

Trends in United States TAVR Practice

An update on where TAVR is going as the technology matures in the United States.

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Transcatheter aortic valve replacement (TAVR) has changed immensely over the last 6 years since the US Food and Drug Administration (FDA) approval of TAVR for high-risk and inoperable patients with symptomatic aortic stenosis in November 2011. Since then, we have seen the introduction of both balloon-expandable and self-expanding TAVR systems, lower-profile delivery systems with resultant marked decreases in sheath size requirements that have changed access routes for performing of TAVR, as well as the expanded indication for TAVR to include intermediate-risk patients.

The most striking trend over the past few years has been the very rapid and broad dissemination of TAVR, with the number of sites performing TAVR procedures markedly increasing, bringing up questions about volume-outcome relationships and the learning curve associated with TAVR. The national coverage decision determined by the Centers for Medicare & Medicaid Services mandate for a national registry has allowed for a more rapid assessment of temporal trends in TAVR in United States practice.

Although the medical devices used in TAVR practice in the United States have been fairly stable over the past several years, 2017 had two events affecting commercial TAVR. The first was the FDA approval of the CoreValve Evolut Pro self-expanding valve (Medtronic) in March 2017, and the second was the expanded indication for the Sapien 3 valve (Edwards Lifesciences) by the FDA to include high-risk patients with a failed surgical bioprosthetic aortic or mitral valve for valve-in-valve treatment. Given the highly effective medical devices in use in the United

States, current efforts are focusing on improving clinical outcomes and decreasing costs with a “minimalist” approach using conscious sedation and percutaneous femoral access in the majority of patients, evaluating the volume-outcome relationship with TAVR, and introducing cerebral embolic protection to attempt to reduce periprocedural stroke risk.

TEMPORAL TRENDS IN VOLUMES AND OUTCOMES

In the most recent Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry annual report, trends in TAVR practice were evaluated from January 2012 through December of 2015.¹ The median

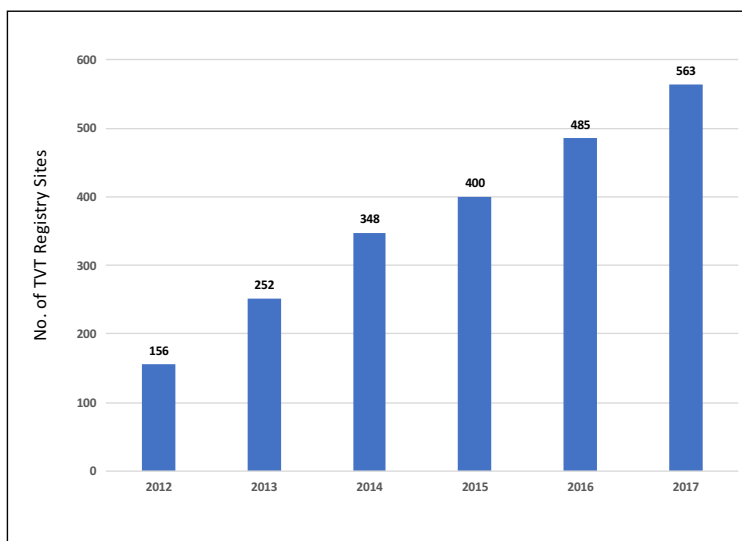


Figure 1. Sites enrolled in the STS/ACC TVT Registry. There has been a continued annual increase since the start of the registry. Modified from Grover FL, Vemulapalli S, Carroll JD, et al. 2016 annual report of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *J Am Coll Cardiol.* 2017;69:1215–1230.

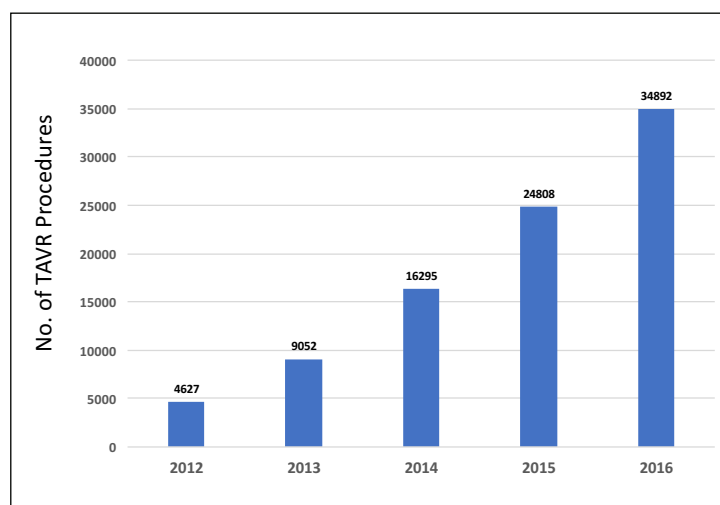


Figure 2. TAVR procedural volume over time based on data from the TVT Registry database. There has been a continued annual increase since the start of the TVT Registry. Modified from Grover FL, Vemulapalli S, Carroll JD, et al. 2016 annual report of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *J Am Coll Cardiol.* 2017;69:1215–1230.

age of patients who underwent TAVR was 83 years and 48% of patients were women at the end of 2015. The median STS risk score was 6%. In-hospital mortality decreased from 5.7% to 2.9%, and 30-day mortality decreased from 7.5% to 4.6%. Balloon-expandable valves were utilized in 66.4% of cases.

Over time, vascular and bleeding complications have significantly decreased, which is undoubtedly related to the decreased sheath size with the newer-generation TAVR systems. By the end of 2015, femoral access was used for 86.6% of TAVR cases, with transapical access accounting for only 6.1% of cases and alternate access (eg, direct aortic, subclavian/axillary) accounting for 6.8%. Major and life-threatening bleeding decreased from 6.9% to 3.9% between 2012 and 2015. With the introduction of the newest-generation TAVR valves, the need for new pacemaker implantation at 30 days has increased from 8.8% to 12%.

Given the technologic advancements in TAVR, it is no surprise that there has been a marked increase in the number and types of sites participating in the TVT Registry (Figure 1) and the number of patients undergo-

ing TAVR in the United States (Figure 2). The staggering growth in TAVR and its impact on temporal trends for isolated surgical aortic valve replacement (SAVR) procedures performed in the United States has recently been evaluated.² In this study, the number of Medicare beneficiaries undergoing isolated aortic valve procedures increased from 47.5 to 88.9 per 100,000 Medicare beneficiaries between 2009 and 2015, driven mostly by increased TAVR volume. During this time, the rate of TAVR use has markedly increased and surpassed SAVR with a tissue valve (Figure 3). Importantly, in-hospital mortality has significantly decreased across all valve types over time, but more so with Medicare beneficiaries undergoing TAVR (Figure 4).

MINIMALIST APPROACH

Based on a single-center experience, it has been suggested that moving away from general anesthesia toward conscious sedation may afford better outcomes and reduce complications and length of stay. In 2012, almost all TAVR procedures were performed with general anesthesia in the United States, including those using transthoracic echocardiography (TTE) for guidance. The “minimalist approach” was first evaluated in a single-center study of 142 patients undergoing TAVR and included local anesthesia, minimal conscious sedation, fully percutaneous access site entry and closure, and TTE guidance.³ There were no significant differences in in-hospital or 30-day mortality, but there

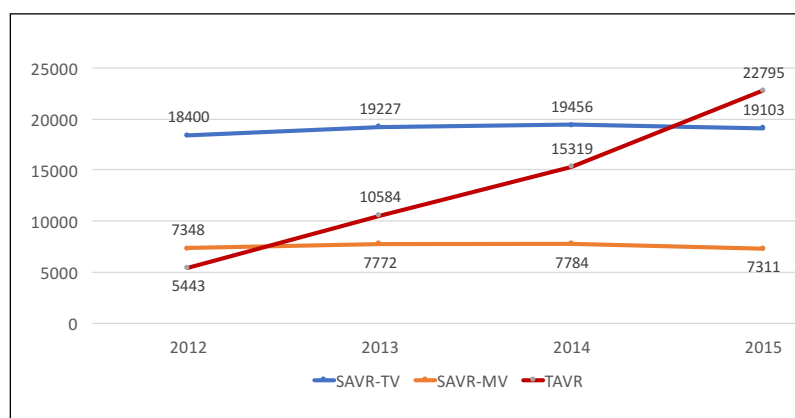


Figure 3. Temporal trends for aortic valve procedures for AVR among Medicare beneficiaries by fiscal year. SAVR-MV, SAVR with a mechanical valve; SAVR-TV, SAVR with a tissue valve. Adapted from Culler SD, Cohen DJ, Brown PP, et al. Trends in aortic valve replacement procedures between 2009 and 2015: has transcatheter aortic valve replacement made a difference? *Ann Thorac Surg.* In press.

was a marked reduction of 2 days in length of stay after TAVR and a reduction in costs of approximately \$10,000 per case using the minimalist approach compared with the standard approach under general anesthesia. This study was limited by the two cohorts (ie, general anesthesia and conscious sedation) undergoing treatment at two different time points with enhanced technique and technology favoring the conscious sedation group.

Hyman and colleagues recently reported on the temporal changes in anesthetic approach and outcomes in patients undergoing elective percutaneous transfemoral TAVR.⁴ In an analysis of 10,997 TAVR cases performed between April 2014 and June 2015, there was a marked increase in the use of conscious sedation compared with general anesthesia. The overall rate of conscious sedation use was 11% in 2014 and increased to 20% by the end of the second quarter of 2015. The proportion of sites that utilized conscious sedation increased from 10% to 28% over this short 15-month period. Overall, the conversion rate to general anesthesia was very low during this period at 5.9%. Using propensity analyses to adequately adjust for baseline demographic and clinical variables, TAVR with conscious sedation compared with general anesthesia was associated with a slightly lower procedural success rate (97% vs 98.6%; $P < .001$).

Imaging guidance for TAVR changed from transesophageal echocardiography to TTE at most sites using conscious sedation. Importantly, use of conscious sedation compared with general anesthesia was associated with a lower rate of adjusted in-hospital mortality (1.5% vs 2.4%; $P = .01$) and lower 30-day mortality (2.3% vs 4.0%; $P < .001$). The combined endpoint of 30-day mortality/stroke was 6.4% versus 4.8% ($P < .001$), respectively. In addition, conscious sedation was associated with reduced intensive care unit length of stay and shorter length of hospitalization by 0.5 days. Findings from this observational registry appear to demonstrate that TAVR is feasible with conscious sedation without sacrificing procedural success rates or evidence of adverse outcomes.

VOLUME-OUTCOME RELATIONSHIPS

With the marked explosion in the number of TAVR centers, it is important to understand whether a

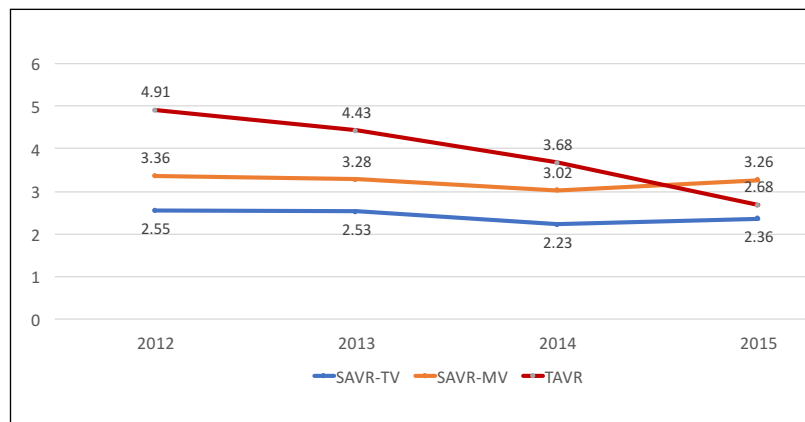


Figure 4. In-hospital mortality rates for selected types of aortic valve procedures by year. SAVR-MV, SAVR with a mechanical valve; SAVR-TV, SAVR with a tissue valve. Adapted from Culler SD, Cohen DJ, Brown PP, et al. Trends in aortic valve replacement procedures between 2009 and 2015: has transcatheter aortic valve replacement made a difference? *Ann Thorac Surg*. In press.

volume-outcome relationship exists for a new technology such as TAVR and whether this has an impact on outcomes at centers starting with TAVR that may have lower annual volumes going forward. To better evaluate this, Carroll and colleagues evaluated consecutive case data from 2012 to 2015 using the TVT Registry.⁵ They found a significant linear association between increased TAVR volume and in-hospital mortality before and after adjusting for baseline patient and procedural characteristics. Similar statistically significant and clinically important associations were found between TAVR volume and outcomes for both vascular and bleeding complications, but there was no association found for stroke. These associations were most pronounced during the first 100 TAVR cases, but beyond this number of cases, procedural risk continued to decline at a more gradual rate.

Using modeling based on the data, estimated in-hospital mortality of a patient with average characteristics of the overall study population was projected to decrease from 3.5% for the first case to 2.15% for 400th case. Whether this volume-outcome relationship persists with improvements in technology over time is unclear, but this needs to be considered during this rapid dissemination phase of TAVR to many hospitals that have much less experienced heart teams with potential for lower annual TAVR volumes. It remains unclear what the optimal number of TAVR sites should be (and their geographic distribution in relation to other sites) in the United States to balance access and quality of TAVR outcomes, and this is an area of controversy that requires significantly more study.

FOCUS ON STROKE PREVENTION

As noted in the most recent annual report and the volume-outcome analyses, site-reported stroke rates have remained around 2% in the TVT Registry, unchanged from the start of TAVR. This is an underestimate of stroke associated with TAVR, because it does not routinely involve formal neurologic adjudication. Unfortunately, the stroke rate does not appear to have been impacted by newer-generation technologies, and there is no signal that a learning curve can impact the rate of stroke.⁵

In June 2017, the FDA approved the Sentinel cerebral protection system (Claret Medical, Inc.), a percutaneously inserted filter system (via the right radial or brachial artery) designed to capture and remove debris dislodged during endovascular procedures. The Sentinel device was evaluated in the prospective, multicenter, randomized SENTINEL study of 363 patients undergoing TAVR who were deemed to be high surgical risk. The rate of major adverse cardiac and cerebrovascular events (MACCEs) in the test and safety arms was 7.3%. The MACCE rate in the control arm (9.9%) was not statistically different from that of the test and safety arms ($P = .405$), although the numerical difference was driven by stroke. The 30-day stroke rates were not statistically significantly different in the device arms versus the control arm (5.6% vs 9.1%; $P = .25$), but there were fewer events in the device arms,⁶ particularly in the < 72-hour postprocedure period when the stroke rate was 63% lower with the Sentinel device versus the control (3% vs 8.2%; $P = .05$).⁷

Despite the lack of a statistically significant reduction in the number or size of strokes in the device versus control arms, debris was documented in 99% of cases of filter use, and the FDA approved the Sentinel device based on its safety profile. An independent, real-world, prospective, propensity score–matched study of 802 consecutive all-comer TAVR patients (280 consecutive protected by Sentinel) recently showed a significant 70% reduction in stroke at 7 days ($P = .03$) and a 70% reduction in combined stroke or mortality ($P = .01$), with one stroke or death avoided for every 21 TAVR patients treated with the Sentinel device.⁸ The Sentinel cerebral protection system is now captured in the TVT Registry for TAVR patients treated after January 1, 2018 to allow for postapproval evaluation of this device. The TVT Registry will provide an opportunity to evaluate the uptake of cerebral protection systems going forward as well as the associated rates of stroke in patients with and without use of cerebral embolic protection.

CONCLUSION

Temporal trends in United States TAVR practice demonstrate a marked increase in use of a percutaneous

transfemoral access approach because of the reduction in sheath size currently needed for TAVR. Overall, in-hospital mortality, major bleeding, and vascular complications have decreased over time. Over the last few years, there has been a significant increase in the use of minimalist approaches with use of conscious sedation, and TTE guidance appears to be associated with reduced length of stay and reduced mortality in observational studies.

One of the biggest trends in United States practice has been a marked increase in the number of centers performing TAVR, with an astonishing doubling of centers in since 2013. Relevant to this increased number of TAVR programs is the recently described volume-outcome association that has been demonstrated using the TVT Registry, with inverse associations between increasing case volume and lower in-hospital mortality, vascular complications, and bleeding. There appears to be an early learning curve for TAVR during the first 100 cases for in-hospital mortality, bleeding, and vascular complications. These findings will need to be studied further in an era of more programs performing TAVR with less experienced heart teams. Finally, the introduction of an FDA-approved cerebral protection system to capture debris during TAVR is a potentially important step in reducing the devastating complication of periprocedural stroke, which has not been impacted by the TAVR learning curve. ■

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