Transcatheter Aortic Valve Replacement in Moderate-risk Aortic Stenosis Patients

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Abstract

The Placement of Aortic Transcatheter Valves (PARTNER) trial showed the effectiveness of transcatheter aortic valve replacement (TAVR) for inoperable patients and non-inferiority for mortality versus open valve replacement. There are three questions concerning the role of TAVR for intermediate-risk patients. These relate to: institutional and surgeon results, physician and hospital alignments, and who will pay.

Keywords

Transcatheter aortic valve replacement, transcatheter aortic valve implantation, aortic valve stenosis, aortic valve replacement

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If you can look into the seeds of time and say which grain will grow and which will not speak then to me. Macbeth; William Shakespeare.

Predictions of the role of transcatheter aortic valve replacement (TAVR) in moderate-risk patients is fraught with potential pitfalls. The matrix of outcomes is interlinked and changes in one cell may have consequences beyond currently observable measures. For example, the Congressional Budget Office (CBO) options for cost reductions ('caps on spending') being presented to lawmakers, reads like rationing for healthcare and new technologies. Moreover, neither Europe, Canada nor Scandinavia are immune and if anything, many are more restricted, such as Belgium. It is thus incumbent upon us physicians to consider options both locally and more globally for the management of our patients.

The previous randomised study of the Placement of Aortic Transcatheter Valves (PARTNER) trial showed that TAVR was superior to medical treatment and that TAVR was equivalent to open aortic valve replacement (AVR) for mortality, although the stroke or transient ischaemic attack (TIA) rate was three times higher. Long-term data are, however, not available for valve durability, particularly in younger patients with longer expected survival. Open surgical treatment is established, highly successful and safe treatment for aortic valve stenosis that both relieves symptoms and very markedly extends survival. The seed of TAVR has been planted, is growing, and only time will tell how TAVR compares with AVR. Thus the use of TAVR in lower risk, and hence younger patients, needs to address safety and durability and also the trade-off of less invasive procedure for greater risk of stroke.

Questions to Address

There are three scenarios to consider. Firstly, the ethical question of what are your institutional results with AVR and TAVR? Secondly, what are your physician and hospital alignments? Thirdly, is the moral

question for greater society of what should we pay for and should healthcare be 'rationed' for the moderate-risk and high-risk elderly?

Results

What are your results? This question should be relatively easy to answer yet it surprises me when we are asked to review cardiovascular programmes how scanty the data can be. Nevertheless, both institutional outcomes and individual surgeon's outcomes should be known based on the Society of Thoracic Surgeons (STS) data or collection of state data such as in New York, Pennsylvania or Massachusetts. In a broader US context, for July 2011 to June 2012, 92,514 aortic valves were sold at a cost of US\$472 million, and in 2010 on average a cardiac surgeon did eight AVRs and an institution 21.^{1,2} To illustrate the point, at the Cleveland Clinic in the year 2011 we did 479 isolated AVRs (we do in total about 1,500 AVRs combined with other procedures), including reoperations, emergencies and endocarditis with a predicted STS mortality score of 3.48 %, but observed mortality was in fact 0.60 % and stroke 1.50 %.³ For 2012 we did 539 patients, STS predicted death was 3.96 %, actual deaths 0.40 % and stroke 1.10 %. From 2001 to December 2007 (before potential influence of TAVR) it was only after the age of 80 years that mortality increased for reoperations to 5.6 %. However, based on careful patient selection no patient operated on over the age of 90 years died during that period. For root sparing procedures, including aortic dissections, it was 1.4 % (n=418) and for minimally invasive approaches for AVR 0.5 % (n=1,572, stroke 0.8 %). For patients <70 years old and primary operations (n=720) it was 0.28 %. Thus, because our operative results are so good this would be a considerable equipoise challenge to perform a prospective randomised study for the use of TAVR in our population. Certainly, for enrolment in the PARTNER 2A trial, this raised an ethical question of equipoise until we analysed our data in December 2012. For 257 transfemoral TAVRs there were 11 conversions (five to transapical [TA], two open AVR for ruptured roots, 4.2 %), one death

(0.4 %) and two strokes (0.8 %). Up to May 2013 for 150 TA patients there were five deaths (3.3 %) and one death out of 85 patients since January 2011 (1.2 %). This compares favourably to the PARTNER A results.⁴ Hence, based on the data, we had the equipoise to enrol in the PARTNER 2A trial in which moderate-risk patients were required to have a STS score of 4–8 %, although later the upper limit was removed at the Food and Drug Administration's (FDA) request. Nevertheless, this is a trial of moderate-risk and also high-risk patients with a new device (Sapien XT) that will help inform patient selection for AVR versus TAVR. Whether the lessons learnt from the PARTNER A trial will apply to the moderate-risk patients, such as the finding that transfemoral (TF) is better for high-risk patients with significant co-morbid disease, at the cost of 4.6 % stroke or TIA versus 1.4 % for open AVR ($p=0.04$), and that AVR or TA is better for more complex cardiovascular cases (like reoperations [$p<0.05$] or with males [$p<0.05$]) remains to be seen.⁵

The STS score has proven to be very accurate for prediction of deaths for the mature and technological plateaued procedure of AVR, even for STS >10 % but with wider confidence limits and receiver operating characteristic (ROC) curve c-statistics of better than 0.8.⁶ However, our attempts at finding a reliable ROC score for TAVR has not been as effective (c-statistic <0.6).⁷ Why should this be? AVR has become a mature technology for which random unpredicted events are rare, such as coronary occlusion (a good surgeon should mostly prevent this) or aortic dissection, and hence patient-related factors can be used in a predictive formula with greater reliability. For TAVR, as with other new innovative and disruptive technologies there are greater risks of both unpredictable and frequent random events. These include: failure to place the valve accurately, sizing problems, conversions, valve embolization, root rupture, ventricular perforation, aortic dissection, vascular access injury, ventricular tears, pacing wire perforations, heart block, entrapped wires or catheters, severe mitral valve regurgitation, severe perivalvular leaks, etc.^{4,8} In the PARTNER A trial, 9.5 % had a failure of successful TAVR insertion based on Valve Academic Research Consortium (VARC) definitions and 10.5 % had severe or moderate perivalvular leak, also a failure by VARC; thus in total, approximately 20 % had a failed procedure. Indeed, there is some evidence that if all complications related to a TAVR procedure are combined and because transapical TAVR is associated with less bleeding and less perivalvular severe leaks, the transfemoral approach has an overall greater risk of complications for all comers. Thus, based on current known outcomes, until TAVR further matures, TAVR in moderate-risk patients should be used with caution but would depend on institutional experience and AVR outcomes.

Alignments

What are your alignments? This question addresses the issue of surgeon and interventional cardiologist alignments in either doing open AVR or TAVR. In Germany, one-third of patients are done by TAVR because institutions get paid more for TAVR and surgeons are essentially employed by the institutions, although numbers do count. However, the German healthcare system has realised this and now a senior surgeon is required to approve patients for TAVR. In Belgium, the government will not pay for TAVR and so surgeons and cardiologists do TAVRs for free and hospitals absorb the costs but limit the annual number they permit, to for example 15. In the US the situation varies from institution to institution. If both cardiologist and surgeon are in private practice, there is little support for moderate-risk TAVR. If surgeons are in combined practice plans there is more accommodation since fees are split and a surgeon gets half of the AVR fee. In institutions where both are on

salary and the perception is for the greater good, accommodation of TAVR is more based on medical imperatives and less influenced by financial potential arbitrations. On the contrary, however, it is likely in the latter scenario that surgeons will be more prepared to give up complex reoperations for TAVR if there are no rewards to do the complex cases, even though previous coronary artery bypass grafting (CABG) patients in the PARTNER A trial did much better ($p<0.05$) with open AVR.

Who Will Pay

The moral question of whether society will pay? Centers for Medicare & Medicaid Services (CMS) posed the question of whether "the evidence (is) adequate to conclude that transcatheter aortic valve replacement improves health... for Medicare beneficiaries with severe aortic stenosis"? It is worth noting that CMS has three departments and the evaluation of effectiveness is done by a group separate from the payment department. The issue is that in 2009 (financial data is a minimum of two years behind) CMS spent US\$133 billion on in-hospital patient care (estimate US\$170 billion, 2013); while the total estimated expenditure by CMS in 2013 was US\$1,125 billion according to the CBO, with 36 % of all US patient care paid for by CMS (Medicare, Medicaid, CHIP, etc.). Currently, 42 % of patients are covered by government insurance but our predication is that in a decade it will be 75 %. Consequences are that CMS will determine directly or indirectly the level of reimbursement (for example, exchanges will pay physicians 5 % above Medicare rates and hospitals at the Medicare rate). Hence, with the financial problems, poor job growth and the budget deficit, healthcare will be under increasingly severe 'spending caps' as recommended by the CBO. In turn, CMS will be under pressure to cut costs. Clearly, while AVR and TAVR are among the most effective cardiovascular treatments to improve symptoms, quality of life, Kansas City Cardiomyopathy Questionnaire (KCCQ) score and long-term survival, both treatments cost more than 'medical treatment'.^{9,10} This then is the moral question as to who should receive treatments within the group of patients at increased risk. The determination of CMS for TAVR in high-risk patients was "TAVR provided no mortality benefit but significant risk of harm. ... coverage... should be restricted only to clinical trials rather than registries." Hence, the TVT Registry™/NCDR® database. Furthermore, based on CMS reimbursement on the valves costing US\$32,500, some hospitals lose US\$4,000–14,000 per TAVR (average cost was US\$78,000 with a mean 1.5 nine-year survival gain) and analysts' predict that CMS could end up paying a predicated US\$2.6–6.0 billion per year for percutaneous valves in contrast to half a billion for AVR.¹¹

Conclusion

In conclusion, it is noteworthy that in the recent report published in *The Journal of the American Medical Association (JAMA)*¹² of the first 7,710 patients in the TVT/NCDR registry the STS score was a mean of 7 (for the approval of the device for inoperable patients in the PARTNER B trial it was 11 and also for high-risk patients in PARTNER A it was also 11, and this is the population the device should be commercially used in). Thus, there are already moderate-risk patients (for PARTNER 2A moderate-risk study the Cleveland Clinic mean was STS 7) being done commercially. Furthermore, based on the data shown in their Figure 1, institutions doing small volumes of TAVR, particularly <60 TAVR case volume, were also doing more low-risk STS score patients. If two surgeons in these low volume institutions are approving these cases, then it is likely they feel less confident to tackle higher risk patients, like reoperations, despite the fact these patients do paradoxically better with open AVR. Indeed, between January 1999

and mid-2013, at the Cleveland Clinic, we did 329 reoperations of all types for AVR surgery and the mortality rate was 2.4 % and stroke 1.8 %. Furthermore, for our low-risk patients (n=771) with a STS <4 % risk the mortality rate was 0.3 % between 2011 and 2013, and for 74 % intermediate or high-risk there were no deaths (0 %) for a total of 0.2 % death (n=956 patients). The unanswered questions are the long-term durability of TAVR in younger intermediate-risk patients, the stroke risks, and the effect of perivalvular leaks long-term. PARTNER 2A will likely add information but will show mixed results.

It is unlikely that further successful prospective randomised trials will be done in the intermediate-risk patients to clarify selection of patients. At least for high-risk and inoperable patients the results are encouraging in our experience.¹³

The future use of TAVR for moderate-risk will be determined by your answers to the above questions; and in the US, risk creep, the future decisions of congress, CBO recommendations and CMS reimbursement. ■

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