Results from the PARTNER Trial (Cohort A): Transfemoral TAVI Economically Attractive but Transapical TAVI More Costly

The Cost Effectiveness of Transcatheter Aortic Valve Replacement Compared with Surgical Aortic Valve Replacement in Patients with Severe Aortic Stenosis: Results from The PARTNER Trial (Cohort A) study [NCT00530894; Leon MB et al. *NEJM* 2010], presented by Matthew R. Reynolds, MD, MSC, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA, compared transcatheter aortic valve implantation (TAVI) with surgical aortic valve replacement (SAVR) in patients with high operative risk from cohort A of the PARTNER trial. The study combined cost data with survival and quality of life (QoL) data to estimate the 12-month cost-effectiveness of TAVI.

This study was a 12-month analysis that was based on observed survival, QoL, health care resource use, and hospital billing data. The primary effectiveness measure was quality-adjusted life-years (QALYs)

Three populations were analyzed. The primary population (n=647) for the full cost-effectiveness analysis consisted of patients in whom TAVI or SAVR was attempted, with complete follow-up until death or 1 year. The secondary population (n=657) comprised patients in whom TAVI or SAVR was attempted, including patients who withdrew or were lost to follow-up. The per-protocol population (n=647) consisted of those who were analyzed for procedural resource utilization and costs only and excluded patients in whom TAVI or SAVR was abandoned. Due to the significant interaction between treatment effect and access site, TAVI patients were stratified into transfemoral or transapical approach.

Transfemoral Results:

At 12 months, the average QALYs was significantly higher among the 239 patients who underwent transfemoral TAVI compared with the 217 patients who had SAVR (0.659 vs 0.591 QALYs, respectively; difference 0.068, 95% CI, 0.017 to 0.123). Resource use in the per-protocol population was significantly lower for transfemoral TAVI versus SAVR with respect to procedure duration (244±78 vs 330±102 minutes; p<0.001) and total hospital days (10.2 vs 16.4; p<0.001). Major vascular complications were significantly more frequent in transfemoral TAVI patients versus SAVR patients (13.2% vs 3.2%, respectively; p<0.001). Major bleeding was lower in transfemoral TAVI patients versus SAVR patients (9.4% vs 22.6%, respectively; p<0.001). As noted in Table 1, compared with SAVR, patients who were undergoing transfemoral TAVI had higher procedural costs but slightly lower overall index admission total costs. Total 12-month follow-up costs were not significantly different for transfemoral TAVI versus SAVR ($22,251 vs $21,965, respectively; p=0.97).

Table 1. Index Admission Fees.

Fees	Transfemoral TAVI	SAVR	Δ (p value)
Procedure	$34,863	$14,451	
Non-procedure	$31,192	$54,228	
Total MD fees	$4742	$5773	
Total fees	$71,955	$74,452	$2496 (p=0.53)

Transapical Results:

At 12 months, QALYs were lower in the patients who underwent transapical TAVI compared with SAVR (0.570 vs 0.64 QALYs, respectively; difference -0.070, 95% CI, -0.151 to 0.012). Procedural, index admission, and total 12-month costs were increased with transapical TAVI versus SAVR by roughly $11,000.

Dr. Reynolds concluded that for patients with severe aortic stenosis and high surgical risk, TAVI is an economically attractive and possibly dominant strategy compared with SAVR, provided that patients are suitable for the transfemoral approach. Current results for transapical TAVI compared with SAVR are not attractive from a health economic perspective.

PARTNER Cohort B: TAVI Superior to Standard Therapy at Two Years

Transcatheter aortic valve implantation (TAVI) is the recommended treatment for "inoperable" patients with severe aortic stenosis (AS), based on the 1-year results of the PARTNER trial [NCT00530894; Leon MB et al. *NEJM* 2010]. The objective of this PARTNER trial analysis, presented by Raj R. Makkar, MD, Cedars-Sinai Medical Center, Los Angeles, California, USA, was to evaluate the clinical outcomes of TAVI compared with standard therapy at 2 years in patients with inoperable AS (PARTNER Cohort B).

The PARTNER Cohort B randomized 358 inoperable patients with symptoms of severe AS to transfemoral TAVI (n=179) versus standard therapy (n=179). Included patients were NYHA class II or higher and had severe AS (echo valve area of <0.8 cm^2 [EOA index < 0.5 cm^2], mean gradient >40 mm Hg or jet velocity >4.0 m/s) and a >50% risk of death or serious irreversible morbidity with surgical aortic valve replacement as assessed by a cardiologist and two surgeons). The primary endpoint was all-cause mortality over the length of the trial. Other key endpoints were: cardiac mortality, rehospitalization, stroke, NYHA functional class, days alive and out of the hospital, echo-derived valve area, transvalvular gradients, paravalvular aortic regurgitation, and mortality outcomes that were stratified by STS score.

Eleven patients crossed over from standard therapy to TAVI between 1 and 2 years. All-cause mortality (intention to treat; ITT), including crossover patients, was significantly lower at 2 years for patients who were treated with TAVI versus standard therapy (67.6% vs 43.3%, respectively; HR=0.57; 95% CI, 0.44 to 0.75; p<0.0001). Censoring of the crossover patients did not qualitatively change the results.

A landmark analysis was performed among the survivors at 1 year to ascertain whether there was incremental benefit between Years 1 and 2. Among the 1-year survivors, mortality was 18.2% with TAVI versus 35.1% with standard therapy (HR=0.58; 95% CI, 0.37 to 0.92; p=0.019).

Cardiovascular (CV) mortality (ITT, crossover patients censored) was 31.0% with TAVI versus 62.4% with standard therapy (HR=0.44; 95% CI, 0.32 to 0.60; p=0.0001). The rate of repeat hospitalizations (ITT) was 35.0% in the TAVI group versus 72.5% in the standard therapy group (HR=0.41; 95% CI, 0.30 to 0.58; p=0.0001). The days alive out of the hospital was 699 with TAVI versus 355 with standard therapy (p=0.0003). TAVI improved NYHA functional status and decreased Class III/IV symptoms versus standard therapy (17% vs 64%; p<0.001).

There were more neurological events with TAVI versus standard therapy (16.2% vs 5.5%, respectively; p=0.003). The incidence of stroke at 2 years was 13.8% in the TAVI group versus 5.5% in the standard therapy group (HR=2.79; 95% CI, 1.25 to 6.22; p=0.009). After 30 days, differences in stroke frequency were largely due to increased hemorrhagic strokes in TAVI patients.

In patients who were not suitable for surgery, TAVI was superior to standard therapy, with incremental benefit from 1 to 2 years, markedly reducing the rates of all-cause mortality, CV mortality, and repeat hospitalization, with improved NYHA functional status and decreased Class III/IV heart failure symptoms. Importantly, TAVI patients had significantly increased rates of stroke. TAVI was most beneficial in patients without extreme clinical comorbidities.

Dr. Makkar concluded that the 2-year data continue to support the role of TAVI as standard of care for symptomatic patients with AS who are not surgical candidates.

Transapical TAVI Inferior to SAVR in Operable Elderly Patients

Transcatheter aortic valve implantation (TAVI) is a treatment option for patients with aortic valve stenosis who are either high risk or not operative candidates for conventional surgical aortic valve replacement (SAVR). Transfemoral TAVI requires delivery of the valve system through the iliofemoral vasculature and is limited by peripheral vascular disease (PVD) and small vessel caliber. Transapical TAVI is somewhat more invasive than the transfemoral approach but can be utilized in patients with severe PVD or smaller leg vessels. The role of TAVI in patients who are operable candidates or at lower surgical risk has not been studied. Leif Thuesen, MD, Aarhus University Hospital, Aarhus, Denmark, presented the Prospective, Randomized Trial of Transapical Transcatheter Aortic Valve Implantation versus Surgical Aortic Valve Replacement in Operable Elderly Patients with Aortic Stenosis (STACCATO) trial. The objective of STACCATO was to evaluate the safety and efficacy of transapical TAVI in operable, lower-risk patients.

A total of 72 patients were randomized to transapical TAVI (n=34) or SAVR (n=36). Two patients were excluded after randomization. Eligibility criteria included valvular aortic stenosis (valve area <1.0 cm^2), age ≥70 years (later amended to age ≥75 years), patients who were treatable by either transapical TAVI or SAVR, and expected survival >1 year following successful treatment. The primary endpoint was the composite of 30-day all-cause mortality, major stroke, and/or renal failure that required dialysis.

The study design called for inclusion of 200 patients. After inclusion of 11 patients, the study was put on hold due to 3 potentially serious adverse events in the transapical TAVI group. After inclusion and exclusion criteria were modified (increased age limit to 75 years and exclusion for previous heart surgery), the study was resumed.

After randomization of 70 patients, the independent data safety monitoring board recommended study termination