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BMJ analysis: TAVI is vastly overused

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Brussels, Belgium (updated) - The rapid expansion of transcatheter aortic-valve implantation (TAVI) in Europe is not justified by the clinical evidence, according to a scathing article published online July 31, 2012 in *BMJ* [**1**].

"Given the enthusiasm with which the procedure has been adopted, we might expect the evidence for its efficacy to be solid," **Dr Hans Van Brabandt** (Belgian Health Care Knowledge Center, Brussels) and colleagues write. But, they conclude, "Based on current evidence, and considering efficient use of limited resources, it is difficult to see how healthcare payers can justify reimbursing TAVI for patients suitable for surgery."

Van Brabandt et al conducted a health-technology assessment for the Belgian government that concluded that the country's health system should pay for TAVI only for patients who are ineligible for surgery—only about 10% of those currently considered for the therapy. Their analysis of observational data found that TAVI costs about €20 000 more per patient in Belgium than traditional surgical valve replacement [**2**]. The average initial costs, including the €18 000 for an Edwards Lifescience's **Sapien** valve, are €43 600 for TAVI vs €23 700 for surgical valve replacement.

The analysis also found that transapical TAVI procedures cost more than transfemoral procedures (€49 800 vs €40 900). The authors also note that the transapical approach was linked to a 25.5% one-year mortality rate in the UK TAVI registry and a 20.2% six-month mortality rate in the **FRANCE-2** registry.

The authors cite a guidance from the UK's **National Institute for Health and Clinical Excellence** (NICE) that concluded that the evidence supporting TAVI for patients for whom surgery was possible is not strong and that it should be used for these patients only as part of an appropriately governed clinical trial [**3**]. However, NICE's guidance did not explicitly consider the cost-effectiveness of TAVI, but "these costs should be taken into account by local [**UK National Health Service**] commissioners in decisions about whether to fund the procedure," Van Brabandt et al argue. "If policy makers are willing to pay for TAVI, they should give priority to anatomically inoperable patients."

PARTNER problems?

As reported extensively by heartwire, the most important support for the Sapien valve is the PARTNER trial, which found similar one-year mortality for TAVI and surgery patients for whom surgery was very risky but showed that mortality was significantly lower with TAVI than standard medical therapy in patients deemed inoperable (30.7% vs 50.7%, $p<0.001$). But in both comparisons, the TAVI patients had more strokes and vascular complications.

Van Brabandt et al argue that these data show that TAVI can be justified for inoperable patients on ethical, but not cost-effectiveness, grounds. However, they argue that even this modest claim for TAVI may be undercut by the unpublished data from 90 patients in the randomized continued-access protocol. According to the briefing documents provided to the FDA advisory panel that endorsed Sapien for inoperable patients in July 2011, Kaplan-Meier analysis of those 90 patients shows that 30-day freedom from death is 90.2% for patients implanted with Sapien via the transfemoral route and 97.9% for patients treated only with standard medical care. The one-year survival rates are 65.7% and 78.4% for the TAVI and standard-care groups, respectively.

Van Brabandt et al say that they've tried to get more information on this follow-up trial by contacting the FDA, Edwards, the PARTNER investigators, and the *New England Journal of Medicine* (which published the original PARTNER results) but have not been provided with any more details on this study.

The authors also argue that the control and treatment groups in the PARTNER trial were unbalanced in a way that would favor TAVI for inoperable patients. The control group had more patients with comorbidities,

more with previous MI, and more classified as frail. "All these differences could have arisen from a flawed randomization or by chance, but since they favor TAVI, an analysis that adjusted for prognosis at baseline would have produced a more realistic estimate of the effect size," Van Brabandt et al argue.

The authors also claim that the PARTNER investigators—most notably **Dr Martin Leon** (Columbia University, New York, NY) did not fully disclose their financial interests in the trial. As reported by **heart*wire***, Leon has already responded to these charges and adamantly denies that his financial relationship to Edwards biased the trial results.

Edwards responds

A statement from Edwards notes: "The *BMJ* editorial contains no new data but is simply a repackaging of old, non-peer-reviewed arguments against [transcatheter aortic-valve replacement] TAVR that have been fully and publicly answered.

"Globally, there exists a remarkable body of clinical, quality-of-life, and economic evidence on Sapien, collected over 10 years," according to the company. "These data have been published in more than 350 peer-reviewed publications and extensively presented at public meetings and reviewed by regulators and payers worldwide."

Each center must choose what's best for the patient

Dr Josep Rodés-Cabau (Quebec Heart and Lung Institute, Quebec City), who has been actively involved in tracking real-world TAVI outcomes, especially in Canada, told **heart*wire*** that he does not believe that concerns about overuse of TAVI found at some centers can be generalized to most centers performing the procedure, as most such centers in Europe and around the world have created heart teams with surgeons and interventionalists who collaboratively decide which procedure to perform on a given patient.

"It's very dangerous to generalize and say that it's overused everywhere, because each center has to go through its own exercise of looking at the data they have with the surgical treatment of these high-risk patients—or even moderate-risk patients—and then look at the results they are getting with the TAVI program," he said. "You may have some surprises, and at some centers, maybe the surgical results are much better." He noted that the stroke rate in the surgical patients in the PARTNER trial is lower than what would be expected at many centers.

Rodés-Cabau said that there's good reason to hope that the stroke rates with TAVI will go down over time as operators' technique improves; and as TAVI outcomes improve, so will the cost-effectiveness of the procedure. The SURTAVI and PARTNER II trials will show more clearly whether or not TAVI should be an alternative to surgery in intermediate-risk patients, but until those data are available, physicians must try to make the best choice for their patient based on the data available now. "We have to start somewhere," he said.

He also pointed out that PARTNER showed that quality-of-life improvement postprocedure was more rapid for TAVI patients than for surgery patients—a finding not addressed by Van Brabandt et al. "We have to look more objectively at what we've achieved, and I think it's been very impressive in a very short period of time," Rodés-Cabau said.

The authors declare no conflicts of interest. Rodés-Cabau has previously disclosed serving as a consultant for Edwards Lifesciences and St Jude Medical.

Sources

1. Van Brabandt H, Neyt M, Hulstaert F. Transcatheter aortic valve implantation (TAVI): Risky and costly. *BMJ* 2012; DOI:10.1136/bmj.e4710. Available at: http://www.bmj.com.
2. Neyt M, Van Brabandt H, Devriese S, Van De Sande S. A cost-utility analysis of transcatheter aortic valve implantation in Belgium: focusing on a well-defined and identifiable population. *BMJ Open* 2012; DOI:10.1136/bmjopen-2012-001032. Available here. PUBMED
3. National Institute for Health and Clinical Excellence. Transcatheter aortic valve implantation for aortic stenosis. NICE interventional procedure guidance 421. March 2012. Available here.

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