Editorial Comment

Transcatheter Aortic Valve Replacement
A Revolution in Evolution*

Rishi Puri, MBBS, PhD, Josep Rodés-Cabau, MD

The advent of transcatheter aortic valve replacement (TAVR) was an undeniable revolution in interventional cardiology, fundamentally altering the therapeutic armamentarium toward patients with severe symptomatic aortic stenosis (AS) who are deemed at high or prohibitive surgical risk.

With the worldwide number of TAVR procedures rapidly approaching 200,000, coupled with an amassed knowledge spanning over a decade, we are able to now reflect on the evolution of TAVR and how changes in technology, operator/institution experience, and patient selection have ultimately affected clinical outcomes. With this in mind, in this issue of JACC: Cardiovascular Interventions, Beohar et al. (1) sought to examine how the effects of an evolution in patient selection and procedural characteristics over time would affect clinical outcomes of high-risk AS patients undergoing TAVR in a “real-world” clinical setting: the PARTNER (Placement of Aortic Transcatheter Valve) nonrandomized continued-access scheme. These investigators examined 1,063 consecutive TAVR recipients from March 2009 until January 2012, equally dividing the cohort according to tertiles (T) of time intervals according to date of procedure. During this period, all patients underwent TAVR with a 23- or 26-mm Edwards SAPIEN transcatheter heart valve (THV) (Edwards Lifesciences, Irvine, California). Annular measurements were performed with echocardiography or computed tomography. A central core laboratory was used for ultrasonic analysis. Clinical events were centrally adjudicated by an external committee, and the investigators reported clinical events according to Valve Academic Research Consortium-1 criteria.

From a clinical perspective, although the mean age of patients undergoing TAVR rose, the overall risk profile of these patients declined (median Society of Thoracic Surgeons score was 10.9 during T1 and 9.8 during T3). The incidence of concomitant cardiovascular conditions such as prior presentation with congestive cardiac failure or ischemic heart disease in patients recruited over time did not change; however, the number of patients with a prior (last 6 to 12 months) cerebrovascular event, porcelain aorta, or pulmonary hypertension decreased significantly. Similarly, the inclusion rate of concomitant noncardiovascular conditions such as oxygen-dependent chronic lung disease or prior chest wall irradiation/deformities lowered significantly from T1 to T3. To further reflect the significant evolving trend for recruiting lower-risk patients, the number of so-called “inoperable” (PARTNER cohort B) patients also declined from periods T1 to T3. No changes in echocardiographic parameters were observed over time; however, a number of procedural characteristics did evolve over time, including less post-dilation and a greater number of “fully percutaneous” procedures. In parallel, overall device and procedural success significantly improved. Crude rates of 30-day complications, however, remained similar across T1 to T3, although the rate of moderate-severe paravalvular regurgitation declined significantly over time (from 19.2% to 10.1%). The authors then performed a multivariable analysis, and found that the T3 enrollment period was independently associated with a reduction in all-cause mortality compared with

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T1, but not compared with T2. The 24% mortality rate of the T3 population at 2 years post-TAVR (compared with the 35% corresponding mortality rate of the T1 population) was then placed into perspective by the authors, who compared these results with the 2-year mortality data from the inoperable (43%) and high-risk transfemoral (31%) PARTNER cohorts.

So, does the totality of this data equate to a real evolution in TAVR? Some caveats of the analysis by Beohar et al. (1) warrant consideration to better place these findings into context. As the authors rightly state, their post hoc analysis stemmed from a non-randomized registry, which therefore carries inherent limitations. The evolution and cumulative experience of each operator/heart team was not reported per time frame. Increasing operator/center experience is known to correlate with improved procedural outcomes during TAVR (2,3). However, the increasing operator/heart team experience is frequently mixed with significant improvements in transcatheter valve technology (lower device profile, enhanced antiparavalvular leak properties, retrievability, and so on), making it difficult to estimate the real effect of the learning curve on TAVR outcomes. The fact that operators were using essentially the same valve and sheath type and size during the study period reflects a strength of Beohar’s work (1), such that it allows us to better evaluate the true effect of the learning curve during a relatively “constant” procedural environment.

The progressive decrease in the rate of paravalvular leaks over time is 1 of the most important findings of the study by Beohar et al. (1). Newer imaging algorithms, especially on the basis of 3-dimensional computed tomography aortic annulus measurements, have changed the way in which operators choose the correct THV size (4). As operator experience grew, these aspects likely played a key role in lowering paravalvular regurgitation rates, as well as reducing the need for balloon post-dilation. Importantly, a further decrease in the rate of moderate or severe AR (<5%) has already been achieved with the arrival of newer transcatheter valve systems with enhanced antiparavalvular leak properties (5). However, increasing experience was not associated with a decrease in the rate of periprocedural stroke or major vascular complications. These results suggest that additional measures (i.e., embolic protection devices, improved antithrombotic regimes) may be required to systematically further lower periprocedural stroke rates during TAVR. Despite this, recent evidence does point to a slight decline in peri- and post-TAVR stroke rates in real-world “all-comer” populations, which could already reflect major improvements in the design of newer-iteration THV devices (6,7). The lack of a decrease in major vascular complications over time suggests that in addition to a learning curve effect, further reductions in sheath sizes are required to incrementally lower peri-TAVR vascular complications (5). Also, the learning curve associated with the use of a fully percutaneous closure (vs. surgical cut-down) during the study period may have, in fact, negatively biased the vascular complication rates during T3 (8).

Of note, the main clinical improvement demonstrated in this analysis—significant decrease in mortality rate at 2-year follow-up—likely pertains to more optimal patient selection. Increasing interest now lies in better identifying patients who are unlikely to benefit from TAVR or for whom TAVR is likely to be futile (9). Although there is currently no uniform definition, futility from a TAVR perspective is usually defined by the combination of death and/or absence of functional/quality of life improvement during short-term follow-up post-procedure (6 months to 1 year). Aside from a host of cardiac (left ventricular ejection fraction <30%, severe pulmonary hypertension, low flow, and organic severe mitral regurgitation) and noncardiac (chronic severe lung disease, oxygen dependency, and advanced chronic kidney disease with dialysis dependence) conditions, frailty is increasingly recognized to be a marker of procedural-related futility (10,11). Although the analysis from Beohar et al. (1) did not report on the selection of frail patients across time, it is likely that the benefit witnessed over time also derived from selecting less patients harboring features linked with TAVR-related futility. Also, the lower prevalence of “extreme”-risk patients and those with chronic lung disease and oxygen-dependence likely contributed to improved outcomes (12).

It is therefore reassuring to observe, within the confines of the PARTNER nonrandomized continued-access study, the evolution of TAVR and its favorable effect on outcomes in a relatively short space of time. Indeed, similar observations were noted within the larger GARY (German Aortic Valve Registry), in which a progressive decline in TAVR-related complications from 2011 to 2013 was demonstrated (6). Further improvements in TAVR-related outcomes are likely to arise following ongoing refinement in patient selection. Integrating TAVR-related risk scores during patient evaluation (13-15), which are likely to be further improved by incorporating measures of frailty (9), will contribute toward improving the outlook of patients undergoing TAVR.
How much further can TAVR evolve? Are we reaching a threshold in terms of complication rates? The advent of newer-generation and more slender device iterations coupled with optimized patient selection are already resulting in dramatically lower complication rates compared with earlier TAVR results. A number of clinical trials are currently underway exploring various antithrombotic strategies post-TAVR. Although these trials will further enhance our ability to tailor our therapeutic approach, TAVR will ultimately evolve toward younger, lower-risk patients who harbor less comorbidities. Given that a number of clinical events currently witnessed post-TAVR invariably relate to the burden of pre-existing comorbid illnesses, expanding TAVR to a younger population could result in event rates that are commensurate or even lower than what is seen with contemporary surgical aortic valve replacement. The broader question now pertains to the durability of THV devices; a question that will likely take another 5 to 10 years to resolve. In the interim, the future for TAVR remains bright.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Josep Rodés-Cabau, Quebec Heart & Lung Institute, 2725 chemin Ste-Foy, Québec City, Québec G1V 4G5, Canada. E-mail: josep.rodes@criucpq.ulaval.ca.

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