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Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Diabetes and Severe Aortic Stenosis at High Risk for Surgery

An Analysis of the PARTNER Trial (Placement of Aortic Transcatheter Valve)

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Objectives The goal of this study was to determine whether a less-invasive approach to aortic valve replacement (AVR) improves clinical outcomes in diabetic patients with aortic stenosis (AS).

Background Diabetes is associated with increased morbidity and mortality after surgical AVR for AS.

Methods Among treated patients with severe symptomatic AS at high risk for surgery in the PARTNER (Placement of Aortic Transcatheter Valve) trial, we examined outcomes stratified according to diabetes status of patients randomly assigned to receive transcatheter or surgical AVR. The primary outcome was all-cause mortality at 1 year.

Results Among 657 patients enrolled in PARTNER who underwent treatment, there were 275 patients with diabetes (145 transcatheter, 130 surgical). There was a significant interaction between diabetes and treatment group for 1-year all-cause mortality ($p = 0.048$). Among diabetic patients, all-cause mortality at 1 year was 18.0% in the transcatheter group and 27.4% in the surgical group (hazard ratio: 0.60 [95% confidence interval: 0.36 to 0.99]; $p = 0.04$). Results were consistent among patients treated via transfemoral or transapical routes. In contrast, among nondiabetic patients, there was no significant difference in all-cause mortality at 1 year ($p = 0.48$). Among diabetic patients, the 1-year rates of stroke were similar between treatment groups (3.5% transcatheter vs. 3.5% surgery; $p = 0.88$), but the rate of renal failure requiring dialysis >30 days was lower in the transcatheter group (0% vs. 6.1%; $p = 0.003$).

Conclusions Among patients with diabetes and severe symptomatic AS at high risk for surgery, this post-hoc stratified analysis of the PARTNER trial suggests there is a survival benefit, no increase in stroke, and less renal failure from treatment with transcatheter AVR compared with surgical AVR. (The PARTNER Trial: Placement of AoRTic TraNscathetER Valve Trial; NCT00530894) (J Am Coll Cardiol 2014;63:1090–9) © 2014 by the American College of Cardiology Foundation

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Diabetes mellitus adversely affects morbidity and mortality for all types of cardiovascular diseases (1,2). In patients with aortic stenosis (AS), diabetes is associated with increased hypertrophic remodeling, decreased left ventricular function, and worse heart failure symptoms (3,4). Diabetes has also been associated with increased morbidity and mortality after surgical aortic valve replacement, even after adjustment for comorbidities such as vascular disease and renal dysfunction

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(5,6). The mechanisms for this additional surgical risk are not completely known, although it is hypothesized that the inflammation, oxidative stress, and reperfusion injury induced by cardioplegia and cardiopulmonary bypass are particularly harmful in the setting of diabetes and hypertrophic ventricular remodeling from chronic pressure overload due to AS, thereby causing adverse short- and long-term consequences (7–13). As such, a less-invasive method of valve replacement that avoids the injurious effects of cardiopulmonary bypass may lead to improved clinical outcomes among these high-risk patients with diabetes. Accordingly, we examined the clinical outcomes of patients at high risk for surgery enrolled in the PARTNER (Placement of Aortic Transcatheter Valve) trial to evaluate whether outcomes varied according to diabetes status after treatment with transcatheter versus surgical aortic valve replacement (14).

Methods

Study population. The design, inclusion and exclusion criteria, and primary results of the high-risk cohort (cohort A) of the PARTNER trial have been reported (14). These patients were at high surgical risk as defined by a predicted risk of death ≥15% by 30 days after surgery. After evaluation of vascular anatomy, patients were included in either the transfemoral placement cohort or the transapical placement cohort and randomized to undergo transcatheter therapy with the Edwards SAPIEN heart valve system (Edwards Lifesciences, Irvine, California) or surgical aortic valve replacement. Some patients did not undergo their assigned procedure due to death, refusal, study withdrawal, and/or pre-treatment clinical deterioration. For the current analysis, we included only patients who were randomized to and received the assigned treatment (as-treated population). The diagnosis of diabetes and other clinical characteristics were determined by the enrolling sites. The study protocol was approved by the institutional review board at each enrolling site, and all patients provided written informed consent.

Abbreviations and Acronyms

AS = aortic stenosis
AVR = aortic valve replacement
CI = confidence interval
HR = hazard ratio
KCCQ = Kansas City Cardiomyopathy Questionnaire

Clinical endpoints. Clinical events, including death (all-cause and cardiac), repeat hospitalizations, stroke, renal failure, major bleeding, myocardial infarction, and vascular complications, were adjudicated by a clinical events committee. The primary endpoint of the PARTNER trial and our analysis was all-cause death at 1 year. A detailed report of the classification of deaths among the diabetic and nondiabetic patients treated with transcatheter or surgical aortic valve replacement in the transfemoral and transapical placement cohorts is provided in Online Table 1. Repeat hospitalizations were defined as hospitalization resulting from symptoms of AS (valve-related deterioration, including heart failure, angina, or syncope) or complications of the valve procedure. Stroke was defined as a focal neurological deficit lasting ≥24 h or a focal neurological deficit lasting <24 h with imaging findings of acute infarction or hemorrhage. Renal failure events were defined as the need for dialysis of any sort (hemodialysis, continuous venovenous hemodialysis, peritoneal). Further details on clinical events definitions are provided in Online Table 2. Many of these clinical event definitions are consistent with the VARC-2 (Valve Academic Research Consortium–2) definitions (e.g., cardiac death, stroke, myocardial infarction), but others differ substantially (e.g., renal failure, major bleeding) (15). An independent core laboratory analyzed all echocardiograms (16). The presence and severity of post-procedural prosthesis–patient mismatch and aortic regurgitation were determined according to VARC-2 criteria (15). The Kansas City Cardiomyopathy Questionnaire (KCCQ), a disease-specific health status measure of heart failure, was used to assess health status (17,18).

Statistical analysis. Continuous variables are summarized as mean ± SD or median (quartile), and they were compared by using the Student *t* test or Mann-Whitney rank sum test as appropriate. Categorical variables were compared by using the chi-square or Fisher exact test. Survival curves for time-to-event variables, based on all available follow-up data, were performed with the use of Kaplan-Meier estimates and were compared between groups with the use of the log-rank test. Cox proportional hazards models were used to calculate hazard ratios (HRs) and to test for interactions. KCCQ overall summary scores were compared by using analysis of covariance to adjust for baseline differences in KCCQ scores between groups. All statistical analyses were performed by using SAS version 9.2 (SAS Institute, Inc., Cary, North Carolina).

a member of the PARTNER trial steering committee and consultant for Edwards Lifesciences, a member of the steering committee for the Portico trial (St. Jude Medical), and a member of the scientific advisory board of Thubrikar Aortic Valve. Dr. Thourani is a member of the PARTNER trial steering committee; and is a consultant for Edwards Lifesciences, Sorin Medical, St. Jude Medical, and DirectFlow. Dr. Waksman is a member of the Speakers' Bureau of Boston Scientific, Medtronic, AstraZeneca, Biotronik, and Abbott Vascular. Drs. Tuzcu, Svensson, Smith, and Leon are unpaid members of the PARTNER Executive Committee; and has received travel reimbursements from Edwards Lifesciences for activities related to these positions. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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