

## PARTNER cohort A: Transcatheter valves noninferior to surgery

Apr 3, 2011 Shelley Wood

**New Orleans, LA** - Long-awaited results from [PARTNER](#) cohort A, comparing transcatheter-valve implantation with surgery for severe aortic stenosis, show that the new catheter-based procedure is just as good as surgery in surgery-eligible patients for the primary end point of mortality, with a range of secondary end point findings that will give surgeons and interventionalists plenty to debate in the days to come. Principal investigator **Dr Craig Smith** (Columbia University, New York, NY) will present the one-year results here at the [American College of Cardiology 2011 Scientific Sessions/i2 Summit](#) at 9:15 am CT today. Those results show that PARTNER cohort A, conducted in high-risk aortic-stenosis patients deemed eligible for surgery, met its primary end point, demonstrating that TAVI is noninferior to traditional aortic-valve replacement in terms of all-cause mortality.

At 30 days, deaths were numerically lower in the TAVI group, but not statistically different (3.4% vs 6.5%). By one year, deaths in both groups were nearly identical, ranging from 25% to 26%.

Major strokes—the secondary end point that has been provoking the most speculation in the lead-up to this presentation—were higher in the TAVI-treated patients, both at 30 days (3.8% vs 2.1%) and one year (5.1% vs 2.4%). By contrast, and not unexpectedly, major bleeding was more than twice as common in surgery-treated subjects (19.5% vs 9.3%), and vascular complications were nearly four times higher in the TAVI group (11% vs 3.2%).

Speaking with [heartwire](#), **Dr Michael Mack** (Medical City Dallas Hospital, TX), a surgeon and PARTNER investigator, characterized the trial as "a win for everybody. Surgery looked good; transcatheter-valve replacement looked good."

**Dr John Webb** (St Paul's Hospital, Vancouver, BC) one of the early percutaneous-valve pioneers, also hailed the findings but clearly viewed TAVI as the winner.

"This is a trial of a first-generation transcatheter-valve system, and with operators, many of whom had only done two cases before doing this trial, compared with the very best surgeons, at the very best sites in the United States—a very high bar. And [the patients enrolled] were really just the top 10% of surgical candidates—the worst patients. Despite that, you have a mortality rate that's lower [numerically] with transcatheter-valve implantation. The study was powered as a noninferiority trial, and it met that benchmark."

In all, 699 elderly patients (median age 84.1) with severe aortic stenosis were randomized to either TAVI or conventional surgery at one of 26 centers in the US, Canada (four centers), or Germany (one center). In the TAVI group, patients received the experimental device via the fully transfemoral route (244 patients) or via a transapical (104 patients)

procedure, which is typically used when the femoral artery is deemed unsuited to the TAVI catheters. Not surprisingly, patients in the transapical group were slightly higher risk than patients in either the transfemoral TAVI group or the aortic-valve-surgery group.

### The stroke results

Mack singled out the difference in stroke rates as "the big differentiator" that he expects people will zero in on. Strokes were also a major talking point in the [PARTNER cohort B](#) trial (TAVI vs best medical therapy), although in that group, patients ineligible for surgery, a stroke seemed a smaller price to pay for a huge mortality gain. In cohort A-type patients, stroke will be an even more important consideration.

"You may pay a higher risk of stroke with transcatheter aortic-valve replacement, but you have a quicker recovery with TAVI, and you end up at the same point at one year," Mack says. That said, he thinks people were too fixated on the stroke rates in PARTNER cohort B. "It's almost like the primary focus got lost because of the stroke issue."

Webb, for his part, is less concerned about the stroke rate, which he says will fall considerably as lower-risk patients are treated, as operators gain more experience, and with the newer devices now available. The first-generation **Sapien** (Edwards Lifesciences) device and delivery system were used in PARTNER; his center is now using a fourth-generation device that is much less bulky. Not only will stroke rates decline, he predicts, but vascular adverse events will drop dramatically. Compared with the 11% rate in this study, major vascular complications at Webb's hospital are now down to 2%.

### Speculating on subsets

Webb also pointed to what he thought were important subset findings—the rate of the primary end point in the patients treated with the transfemoral procedure. In an analysis looking at patients "as-treated," rates of the primary end point at 30 days in the transfemoral subset were just 3.7%, vs 8.2% in those treated with surgery, a statistically significant difference. "It's hard to make a noninferiority study sound exciting, but the point is that, overall, TAVI was better than equivalent, it was noninferior, it had a lower mortality [numerically], and the percutaneous group had a dramatically lower mortality," Webb said.

An open question highlighted by Mack is valve durability and rate of paravalvular leaks with transcatheter valves. "We do have an idea of what valve durability is with surgery and that's 15 to 20 years, and we have virtually no paravalvular leaks. That may or may not be significant in the long term for transcatheter valves; right now, so far, it doesn't seem to be a major issue."

What the future holds

Industry analysts have predicted the **FDA** may approve the Sapien device as early as late fall 2011, at least for surgery-ineligible patients. The device is already CE Mark-approved in Europe and on the market in other countries worldwide. A US randomized clinical trial of the **CoreValve** (Medtronic) device—the other major transcatheter valve in clinical testing in the US and approved in Europe—now has 35 sites "activated." As excitement mounts in the US, Mack has one more reminder for physicians.

"What we have learned through this trial is that there are clearly patients who are not candidates for surgery now who can be helped by this, but we've also learned that there is a ceiling to this, and not everybody is a candidate for transcatheter-valve therapy. I think we have found through both trials, A and B, that there were patients that we enrolled early on that we would not enroll today, because they were too old, too frail, or too debilitated, and they can't even withstand a transcatheter procedure."

He continued: "I also think that, as great as the results for cohort B were, and as great as these results are from cohort A, you still have a therapy in which between 25% to 35% of patients are dead at one year. So you have to ask, is that an appropriate use of expensive technology?"

Going forward, says Mack, surgeons and interventionalists, in collaboration, need to do a better job of recognizing when comorbid diseases are too advanced.

"We really need to be more selective about who we think has the greatest chance of surviving one, two, three, and five years out. I would be disappointed if, in the next series, the one-year survival doesn't climb up to 80%, 85%, and 90%."

It should do that, he notes, as lower-risk populations are treated. "If you look at the one-year survival of all patients undergoing valve-replacement surgery in the US today, it's 93%. So I think that's the target to aim for."

### **Cohort B and a publication scuffle**

As previously reported by *heartwire*, the [PARTNER cohort B](#) results testing TAVI against best medical therapy were first released at the [2010 TCT meeting](#). In that randomized comparison, the relative risk reduction in all-cause mortality was 46% compared with medical therapy (a 20% absolute difference), and cardiovascular mortality risk was reduced by 61% compared with patients receiving the best medical care, including balloon valvuloplasty. Risk of a composite end point of dying or needing repeat hospitalization was also lower in TAVI-treated patients. In that arm of the trial, the risk of stroke and of vascular complications was higher in the TAVI group.

In a controversy that still rankles, the PARTNER cohort B investigators had agreed to simultaneously publication of their results in the *New England Journal of Medicine* when the presentation was made on a Thursday morning. Inexplicably, the journal released them early online on Wednesday evening.

Speaking with **heartwire**, co-principal investigator for PARTNER, **Dr Martin Leon** (Columbia University), said that the cohort A results will not have simultaneous publication "by intention."

"One of the reasons we did that was that when we worked so hard to get [cohort B] published simultaneously, it was prereleased, and it took a lot of the shine out of the presentation and was frustrating for us, and we could not convince the journal to hold off on that. So it was such stress for everybody, having data that were potentially being exposed, that I think we wanted to reduce the stress level. So it has been submitted to the *NEJM* but will not be presented and published simultaneously."

### **Related links**

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[TAVI specialists expect surgical valves to survive, as more surgeons also do TAVI](#)

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