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Comprehensive Analysis of Mortality Among Patients Undergoing TAVR

Results of the PARTNER Trial

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ABSTRACT

BACKGROUND Patients with severe aortic stenosis (AS) who were deemed too high risk or inoperable for conventional aortic valve replacement (AVR) in the PARTNER (Placement of Aortic Transcatheter Valves) trial were randomized to transcatheter aortic valve replacement (TAVR) versus AVR (PARTNER-A arm) or standard therapy (PARTNER-B arm).

OBJECTIVES This study compared when and how deaths occurred after TAVR versus surgical AVR or standard therapy.

METHODS The PARTNER-A arm included 244 transfemoral (TF) and 104 transapical (TA) TAVR patients, and 351 AVR patients; the PARTNER-B arm included 179 TF-TAVR patients and 179 standard therapy patients. Deaths were categorized as cardiovascular, noncardiovascular, or uncategorizable, and were characterized by multiphase hazard modelling.

RESULTS In the PARTNER-A arm, the risk of death peaked after randomization in the TA-TAVR and AVR groups, falling to low levels commensurate with the U.S. population within 3 months. Early risk was less in TF-TAVR patients, resulting in initial superior survival; between 12 and 18 months, risk increased, such that within 2 years, TF-TAVR and AVR patients had similar survival rates. Cardiovascular, noncardiovascular, and uncategorizable deaths for TF-TAVR were 37%, 43%, and 20%, respectively, versus 22%, 41%, and 37%, respectively, for TA-TAVR and 33%, 43%, and 24%, respectively, for AVR. In the PARTNER-B arm, risk with standard therapy was 60% per year; TF-TAVR reduced risk to 20% per year, resulting in 0.5 years of life added within 2.5 years.

CONCLUSIONS In inoperable AS patients, TAVR substantially reduced the risk of cardiovascular death. In high-risk patients, TA-TAVR and AVR were associated with elevated peri-procedural risk more than with TF-TAVR, although cardiovascular death was higher after TF-TAVR. Therefore, TF-TAVR should be considered the standard of care for severely symptomatic inoperable patients or those at high risk of noncardiovascular mortality after conventional surgery. (THE PARTNER TRIAL: Placement of AoRTic TraNscathetER Valve Trial; NCT00530894) (J Am Coll Cardiol 2014;64:158–68) © 2014 by the American College of Cardiology Foundation.

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Symptomatic aortic stenosis (AS) has a dismal prognosis. Despite this, up to two-thirds of patients with severe AS do not undergo surgical aortic valve replacement (AVR) due to their comorbidities (1–6). Thus, after some small, but promising feasibility studies and trials, the applicability of transcatheter aortic valve replacement (TAVR) for these high-risk patients has evolved rapidly (6–10). The 2-armed randomized PARTNER (Placement of Aortic Transcatheter Valves) trial was designed to test the procedure for safety and effectiveness. Patients in the PARTNER-A arm were considered high risk for surgery; patients in the PARTNER-B arm were considered inoperable.

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This detailed analysis reports on deaths among patients in both trial arms, including those that occurred between randomization and the procedure, focusing on when and how the deaths occurred (11–14).

METHODS

PATIENTS. A total of 3,105 patients were presented to a Web-based review panel for potential inclusion in the PARTNER trial. All patients were required to have a Society of Thoracic Surgeons (STS) score of >10%, unless comorbidities that were not part of the score assessment were present (e.g., radiation heart disease, cirrhosis, or porcelain calcification of the aortic arch without a distal landing site for a replacement graft). Patients were required to have an aortic valve area <0.8 cm^2 and either a mean transaortic gradient of >40 mm Hg or a transvalvar velocity of >4.0 m/s (11–14). High-risk patients were required to have a >15% probability of 30-day mortality, as deemed by the surgeon, irrespective of the STS score.

Of the reviewed patients, 699 were considered high risk for open surgery (PARTNER-A), and 358 were considered inoperable (PARTNER-B). Before randomization, a determination was made as to whether each patient was suitable for the transfemoral (TF) or the transapical (TA) approach. Of PARTNER-A patients, 348 were randomized to TAVR—244 to a TF approach (TF-TAVR) and 104 to a TA approach (TA-TAVR) (depending on vascular access)—and 351 were randomized to AVR (12).

The inoperable PARTNER-B subset was defined as those patients who were deemed by 2 cardiac surgeons as having a >50% probability of death or irreversible severe morbidity after AVR (11). Of PARTNER-B patients, 179 were randomized to TF-TAVR and 179 to standard therapy (medical management with or without balloon aortic valvotomy).

Baseline patient characteristics were similar among subsets of both PARTNER-A and PARTNER-B arms (11–14). The trial was approved by the U.S. Food and Drug Administration and the institutional review board at each participating center. Additional trial details are described in earlier publications (11–14). All patients who underwent TAVR received the Edwards Sapien valve (Edwards Lifesciences, Irvine, California).

ENDPOINTS. The primary endpoint was all-cause mortality from time of randomization (intent-to-treat). The Online Appendix provides analyses of as-treated mortality in PARTNER-A. Secondary endpoints were categories and subcategories of deaths.

All-cause mortality. Median follow-up was 2 years for PARTNER-A patients, and 10% of the survivors were followed for more than 3 years; 1,154 patient-years of follow-up were available for analyses. Median follow-up was 1.3 years for PARTNER-B patients, and 10% of the survivors were followed for more than 3.2 years; 541 patient-years of follow-up were available for analyses. All time-related depictions were truncated at 2.5 years. Mortality information was current as of April 25, 2012.

Categorization of deaths. The PARTNER Trial Clinical Events Committee reviewed documentation concerning every death that occurred after randomization, initially blinded according to randomized group, then unblinded. Each death was

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis
AVR = surgical aortic valve replacement
CL = confidence limit
STS = Society of Thoracic Surgeons
TA = transapical
TAVR = transcatheter aortic valve replacement
TF = transfemoral

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