Cost-Effectiveness of Transcatheter Aortic Valve Replacement

Running title: *Hlatky et al.;* Cost-effectiveness of transcatheter *AVR*

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Patients with symptomatic aortic stenosis have a poor prognosis, and medical therapy has little, if any, effect upon their natural history. Surgical aortic valve replacement (AVR) is risky, yet it appears to be effective in extending life expectancy and reducing symptoms due to aortic stenosis. In this setting, the development of transcatheter AVR appears to be a breakthrough technology, potentially offering the benefits of surgical AVR without the need for an operation¹. Early clinical experience with transcatheter AVR has been promising, and set the stage for a randomized trial to provide the definitive test of its efficacy. The concurrent PARTNER (Placement of AoRTic TraNScatheter Valves) trials²,³ compared transcatheter AVR with medical therapy among patients at prohibitive risk of surgery (PARTNER Cohort B), and compared transcatheter and surgical AVR among patients at high, but acceptable risk of surgery (PARTNER Cohort A). The PARTNER Cohort B trial showed that transcatheter AVR reduced mortality by 50% among inoperable patients and also improved quality of life². Transcatheter AVR was clearly a great improvement over medical therapy among elderly patients (average age of 83 years) with inoperable aortic stenosis.

Transcatheter AVR is a successful new medical technology, but new medical technologies are also the prime drivers of increasing medical costs in the United States. Since the rising cost of health care has the potential to bankrupt the country, policymakers rightfully ask for evidence that any new technology provides sufficient clinical value to justify its costs. Cost-effectiveness analysis provides an explicit framework to assess the value of medical interventions. The fundamental principles of cost-effectiveness analysis are simple: how much does the new technology improve clinical outcomes compared with the next best alternative, and how much does it cost compared with the next best alternative? The difference in clinical effectiveness (measured in quality-adjusted life-years) is divided by the difference in costs yield
the incremental cost-effectiveness ratio. While there is no absolute level of the cost-effectiveness ratio that indicates an acceptable value in the United States, interventions that cost less than $50,000 per quality-adjusted life-year (QALY) added are readily accepted, whereas interventions that cost more than $100,000 per QALY added are generally considered to be too expensive. Interventions between $50,000 and $100,000 per QALY are in an intermediate zone, but are accepted more often than not.

This framework for assessing cost-effectiveness has several implications. First, clinical effectiveness is the most important determinant of cost-effectiveness—simply put, an intervention has to be effective before it can be cost-effective. Second, cost-effectiveness is always interpreted in context—a treatment is compared with the next best alternative for a specific indication in a particular set of patients. The very same intervention can be highly cost-effective for one indication, yet not at all cost-effective for another indication (e.g., statin treatment for survivors of a myocardial infarction versus primary prevention in young, low-risk individuals).

Partner Cohort B Economic Outcomes

In light of this background, the analysis of the economic outcomes and cost-effectiveness of transcatheter AVR in Cohort B of the PARTNER trial reported by Reynolds and associates is timely and important. The authors assessed economic outcomes as part of a randomized clinical trial, thereby capitalizing on the trial’s ability to control treatment selection bias when comparing therapies. Of course, the generalizability of trial results, including the economic outcomes, to less selected patient populations is always an issue.
Since the key determinant of cost-effectiveness is clinical effectiveness, the method of quantifying the effectiveness of transcatheter AVR is the most important aspect of the report by Reynolds and associates. The mean follow-up among surviving patients in Cohort B of PARTNER was only 18 months (the maximum was 30 months), which is too short to measure the full effect of transcatheter AVR on life expectancy. If life expectancy were measured using only the observed follow-up, transcatheter AVR would increase life expectancy by 0.5 years (from 1.2 years with medical therapy to 1.7 years with transcatheter AVR). The truncated observation period in a clinical trial introduces a potential bias into the cost-effectiveness analysis to the extent that the full costs of an intervention are captured, but its full effectiveness is not. (This has been an issue in assessments of the implantable cardioverter defibrillator and coronary bypass surgery.) So Reynolds and associates projected future life expectancy of surviving patients using an exponential survival hazard function fitted to the observed survival patterns after recovery from the procedure. Their extrapolation suggests that transcatheter AVR increased life expectancy compared with medical therapy by 1.9 years instead of 0.5 years (from 1.2 years to 3.1 years). Note that this extrapolation is somewhat speculative, as it is based on the assumption that the observed survival patterns will continue indefinitely, but they might not if the implanted aortic valves began to fail after a few years. This underscores the need for long-term studies to assess the durability of transcatheter aortic valves.

The second aspect of clinical effectiveness is the extent to which transcatheter AVR improves quality of life. In Cohort B of PARTNER, the patients who survived those transcatheter AVRs had better quality of life—consistent with the reduction in the severity of their aortic stenosis. As a result, patients who underwent transcatheter AVR had a 278% increase in their projected lifetime QALYs, somewhat higher than their 232% increase in life expectancy.
This observation is also important—if transcatheter AVR merely prolonged a miserable existence, it would not be very beneficial to patients.

The data from PARTNER (Cohort B) show that transcatheter AVR improves both life expectancy and quality of life to a clinically important degree compared with medical therapy. The next question is its effect on healthcare costs. The cost of the transcatheter AVR itself is an important consideration, but this cost is a predictable expense for the transcatheter AVR strategy: Reynolds and associates estimate the cost of the procedure at $78,500. The interesting question is whether having a transcatheter AVR might reduce subsequent medical costs by, for instance, reducing hospitalizations for heart failure due to aortic stenosis. Here the randomized design is important, as patients undergoing transcatheter AVR are clinically similar to the comparison group that was treated medically. Reynolds and associates showed that over the subsequent 12 months the patients assigned to transcatheter AVR had 1.2 fewer hospital admissions and lower costs by $24,300 than the medically treated patients. Thus, over a fixed calendar time, they documented partial “payback” of the initial costs of transcatheter AVR.

Cost-effectiveness analysis uses a lifetime perspective, however, and here the PARTNER results are quite interesting. Because the transcatheter AVR patients lived longer (by 1.9 years), they had a longer time to accrue follow-up medical costs. The estimated higher lifetime costs ($79,800) of patients assigned to transcatheter AVR turned out to be almost exactly the same as the cost of the initial transcatheter AVR procedure ($79,500), because the lower costs per year of follow-up were almost exactly counter-balanced by increased medical costs in follow-up due to their longer life-expectancy.
So, in the intention-to-treat analysis, a strategy of transcatheter AVR increases costs, and improves outcomes compared with medical therapy, with a cost-effectiveness ratio of $50,200 per life-year added (or $61,900 per QALY gained). These estimates were not greatly changed by reasonable variations in assumptions of the cost-effectiveness model. The authors estimate there is a very high probability the cost-effectiveness ratio is below $100,000 per life-year added, but there is also a very good chance the cost-effectiveness ratio is above $50,000 per life-year added. Overall, transcatheter AVR for elderly patients with severe, inoperable aortic stenosis looks like a reasonable value for the money spent on the procedure.

**Generalizability**

The results of the nicely done analysis by Reynolds and associates apply to patients like those in the Cohort B of the PARTNER trial. It is important to emphasize that these results cannot be extended to transcatheter AVR performed in other populations or for other indications. Most important, these results do not apply to patients who could get a surgical AVR—for this population we must await the results of the economic analysis of the Cohort A of the PARTNER trial comparing surgical AVR with transcatheter AVR. Nor do these results apply to asymptomatic patients with severe aortic stenosis, or to any patients with mild or moderate aortic stenosis. Furthermore, operator experience will surely have a great effect on the outcomes of transcatheter AVR, and experience levels will vary greatly in routine practice, thereby affecting the clinical effectiveness (and cost-effectiveness) of the procedure in typical patients. Finally, transcatheter AVR is an evolving technology, and the outcomes are likely to change over time and with different device systems. In spite of all these caveats, the results of Reynolds and
associates suggest that transcatheter AVR may be a good value in properly selected symptomatic patients with aortic stenosis who are at too high a risk to have surgical AVR.

**Conflict of Interest Disclosures:** None

**References:**


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