Is There Life After Transcatheter Aortic Valve Replacement?*

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Acceptance of new technology depends on early clinical trials of safety and efficacy followed by the requisite “midterm” and finally “long-term” follow-up. We prefer to rely on the results of randomized trials for understanding how new technology might fit into patient care strategy. But trials are flawed by recruitment and may be slow to enroll, which makes for a long wait for initial results and thus follow-up. In addition, patients must meet many criteria to enter a trial, which frequently results in a small percentage of candidate patients actually being studied. That may make expansion of new technology to the general population tricky. All of the aforementioned were particularly true for transcatheter aortic valve replacement (TAVR). For interventionalists in the United States, it was a long wait for the results of the randomized PARTNER (Placement of AoRTic TraNscathetER Valve) and CoreValve trials and, finally, Food and Drug Administration approval of TAVR technology. However, TAVR was quickly embraced because of its clear-cut mortality benefit at 1 year in nonoperative patients and its equivalence in the PARTNER A trial to surgery in high-risk patients. The downside is that TAVR has risk, and we discuss with patients the issues of vascular complications, stroke, bleeding, emergency surgery, and even death, and also the likelihood of symptom improvement. But what can we tell our patients about long-term outcome? Will patients after TAVR live as long as people without aortic stenosis? Sufficient patients enrolled in the PARTNER A trial still have not had enough follow-up to allow any evaluation beyond 3 years. Does ridding them of aortic stenosis put them back on a “life curve” of an age-matched general population, or are there latent factors or factors actually produced by their TAVR (e.g., paravalvar leak [PVL]) that might change their long-term outlook?

The faster road to technology approval in Europe has given us more information to help answer that question. Patient registries for TAVR, which arguably give us insight into “real-world” care, have been around in Europe since TAVR began. Registries are not perfect because they depend on careful and complete data collection and thus are potentially flawed by inaccuracies that might bias outcomes. But data are data, and much can be learned, especially if registries are carefully overseen. One such database is the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) registry. In this issue of JACC: Cardiovascular Interventions is a report of 870 patients from that registry with “long-term” follow-up for more than 5 years (1). It is important to note that the U.K. TAVI registry enrolls every TAVR done in the United Kingdom. Choosing patients for TAVR in the United Kingdom may be different than doing so in other countries because of geographic or financial constraints, which may influence outcomes. But, as in commercial use of TAVR in the United States, patients in the registry are a mix of high-risk and inoperable patients who received either an Edwards balloon-expandable valve (Edwards Lifesciences, Irvine, California) or the self-expandable Medtronic CoreValve (Medtronic, Minneapolis, Minnesota). The U.K. TAVI registry 5-year mortality tracking is an enviable 97.7%. There are other data on 5-year outcomes from Canada (2) and from the PARTNER B trial (3). How do

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these data compare, and how does the current report complement what we already know about the longer-term outcomes of TAVR?

A previous report of the same 870 patients in the U.K. TAVI registry showed survival at 30 days was 92.9%. It was 78.6% and 73.7% at 1 year and 2 years, respectively (4). For purposes of comparison, in the randomized PARTNER A, 30-day survival was 96.4% for TAVR, and 1-year survival was 75.8% (5). For the higher-risk PARTNER B trial, 30-day survival was 95.0%, 1-year survival was 69.3%, and survival at 3 and 5 years was 66.6% and 59.1%, respectively (3). In the U.K. TAVI registry, as in the PARTNER trials, there was a marked attrition in survival between 30 days and 1 year. For the purist, such comparison might not be appropriate, but on balance, it seems that the U.K. TAVI registry patients and those in other reports had survival outcomes that were overall pretty similar.

In the short term, interventionalists are concerned with procedural and periprocedural issues (access, renal failure, severe chronic obstructive pulmonary disease, left ventricular ejection fraction, stroke, frailty, and so on) that have been shown to predict poor early outcome. Longer term, do these issues continue to play a role, or are there others? “TAVR-related” factors might become new players on the scene. Patient/prosthetic mismatch (PPM), prosthetic valve deterioration, pacemaker need, and aortic regurgitation from PVL are on that list. Some of these have already been studied. Post-hoc analysis of the PARTNER A trial has shown that PPM is less common in TAVR than in surgical aortic valve replacement (20% vs. 28%) (6). Patients with small aortic annuli are more likely to have PPM, making TAVR a good choice for such patients.

Pacemaker need has been well studied and varies between types of TAVR valves. It appears that in the short-term and midterm, mortality in such patients is not affected (7), although a recent report from the PARTNER trials shows increased repeat hospitalizations (8). In the U.K. TAVI registry, there is a trend toward improved late survival in CoreValve patients who have a higher incidence of pacemaker need than patients with balloon expandable TAVR. Longer-term studies are clearly needed to help sort out how pacemaker need affects outcomes of TAVR.

Lastly, prosthetic valve failure (either regurgitation or stenosis) does not appear to be problematic despite early warnings from tissue engineers and surgeons. In the Toggweiler et al. report (2), mean aortic valve area increased to 1.67 ± 0.41 cm² after TAVR and was 1.40 ± 0.25 cm² at 5 years (an average area decrease of 0.06 cm²/year with an equivalent small increase in aortic valve gradient [0.27 mm Hg/year]). In the 5-year follow-up of PARTNER B patients, valve durability was also demonstrated (3). Although a single patient does not make a series, anecdotally, the longest survivor of the early TAVR experience, in Rouen, France, is now 9 years post-TAVR with no evidence of prosthetic valve dysfunction (A. Cribier, personal communication, December 2014).

Perhaps most intriguing in the U.K. TAVI registry report is the emergence of new factors and the absence of old factors as predictors of long-term survival. Renal failure, chronic obstructive pulmonary disease, left ventricular dysfunction, and atrial fibrillation were shown at both 3 and 5 years to be independent predictors of mortality. Age and presence of coronary artery disease have now emerged as independent predictors for the first time. All are patient-specific and not related to the TAVR procedure. Surprisingly, moderate or severe PVL did not reach significance. The U.K. TAVI registry authors point out that the explanation may be that their registry does not differentiate all-cause mortality from cardiovascular mortality, and cardiovascular mortality has been shown to be significantly affected by the presence of moderate or greater PVL at 5 years by others (2,5). Also, the degree of PVL was not adjudicated by a core lab, furthering potential underreporting. It seems likely that PVL will continue to be a factor, but longer-term outcomes from the PARTNER trials should help us to understand this contradiction.

The most important take-home message from this U.K. TAVI registry report is that the initial steep drop in survival seen in the first year after TAVR becomes less steep in ensuing years. The same steep survival drop was also seen in the early PARTNER data. In the PARTNER A trial, 30-day mortality was 3.4% for TAVR, and 1-year mortality was 24.2%. For the PARTNER B trial, TAVR 30-day mortality was 5.0%, and at 1 year, mortality was 30.7% (3). After overcoming early mortality risk, survival of TAVR patients improves. Mortality drops to around 6% to 8% per year after patients recover from their TAVR. These data are similar to survival in elderly patients in their 8th and 9th decades who have undergone surgical aortic valve replacement (9,10). TAVR, like surgery, relieves aortic stenosis and its associated death threat, and patients seem to join the survival curves historically seen in the general population from actuarial tables of populations older than 80 years. It is not surprising...
that the presence of CAD and other comorbidities in TAVR patients affects them long term, but whether “TAVR-induced” factors such as PVL and pacemaker need contribute to long-term outcomes needs further study.

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