EuroIntervention 2011;7:903-904

What is the evidence allowing us to state that transcatheter aortic valve replacement via the femoral artery is a more attractive option compared to transapical valve replacement?

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Recently, transcatheter aortic valve replacement (TAVR) has been shown to result in similar 12-month survival as surgical aortic valve replacement (SAVR) for high-risk patients with severe aortic stenosis[1]. For patients deemed inoperable TAVR showed a 20% survival benefit at one year compared to medical treatment[2].

The PARTNER Trial

During the focused late-breaking clinical trial session at TCT in San Francisco new data on TAVR were presented. Good news came from the PARTNER B trial which tested TAVR with the SAPIEN device (Edwards Lifesciences, Irvine, CA, USA) in inoperable patients against best medical care. Data showed that survival curves are continuing to diverge. By two years, 67.6% of patients in the medical group had died, compared with 43.3% in the TAVR group, a difference of 24.3%. The number needed to treat to save one life therefore dropped to four patients, which was five patients at one year.

The potential cost-effectiveness of TAVR versus SAVR in the PARTNER trial was examined and the results were presented by Matthew Reynolds. Health-state utilities were estimated using the EuroQOL (EQ-5D) at baseline, one, six and 12 months. Medical resource utilisation data were collected on all study patients, and hospital billing data were collected for both index and follow-up hospitalisations for any cause. The costs of the SAPIEN valve were projected at $30.000. The objectives of the study were to combine cost data with survival and quality of life (QoL) data in order to estimate the 12-month cost-effectiveness of TAVR compared with AVR. The secondary objective was to explore potential differences in costs and cost-effectiveness of TAVR vs. SAVR for the transfemoral and transapical populations.

The PARTNER A cohort randomised patients with severe, symptomatic aortic stenosis and high surgical risk to either TAVR (N=348) or SAVR (N=351), and followed them for a minimum of 12 months. The PARTNER A study was designed to test the SAPIEN valve against surgery in high-risk patients. Patients randomised to TAVR had a *transfemoral-first approach*; only when the patient was unsuitable for transfemoral valve delivery did they undergo a transapical procedure. This type of study design is biased towards finding more favourable results with transfemoral TAVR.

Quality of life data of the PARTNER A trial was presented by David Cohen. He showed that there was a quality of life benefit of transfemoral TAVR compared to surgery at one month, but similar benefits at later time points. For the small group of transapical patients (n=104) the quality of life measurements tended to be slightly better with surgical AVR at six months only. From a clinical standpoint this is difficult to explain.

Transfemoral TAVR provided small but significant advantages in 12-month quality adjusted life expectancy. TAVR was associated with higher procedural costs, but slightly lower index hospitalisation and costs at one year. The study also indicated that for the transapical approach there was no difference in quality of life compared to SAVR at one year and the costs were somewhat higher compared to surgery (about $10,000/patient) due to the same length of hospital stay as with surgery. Transcatheter aortic valve replacement therefore seems an economically attractive intervention especially for the transfemoral approach.

STACCATO

In the STACCATO trial patients were randomised to transapical TAVR or surgical AVR. The design of the trial can be criticised. The

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PCR online

DOI: 10.4244/EIJV7I8A143

only inclusion criteria was that patients had to be older than 70 years of age. As a result, the enrolled patients had a mean STS score of only 3.1 and 3.4 in the TAVR and SAVR groups, respectively. So far TAVR has only been investigated in high-risk or inoperable patients, while this trial looked at patients at low risk for SAVR.

The primary endpoint of the trial was a composite of all-cause death, stroke, and renal failure requiring haemodialysis.

The sample-size calculation of the trial was based on data that did not correspond to current outcomes. A surgical event rate of 13.5% was anticipated, which, based on data from the STS database, is far too high. The STS score of 3.1-3.4% corresponds to similar mortality rates, and is the same as reported by O'Brien et al.[3] This mortality risk coincides with only a 1.5% stroke rate (total event rate would be ±5%). Although the addition of renal failure requiring haemodialysis would increase the event rates somewhat, this will never be 13.5%.

In the TAVR arm, only a 3% event rate was expected, which is much lower than in most European registries or the PARTNER trial. Two Danish centres participated after more than 40 TAVR procedures had been performed. Whether these were transfemoral or transapical cases was not presented.

The trial was first stopped after inclusion of 11 of the 200 planned patients due to three adverse events in the TAVR group. The inclusion and exclusion criteria were modified and after enrolling 70 patients the study was stopped again due to an excess of events in the transapical patients. The events that occurred, however, are more related to TAVR in general than to the transapical route. Primary endpoints included one patient who died on the waiting list, two major strokes (day 16 and 27), one left coronary blockage and one patient that needed dialysis. Other events were TIA (n=1), left main occlusion during balloon valvuloplasty (n=1), aortic rupture (n=1), severe paravalvular leakage (n=2), valve embolisation (n=1), abnormally positioned heart (n=1) and bleeding complication (n=1). It is clear that only the bleeding event might possibly be attributed to the transapical route.

Multislice computed tomography (MSCT) was not used in the pre-operative assessment for valve sizing, and this could have led to valve under-sizing and the high rate of paravalvular leakage[4]. MSCT could also have been used to assess the annulus to left main distance and potentially avoid coronary ostia blockage.

The conclusion that "transapical aortic valve replacement is inferior to surgical valve repair" seems not to be justified. Transapical AVR has the advantage of being an antegrade approach as opposed to all the other techniques; the transaortic, subclavian artery and transfemoral being retrograde. This may have potential advantages like reduction of periprocedural strokes due to a minimum of manipulations in the aortic arch.

It is important to note that the STACCATO trial was designed three years ago and the PARTNER trial enrolled patients up until two years ago – techniques have changed since then. In the PARTNER trial, the first generation of the SAPIEN device was used, while in Europe new generation devices and improved techniques are currently employed. Thus the results from these studies cannot be translated to other devices or newer generations of these devices, and new studies with these devices are necessary in order to define the role of transapical valve replacement. Sizing of the valve has improved by the use of MSCT, incisions for transapical replacement have become smaller and the spreading of the ribs reduced, leading to less postoperative pain. The centres in the PARTNER trial did not have any previous experience with TAVR and still achieved remarkably good results. These will improve even further with experience. Procedural times for transapical TAVR were 224 min in the PARTNER US trial much longer than the 132 min in the PARTNER EU trial. The transapical group in the PARTNER trial was rather small; only 104 patients were enrolled at a large number of sites with, therefore, little experience for a technically more demanding procedure than transfemoral replacement. The transfemoral and transapical groups were not powered to look at the quality of life or cost-effectiveness endpoints separately, and it is very likely that in an inexperienced centre the costs will be higher.

The costs of the procedure depend very much on the cost of the device and it is to be expected that in the coming years, with more competition, the costs of the device will come down and transapical TAVR will mimic the cost of surgical AVR.

Conclusion

From the data presented at TCT it is clear that TAVR will play an important role in the future. To which extent the valve will be replaced transfemorally or transapically cannot be concluded from the data, but will need additional research.

Conflict of interest statement

The authors have no conflict of interest to declare.

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