Transcatheter Aortic Valve Replacement in the Asian Population
What Did We Learn and Not Learn?*

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Transcatheter aortic valve replacement (TAVR) has entered the main stream of interventional cardiology and cardiac surgery practice in the United States. It offers hitherto clinical benefits unobtainable to many patients who are deemed too high risk for traditional cardiac surgery requiring open chest, cardiopulmonary bypass, high level of anticoagulation, and ventricular standstill. The PARTNER (Placement of Aortic Transcatheter Valves) family of trials as well as the CoreValve U.S. High-Risk trial has offered strong evidence that TAVR resulted in better clinical outcomes in inoperable/extreme risk patients than medical therapy. In high-risk patients, TAVR offers equivalent if not better clinical outcomes (1,2). Continue access data has also shown that the clinical outcomes continue to improve as devices size reduced further and the team experience accumulated over time (3). Furthermore, the U.S. TVT (Transcatheter Valve Therapy) registry has been set up as a mandated post-market registry that track the clinical characteristics as well as outcome for all patients undergoing TAVR for 1 year (4).

Results of the PARTNER IIA trial, which is a randomized study of TAVR versus open aortic valve surgery in intermediate risk patients, will have been presented at the American College of Cardiology 2016 by the time this issue is published. It will likely show that TAVR in intermediate risk patients will be non-inferior to open surgery, confirming the result from a propensity matched dataset (5). Aortic stenosis patients with low-risk profile will soon be tested in clinical trials as well.

The number of cath labs performing TAVR has exploded in the United States with more than 400 cath labs performing such procedure in 2015. The worldwide volume is over 70,000 case in 2015 and likely quadrupled to over 280,000 by 2025. The application of TAVR started first in Europe with the initial case performed in 2002 and commercialization soon after. The adoption of TAVR has been somewhat uneven across different European countries varying from 160 TAVR units/million inhabitants to 10 to 20 per million, determined mainly by local health policy and reimbursement. The current U.S. adoption is around 70 per million inhabitants.

For Asia, the adoption has been slow due to lack of operators/heart team, the high cost of the device, and general lack of government funding. The smaller aorta size and smaller peripheral vessels in the Asian population are also of significant concerns to physicians for increase complications.

In this issue of JACC: Cardiovascular Interventions, Yoon et al. (6) describe the TAVR experience (Sapien XT and CoreValve Classic) in Asian countries as collected by an international and multicenter registry involving 11 centers in 5 countries from 2010 to 2014. This study enrolled 848 patients in a consecutive, all-comers fashion in Korea, Japan, Taiwan, Hong Kong, and Singapore (total population of about 214 million). Only patients with valve-in-valve procedure and TAVR involving other valves were excluded (total of 25 patients). The mean Society of Thoracic Surgeons (STS) score was 5.2 ± 3.8%. The clinical outcome was excellent with procedure success rate of 97.5% and 30 days and 1-year mortality of 2.5% and 10.8%, respectively. The percent of bicuspid valve is small.
(5.8%) at 49 patients. The outcomes of these Asian patients are in line with clinical trials performed so far.

What can we learn from a registry like this? We learn that this technology is being adopted in selected patients across centers of excellence in Asia with superb clinical outcomes. Centers are generally using one valve or another, minority of the centers are using both valves. It speaks to the need of training and knowing the nuance of deployment of these devices. The incidence of adoption is very low at this time, about 1 TAVR per million per year. Even though these 11 centers volume do not represent all the TAVR cases done in these 5 countries, they do likely represent the majority. The best estimate is 2 to 3 TAVR per million per year, though as we know informally from our Asian colleagues, the volume of TAVR has continue to increase significantly. This selected registry also speaks to the need of mandatory reporting of TAVR in each country to better understand the characteristics and outcome of these patients.

What is it that we cannot learn from a registry like this? We do not know the screen failure rate in these Asian countries. The heart team will select out patients who fit the requirements (e.g., annular dimensions and peripheral artery size) of the available valves; we do not really know how many patients are rejected base on annular size and access site requirements. Because there is no core lab so many of the measurements, especially post-procedure, perivalvular leak can be underestimated. There are fair amount of comparisons between the 2 valves in this report though clearly there are enough confounders to make a direct comparison impossible; however, it provides a glimpse of how 2 valves (though both are not the latest generation) fare in the real world.

How does this Asian Registry compared to the U.S. TVT Registry? The recent update published in 2015 (4) involves 26,414 patients with a similar age (82 years) and slightly more male dominant (50.5%) than the Asian registry. The STS score is higher (8.34% vs. 5.2%) in the U.S. registry, this potentially can be explained by either a frail but low STS score or the presence of hostile chest or aorta in the Asian population. The 30-day mortality in the Asian registry is 2.5% while the in-hospital mortality in the U.S. registry is 4.4% in 2014. This discrepancy can pretty much be explained by the difference in the STS score. Other more interesting comparisons such as body mass index, annular dimensions and coronary heights, and access site size are not readily available from the 2 registry reports. An ethnicity substudy using the PARTNER database did not show a mortality or clinical difference between African American and Caucasian American individuals (7). Women fare better than men in TAVR, though there were more vascular complications (8).

The notion that Asians have smaller annular dimensions and limited femoral access is an intriguing question. Unfortunately this registry was unable to shed light into this question since only those patients with suitable annular dimensions can receive the smallest Sapien or CoreValve. Is there actually a correlation of annular dimension, iliofemoral dimensions with height, weight or body mass index, and ethnicity? This data is extremely important for helping with future TAVR valve development in the Asian populations.

The presence of bicuspid valve in Asian population is thought to be higher than the Western population, though clinical data is scant. Higher patient population of bicuspid valve in the Asian Registry can be due to true higher incidence or the enrichment of more bicuspid valve due to enrollment of lower risk/younger patients who likely have bicuspid valve disease. However, the literature on TAVR in bicuspid aorta valve shows a higher incidence of paravalvular leak. Mylotte et al. (9) reported an incidence of 

$\geq 2$ grades in 28.4% of patients (balloon system 19.6%; self-expanding 32.2%). The preponderance of using Core Valve for treatment of bicuspid aortic stenosis in this study may be due to belief that the noncircular annulus and the presence of the supra-annular valve within the CoreValve may fare better, though the literature is not consistent in this aspect. If indeed the incidence of bicuspid aorta valve is higher in the Asian population, it is an important area to focus on to determine what valve, technique, and imaging is required to achieve better results in this population.

Post-market registries are helpful for us to understand how new technology behaves when it is used in the real world. However, to make them more useful, these registries should be mandatory, especially for the first few years. Each registry in each country may end up to be in similar format, though not identical, making data comparison more difficult. It would be ideal that we all collect the same fields, use the same definitions, and the same electronic collecting form. The datasets can be shared, transparent, and combinable and can be used to do cohort analysis. This is a very important technology and the performance of it needs to be monitored and a worldwide uniform, shareable registry should be a great goal to aim for.

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