scores were considerably lower than in the PARTNER high-risk surgical trial by Smith and colleagues.[5] It is possible that risk score creep has already occurred, even with the rational dispersion of this technology. The transfemoral approach was most commonly used, accounting for 64% of all cases, whereas the transapical approach led among the alternative access cases, accounting for 29% of the total procedures performed. Device implantation success (defined as successful vascular access, deployment of a single device in the proper anatomic position, appropriate valve function excluding aortic insufficiency < 2+ [ie, moderate], and successful retrieval of the delivery system) was achieved in 92% of the patients. Conversion to open surgery, although rare (1%), was associated with exceptionally high mortality (49%). The majority of TAVR procedures (57%) were performed in a hybrid operating room. Other patients underwent TAVR in a hybrid catheterization laboratory (28%), and a minority of procedures were performed in a catheterization lab (14%).

The in-hospital mortality rate was a very respectable 5.5%. Major in-hospital complications included stroke (2%), major vascular injury (6.4%), acute renal insufficiency (5.5%), and major bleeding (3.5%). The need for a new pacemaker or implantable cardiometer-defibrillator occurred in 6.6% of patients. The median stay in the intensive care unit was 46 hours, and the median hospital stay was 6 days. The 30-day follow-up data were derived from 3,133 patients treated at 114 different hospitals. At 30 days, mortality was 7.6%, with

52% of these deaths attributed to a noncardiovascular cause. Among those patients with available follow-up, the incidence of New York Heart Association class III or IV heart failure during the follow-up period was 12%.

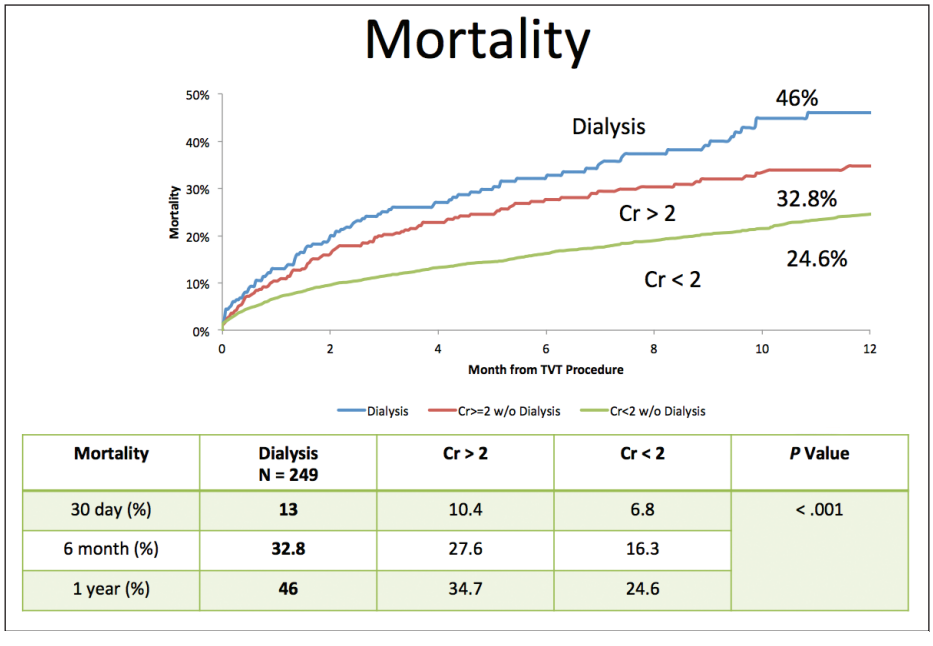
In general, the data from the registry closely paralleled the outcomes seen in the randomized clinical trials that led to commercial approval.[4,5] These early results are undoubtedly due in large part to the heretofore-unseen level of effort put forth by industry and our professional societies to prepare, train, and then guide clinicians through the postapproval launch of this technology. Furthermore, these real-world United States registry results compared favorably with multiple TAVR registries in Europe[8-11] and are indicative of the generalizability of randomized trial results when introduced by rational dispersion.



	HR	P
8-15 vs <8%	1.441	<0.001
>15 vs <8%	1.785	<0.001

	HR	P
8-15 vs <8%	1.037	0.855
>15 vs <8%	1.151	0.619

Figure 2. Effect of STS PROM on 1-year mortality and stroke.



Mortality	Dialysis N = 249	Cr > 2	Cr < 2	*P* Value
30 day (%)	**13**	10.4	6.8	< .001
6 month (%)	**32.8**	27.6	16.3	
1 year (%)	**46**	34.7	24.6	

Figure 3. One-year mortality in patients with and without ESRD following TAVR. Cr = creatinine.

DATA PRESENTED AT RECENT MEETINGS

The remaining data from the TVT registry have been presented in professional society meetings of the STS and ACC. At the 50th annual meeting of the STS in January 2014, Brennan and colleagues assessed all aortic valve replacements (215,767 surgical aortic valve replacements and 11,436 commercial TAVRs) performed in the United States from 2008 to 2013.[12] The authors noted a gradual increase in the annual aortic valve replacement volume across the country. Although this growth was larger at TAVR centers (evidencing the "halo effect"), non-TAVR centers have experienced growth as well (Figure 1). There has also been a steady decrease in the STS PROM observed-to-expected ratios for in-hospital mortality related to surgical aortic valve replacement; this effect has been the most dramatic at centers with TAVR programs. Notably, there has been a slight increase in the overall trend in the STS PROM observed-to-expected mortality ratio for TAVR patients since the commercial launch

for the Sapien device (0.36 from the second quarter of 2010–2011 vs 0.61 from the third quarter of 2011 to the second quarter of 2013).

At the recent ACC annual meeting in March 2014, Holmes and colleagues presented the summary of 1-year data from the TVT registry.[13] These data included 5,980 patients, of which 97% were successfully linked to CMS claims data. At 1 year, the overall all-cause mortality was 26.2%, which remains comparable to previous studies. The overall stroke incidence was 3.6%. Interesting patient sex differences among the primary outcomes were identified. Men had a higher overall 1-year mortality rate (29.2% vs 23%), whereas women had a higher incidence of stroke (4.3% vs 2.9%) at 1 year. A highly impactful observation is the increased 1-year mortality in patients with higher STS PROM. In those with an STS PROM > 15, the mortality was 40% compared to 20.9% in those with an STS PROM < 8% (Figure 2). These early differences should prompt further investigation into targeted strategies to mitigate potential risks responsible for these outcomes.

Importantly, a majority of patients (55.8%) did not require repeat hospital admission in the 6 months immediately following the procedure. An additional 26% only required one readmission. This is dramatic evidence of effective therapy considering that most of the patients (83.4%) had New York Heart Association class III/IV symptoms prior to therapy.

Of particular interest were the outcomes among patients with end-stage renal disease (ESRD), as presented by Mack and colleagues at the 2014 ACC annual meeting.[14] These patients have been excluded from all prior randomized trials and represent an extremely challenging patient population. Mack et al compared 528 patients with a preoperative requirement of renal replacement therapy to 11,749 TAVR patients without preoperative ESRD. Although patients with ESRD tended to be younger than the nondialysis patients, they had significantly higher STS PROM scores (14.43% vs 6.76%; $P < .0001$). In-hospital mortality and VARC-defined major bleeding were higher for the dialysis patients (8.9% vs 5.1%; $P < .0001$; and 6.4% vs 3.2%; $P < .001$; respectively). They noted an all-cause 1-year mortality of 46% in the dialysis patients compared to 24.6% mortality in those with a preoperative creatinine of < 2 mg/dL (Figure 3). ESRD was the second highest predictor of mortality after TAVR, behind STS PROM > 15%.

CONCLUSIONS

The success of the TVT registry is contingent on an army of qualified and cooperative multidisciplinary teams. This ambitious undertaking will provide a new frontier of postmarket data collection, which should allow for a more rapid, yet safe, dissemination of new transcatheter technology in the United States. ■

Eric L. Sarin, MD, is an Associate Professor of Surgery at Emory Structural Heart and Valve Center, Division of Cardiothoracic Surgery, Joseph B. Whitehead Department of Surgery, Emory University School of Medicine in Atlanta, Georgia. He has stated that he has no related financial interests to disclose.

Michael J. Mack, MD, is Professor of Surgery at Heart Hospital Baylor Plano, Baylor Healthcare System in Plano, Texas. He has disclosed that he is on the TVT steering committee.

Hanna A. Jensen MD, PhD, is a Clinical Research Fellow at Emory Structural Heart and Valve Center, Division of Cardiothoracic Surgery, Joseph B. Whitehead Department of Surgery, Emory University School of Medicine in Atlanta, Georgia. She has stated that she has no related financial interests to disclose.

Vinod H. Thourani, MD, is Professor of Surgery at Emory Structural Heart and Valve Center, Division of Cardiothoracic Surgery, Joseph B. Whitehead Department of Surgery, Emory University School of Medicine in Atlanta, Georgia. He has disclosed that he is on the TVT steering and publications committees, has participated in research and the advisory board for Edwards Lifesciences and St. Jude Medical, and has participated in research for Sorin Medical and Medtronic. Prof. Thourani may be reached at (404) 686-2513; vthoura@emory.edu.

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