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Letters

RESEARCH CORRESPONDENCE

Is Transcatheter Aortic Valve Replacement Superior to Surgical Aortic Valve Replacement?

A Meta-Analysis of Randomized Controlled Trials

Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of patients with severe, symptomatic aortic stenosis. Randomized controlled trials (RCT) have shown similar outcomes of TAVR versus surgical aortic valve replacement (SAVR) (1-5). In particular, the recently published SURTAVI (Surgical Replacement and Transcatheter Aortic Valve Implantation) and PARTNER (Placement of Aortic Transcatheter Valves) 2 cohort A trials reported a similar risk of death from any cause or disabling stroke in intermediate-risk patients undergoing TAVR or SAVR (3,4).

Considering the release of these new data (4), we performed an updated study-level meta-analysis of published RCTs directly comparing TAVR versus SAVR in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The pre-specified primary endpoint was the risk of death or disabling stroke at 1 year as reported by the included trials in the as-treated or modified intention-to-treat populations. Risk for bias among included RCTs was evaluated with the Cochrane assessment tool. Risk ratio with 95% confidence intervals was calculated using a fixed-effects model, given the lack of heterogeneity across trials. We used the Cochrane Q statistics and I^2 values to test heterogeneity across studies. Analyses were performed using Stata version 14.1 (Stata Corp., College Station, Texas).

Four RCTs (1-4) were included for a total of 5,002 patients randomly allocated to TAVR (n = 2,592) or SAVR (n = 2,410). The NOTION (Nordic Aortic Valve Intervention) trial was excluded because the composite of death or disabling stroke was not reported (5). The overall risk of bias was low in all included studies. As summarized in **Figure 1**, TAVR was associated with a lower risk of death or disabling stroke at 1 year (risk ratio: 0.87; 95% confidence interval: 0.76 to 0.99; p = 0.03) with no evidence of heterogeneity across studies (I^2 = 0%). Sensitivity analyses indicated consistent results irrespective of device used (balloon-expandable vs. self-expandable devices; $p_{interaction}$ = 0.51) and patients' surgical risk profile (high-risk vs. intermediate-risk; $p_{interaction}$ = 0.89). Risk estimates were also consistent after exclusion of each included RCT.

Individual RCTs were designed to demonstrate noninferiority of TAVR to SAVR and were not powered to evaluate superiority in terms of clinical outcomes. Only the U.S. CoreValve High Risk trial reported a significantly lower risk of our pre-specified primary endpoint in the TAVR group (2), whereas the PARTNER 2 trial detected a significant reduction only in the transfemoral access TAVR subgroup (3). Pooling the evidence derived from 4 pivotal RCTs with a total of 5,002 patients, our meta-analysis suggests that a less-invasive transcatheter approach (TAVR with any access site) could provide a significant clinical benefit over a standard surgical strategy in patients with severe, symptomatic aortic stenosis. However, consequences of TAVR-specific adverse events (e.g., residual aortic regurgitation, need for pacemaker implantation, overt or covert cerebral injury, vascular complications) and durability of bioprosthetic transcatheter valves over time could affect long-term outcomes and therefore requires future careful assessment.

The main limitations of our meta-analysis are the lack of patient-level data and the inherent limitations of included trials (unplanned withdrawals in the surgery group, limited use of the latest-generation transcatheter bioprostheses, lack of long-term follow-up, lack of assessment of subclinical valve-leaflet thrombosis).

In conclusion, this meta-analysis indicates that TAVR might be associated with a significantly lower risk of death or disabling stroke at 1 year, irrespective of the type of valve implanted and the surgical risk of treated patients.

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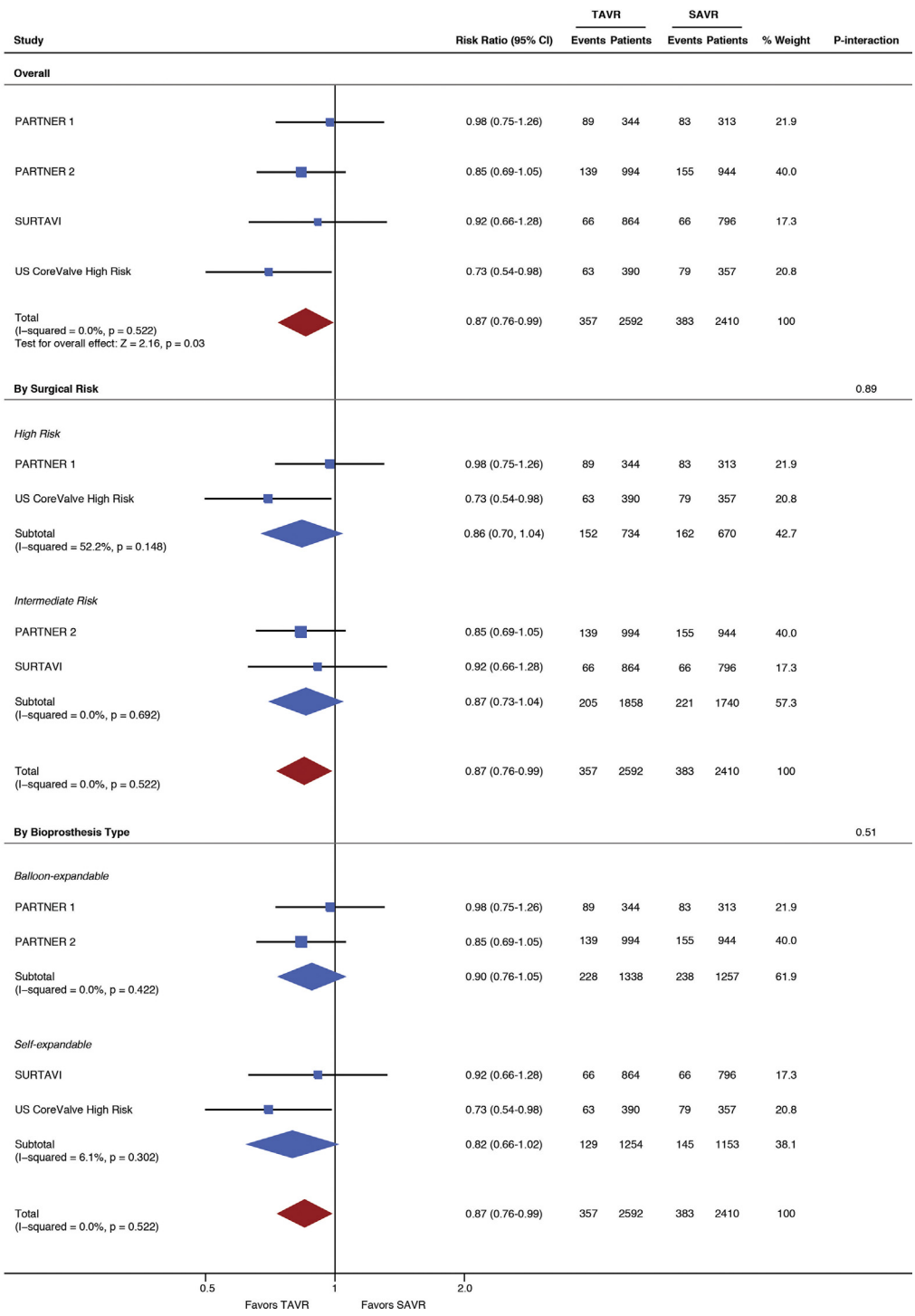
FIGURE 1 Death or Disabling Stroke in Patients Undergoing TAVR Versus SAVR



The extracted number of events was based on as-treated or modified intention-to-treat analysis in each trial. Forest plot displays summary risk ratio and 95% confidence interval for the combined endpoint of death or disabling stroke at 1 year. Sensitivity analyses based on patients' surgical risk and type of transcatheter valve are also shown. CI = confidence interval; PARTNER = Placement of Aortic Transcatheter Valves; SAVR = surgical aortic valve replacement; SURTAVI = Surgical Replacement and Transcatheter Aortic Valve Implantation; TAVR = transcatheter aortic valve replacement.

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RESEARCH CORRESPONDENCE

First Experience With the Coronary Sinus Reducer System for the Management of Refractory Angina in Patients Without Obstructive Coronary Artery Disease

The Coronary Sinus (CS) Reducer (Neovasc Inc., Richmond, British Columbia, Canada) is a percutaneous device implanted in the CS to create a controlled narrowing of the lumen leading to an increase in coronary venous pressure, capillary and arteriolar dilatation, and restoration of the endocardial/epicardial blood flow ratio typically impaired in ischemic myocardium. A single randomized clinical trial and several observational studies have demonstrated Reducer safety and efficacy in patients with obstructive coronary artery disease and refractory angina, who are not candidates for revascularization (1–3). Recurrent angina following successful percutaneous coronary interventions (PCI) is common: a focused analysis of the SYNTAX trial reported a prevalence of recurrent angina of 28.5% at 1 year and 25.9% at 5 years after PCI (4). In particular, patients with refractory angina and evidence of myocardial ischemia despite optimal medical therapy and angiographically successful percutaneous revascularization frequently present to clinicians (5). Coronary microvascular dysfunction seems to be the underlying pathophysiological mechanism.

Because no data are available with regards to Reducer performance in this patient group, we address this issue with this preliminary study.

Between 2015 and 2016 all patients referred to 2 Italian institutions (San Raffaele Hospital, Milan, Italy; ASST Bergamo Est, Bolognini Hospital, Seriate, Italy) undergoing coronary angiography because of chronic stable angina (Canadian Cardiovascular Society [CCS] class 3 to 4) with noninvasive evidence of myocardial ischemia despite optimal medical therapy (OMT) were screened.

Eight patients with evidence of complete revascularization and nonobstructed epicardial coronary arteries (absence of coronary plaques, <50% narrowing in all epicardial coronary arteries, or a negative intracoronary fractional flow reserve test in case of intermediate lesions) underwent compassionate CS Reducer implantation for the treatment of microvascular angina. All patients had previously undergone at least 1 PCI.

Four (50%) patients were women. Median age was 61.5 years (range 50 to 68 years). Seven patients were in CCS class 3, and 1 was in class 4 despite OMT (median number of anti-ischemic drugs used was 3; range 2 to 4). Median left ventricle ejection fraction was 58.0% (interquartile range [IQR]: 55.0% to 61.5%).

No cases of death, need for coronary angiography/PCI, or hospitalization for angina were noted during the follow-up period. Median CCS class improved from 3.0 (3 to 4) to 1.5 (1 to 3) ($p = 0.014$) (**Figure 1A**). At 1 year, this benefit was maintained for 3 of the 5 patients assessed. Discontinuation of at least 1 antianginal agent was possible in 3 of 8 (37.5%) patients.

A significant improvement in most of the questionnaire domains of the Seattle Angina Questionnaire was observed. Physical limitation improved from 46.0 (IQR: 40.5 to 53.3) to 64.0 (IQR: 53.0 to 80.0) ($p = 0.028$), angina stability from 40.0 (IQR: 21.3