



## Editorial

# Will percutaneous valves replace the surgical valves: Another one bites the dust?



## A B S T R A C T

## Keywords:

TAVI  
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Trans-cutaneous valve implantation (TAVI) has witnessed rapid evolution in terms of technical design, efficacy, and safety outcomes. This has led to expanding indications of TAVI from inoperable to high surgical to now even lower surgical risk patients. However, its cost and applicability only in elderly patients with degenerated valves is a cause of concern limiting the use of this technology. Further evolution may lead to its application in lower risk essentially younger patients with broader etiologic sub-groups.

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## 1. Introduction

The goal of modern medicine is to fight death and decrease disease and disability. To achieve this goal, the whole field evolves in a way that therapy becomes more and more efficacious (prolongs life) as well as safer and less disabling. Thus, there is an ongoing quest to make therapy less invasive and more convenient, of course without losing any of its efficacy. Thus, there is a constant shift toward a simpler form of treatment, from surgical to interventional to intravenous or even oral. Thus, it is not surprising that we have seen more number of patients being treated with percutaneous coronary interventions (PCI) than coronary artery bypass grafting (CABG) and still more patients being treated with medical therapy like statins or anti-anginals than PCI. Logically, one would expect that less invasive therapy would first be applied in less sicker patients before being applied to really sick ones. However, one of the principal precepts of medicine is “**Primum non nocere**” which is a Latin phrase that means “**first, do no harm.**” This fundamental principle of medicine reminds the health care provider that they must consider the possible harm that any intervention might do even before considering the possible benefit. Its real world application in medical practice that translates into any newer intervention/therapy being used first in only “no-option patients.” Only when benefit is well established in these patients, way beyond possible harms can the new therapy be applied in less sicker sub-sets. Percutaneous valve therapy is no exception. Initially applied to inoperable or high-risk surgical patients (Society of Thoracic Surgeons score >10%, surgeon assessed risk of mortality >15%), there is now some evidence to suggest that patient selection for trans-cutaneous valve implantation/replacement (TAVI/TAVR) is now shifting toward lower surgical risk patients.<sup>1,2</sup>

## 2. Comparison of outcome

Over the years, there has been a gradual improvement in the outcomes and a reduction in complication rates related to gain in proficiency (overcoming the learning curve) and technological advances in the device technology. In the surgically inoperable group (PARTNER Trial cohort B), patients treated with TAVI had a lower mortality rate compared with those treated only with medications/medications and balloon aortic valvuloplasty (20.5% vs. 44.6% mortality; hazard ratio, 0.39; 95% confidence interval [CI], 0.27–0.56;  $P < 0.001$ ).<sup>3</sup> In high-risk surgical group offered surgical aortic valve replacement (SAVR), there were no differences in mortality at 30 days, 1-year, or 2-year follow-up (30 days – 3.4% for the TAVI arm vs. 6.4% for the SAVR arm; 1 year – 24.2% for the TAVI arm vs. 26.8% for the SAVR arm; 2 year – 33.9% for the TAVI arm and 35.0% for the SAVR arm).<sup>2,4</sup> Newer devices with lower strut thickness, better frame geometry, and lower profile may have even better outcomes. In the PARTNER II trial, the rate of death from any cause or disabling stroke was similar in the TAVI group vs. the surgery group at 2 years (the event rates were 19.3% in the TAVI group vs. 21.1% in the surgery group; hazard ratio in the TAVI group, 0.89; 95% CI, 0.73–1.09;  $P = 0.25$ ). On the other hand, in sub-group where the transfemoral-access was obtained for TAVI, the rate of death or disabling stroke was even lower than surgery (hazard ratio, 0.79; 95% CI, 0.62–1.00;  $P = 0.05$ ).<sup>5</sup>

### 2.1. Valve function

Typically, orifice areas are larger than comparable surgical prostheses related to not only absence of a bulky sewing ring but also the ability to implant oversized prostheses after balloon dilation. Echocardiographic evaluation of both currently available

valves typically documents gradients of under 10 mmHg and effective orifice areas of over 1.5 cm<sup>2</sup> in the TAVI patients.<sup>6</sup> In the PARTNER 2 trial, the improvements in aortic-valve areas and gradients at all time points were significantly greater after TAVI than after surgery.<sup>5</sup>

## 2.2. Stroke rates

Stroke rates have been classically higher with TAVI than SAVR. In the PARTNER A trial, the neurologic events, were higher with TAVI even with femoral artery access, 4.6% vs. 1.4% for SAVR ( $P = 0.05$ ).<sup>2</sup> The mechanism of these neurologic defects seems to be related to release of embolic debris from degenerated aortic valve and aorta. However, with newer low profile devices, which may cause less injury while negotiating arch of aorta this difference also disappears. In the PARTNER 2 trial with newer balloon-expandable SAPIEN XT<sup>®</sup> heart-valve system, at 2 years, the rate of disabling stroke was 6.2% after TAVI and 6.4% after surgery. Even earlier, 30 days and 1-year rates were similar.

## 2.3. Valvular regurgitation

Although no head-to-head comparison is available, paravalvular leak (PVL) is more frequently seen after TAVI than after SAVR (in the PARTNER trial, moderate/severe in 12% in TAVI patients' vs. 4% in SAVR patients).<sup>1,2,7</sup> The use of self-expandable TAVI (CoreValve<sup>®</sup>) is one of the major determinants of significant PVL after TAVI. In FRANCE II registry, self-expandable prosthesis was associated with a moderate to severe PVL rate of 19.8%, compared with 12.2% for balloon-expandable prosthesis.<sup>8</sup> The concern with these regurgitant lesions is that they may not be innocuous. Numerous studies have identified AR  $\geq 2+$  to be an independent predictor of short- and long-term mortality.<sup>9</sup> Another concern about PVL has been potential worsening during extended follow-up. Data from the PARTNER trial revealed mixed outcomes. At 2-year follow-up, it increased by  $\geq 1$  grade in 22.4% of patients, remained unchanged in 46.2%, and improved by  $\geq 1$  grade in 31.5% of patients.<sup>10</sup>

## 2.4. Conduction abnormalities

Conduction abnormality is another complication which is much higher in TAVI as compared to SAVR. While the most common conduction disturbance is left bundle branch block but serious conduction abnormalities requiring pacemaker implantation are the dreaded ones.<sup>11</sup> Three factors have been consistently associated with new development of conduction defects: the previous existence of right bundle branch block, self-expanding TAVI (22% with CoreValve<sup>®</sup> – CoreValve US Pivotal extreme risk iliofemoral study and 3.4% with Edwards valve – PARTNER Cohort B trial), and the deep implantation of the prosthesis.<sup>3,12</sup>

## 2.5. Other complications

While large number of complications can rarely occur after/during TAVI: arterial dissection, perforation, myocardial ischemia, and cardiogenic shock, a complication unique to this device is the possibility of coronary obstruction by the percutaneous valve or even native valve.<sup>13</sup>

## 2.6. Prosthetic valve degeneration

Structural valve degeneration (SVD) is the main cause of SAVR failure; the reported incidence being <1% at 1-year, 10–30% at 10-year, and 20–50% at 15 years.<sup>14</sup> In a recent study, rate of TAVI degeneration was 4.5% at a mean follow-up of nearly 2 years.

Absence of anticoagulation therapy (at discharge), a valve-in-valve (TAVI in a surgical valve) procedure, the use of a 23-mm valve, and a high BMI were found predictors of SVD.

## 3. Current value of TAVI technology

TAVI is really an exciting technology much in tune with medical philosophy of moving away from invasiveness to less invasive options likely to improve quality of life. However, at the moment, it comes at a huge cost which seems disproportionately higher than the surgical alternative. In the current context, perhaps resource-rich communities/developed world is better placed to experiment and fine-tune this technology. Developing world on the other hand is focused on cost-effectiveness of a therapy and challenged with avoiding a waste.

### 3.1. What is waste?

What is a medically wasteful therapy – any therapy that is often not beneficial and may cause harm and rapidly escalates cost of healthcare. The U.S. by far wastes higher on health care than any other country (48% higher health-care spending than next highest spending country Switzerland but nevertheless does not appear to achieve substantially better health benchmarks compared to other developed countries).<sup>15</sup> Further, the spending is not uniform, almost half of all health care spent on just 5% of the population; adults aged 65 and older had the highest health care spending. Interestingly, some estimate that 30% of that price tag may be waste: overtreatment, failures of care coordination, failures of care delivery, administrative complexity, etc. and totally avoidable. Not only this wasteful spending sometimes medically harmful but with limited budgets leads to cost cuts in essential areas like preventive medicine and care for young but also basic necessities like food and housing. Kaiser Health Tracking Polls found that to meet growing medical expenses 11% used up almost all their savings, many not only used up all their savings but had to take loan and 11% were hounded by a collection agency when they were unable to pay their loans, and 7% reporting being unable to pay for basic necessities like food, heat, or housing.<sup>16,17</sup> One can imagine that this is a situation in a market dominated by insurance what will happen in those regions where >90% “people pay from their pocket,” like India.<sup>18</sup>

### 3.2. Impact of age

Aging population presents both challenges and opportunities. They can strain/drain personal and social resources but at the same time older people are a wonderful knowledge and experience resource not only for their families and communities but even in the formal or informal workforce. They can help us avoid making the same mistakes again. The societies that adapt to this changing demography can reap a sizeable “longevity dividend”, and will have a competitive advantage over those that do not. Essentially all societies practice some form of resource-transfer schemes, directly as Social Security or indirectly through family resources. However, shrinking working populations and enlarging elderly populations are putting a huge strain on this classical arrangement so much so that it even warrants novel policy decisions related to the provision of health services for the elderly. These decisions have to encompass new technological, fiscal, and ethical perspectives. Should health care delivery be related to economic productivity? Is there a point where you have to say “Thus far and no more?” Or is differential treatment by age always an example of “age bias” we should avoid as a matter of justice? On the other hand, we do treat people differently at different ages (same guidelines/therapeutic options in many cases do not apply to elderly). The underlying

philosophy is that if we treat a disease in “young,” the individual becomes completely healthy. But what goes wrong with our bodies as we grow older are underlying biological processes of aging that advance regardless of the diseases that are commonly expressed throughout the life course. Thus, from a treatment perspective, an elderly is always different from young and disease in them cannot be considered an isolated event. If we extend this differentiation to treatment options and financial cut-offs, it should not be inherently unfair as long as we do not create inequalities across persons, and the same rules for different treatment apply across their lifespan. Moreover, health in older age is not achieved in isolation from the rest of the life course, investments now in health at younger and middle ages are likely to yield a healthier and longer-lived older population in the future and thus we might have to be willing to trade away some care we might give ourselves late in life.<sup>19</sup> We have to focus on what makes life as a whole better for us rather than thinking about “us” now vs. “them” now. Thus, ideal goal of therapy in elderly should not be mere prolongation of life but prolonging it in a way that they can remain healthy and participative in community discourse. Indeed, if we can ensure older people live healthier as well as longer lives, if we can make sure that we are stretching life in the middle and not just at the end, these extra years can be as productive as any others.

#### 4. What lies ahead: emerging TAVI technologies

With the evolution of technology, newer generation devices have a lower strut thickness, better frame geometry, and lower profile. Further, they may provide a better supra-, infra-, or intra-annular sealing. Introduction of new delivery system makes them more amenable to controlled deployment, repositioning, or removal as also preventing deep implantation of device. Further fine-tuning the technique and developing new strategies for “bed preparation” such as pre-implantation calcification debulking may ensure adequate valve expansion and annulus sealing. Finally, careful selection of patients and valve type may all lead to a dramatic reduction in already low complications so much so that TAVI may become an alternate to SAVR even in low-risk and younger patients.

#### 5. Evolution of TAVI technologies

Apart from a model of wasteful health-care economies fueled primarily by insurance sector, TAVI will become really useful in global health scenario when it will be applied to a wider population base and in those in productive age-groups. Its real value will be proven when patients will start paying from their own pockets. In other words, the innovation will have to move in a way that it can

be applied to younger populations, in regurgitant lesions, for non-degenerative sub-sets of valve diseases, and a much lower cost.

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