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Sex-Specific Outcomes of Transcatheter Aortic Valve Replacement With the SAPIEN 3 Valve

Insights From the PARTNER II S3 High-Risk and Intermediate-Risk Cohorts

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ABSTRACT

OBJECTIVES The purpose of this study was to identify sex-specific outcomes of intermediate risk patients undergoing transcatheter aortic valve replacement with the SAPIEN 3 valve.

BACKGROUND A survival difference has been observed in women as compared with men in inoperable and high-risk patients receiving early-generation balloon-expandable valves for transcatheter aortic valve replacement (TAVR). Whether a sex-specific outcome difference persists with newer-generation valves and in lower-risk patients is unknown.

METHODS The PARTNER (Placement of Aortic Transcatheter Valves) II S3 trial included high-risk (HR) (Society of Thoracic Surgeons risk score >8% or heart team determination) and intermediate-risk (IR) (Society of Thoracic Surgeons risk score 4% to 8% or heart team determination) patients with severe symptomatic aortic stenosis who were treated with TAVR with the SAPIEN 3 valve. Patient characteristics and clinical outcomes at 30 days and 1 year were compared by sex.

RESULTS Between October 2013 and December 2014, 1,661 patients were enrolled: 583 were HR (338 men, 245 women) and 1,078 were IR (666 men, 412 women). In both cohorts, women were more likely than men to be frail (22% vs. 13%; $p < 0.001$), but less likely to have comorbid conditions of renal insufficiency, coronary artery disease, atrial fibrillation, or chronic obstructive pulmonary disease. Women were more likely to receive ≤23-mm valves (74.1% vs. 11.1%; $p < 0.001$) and were less likely to receive 29-mm valves (1.4% vs. 35.1%; $p < 0.001$). In the combined cohorts, there was no difference in mortality for women compared with men at 30 days (2.0% vs. 1.2%; $p = 0.20$) or 1 year (9.3% vs. 10.2%; $p = 0.59$). There were no differences in disabling stroke or any stroke at 30 days or 1 year; however, women had an increased rate of minor stroke at 30 days (2.1% vs. 0.7%; $p = 0.01$). Female sex was associated with increased major vascular complications (7.9% vs. 4.4%; $p = 0.003$), but not with moderate or severe paravalvular regurgitation. Notably, similar outcomes regarding sex-specific outcomes were obtained within stratified analyses of the HR and IR cohorts.

CONCLUSIONS The study found no apparent sex-specific differences in survival or stroke in this trial of TAVR. This may reflect the changing demographic of patients enrolled, use of newer-generation valves with more sizes available, and more accurate valve sizing techniques. (J Am Coll Cardiol Intv 2018;11:13–20) © 2018 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

MDCT = multidetector computed tomography

PVL = paravalvular leak

S3 = SAPIEN 3

S3HR = SAPIEN 3 valve in high risk or inoperable

S3i = SAPIEN 3 valve in intermediate risk

SAVR = surgical aortic valve replacement

STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality

TA = transapical

TAo = transaortic

TAVR = transcatheter aortic valve replacement

TF = transfemoral

Over the previous decade, transcatheter aortic valve replacement (TAVR) has become the therapy of choice for patients with severe aortic stenosis who are not candidates for surgery (1,2) or who are at high risk for morbidity or mortality due to surgery (3,4). More recently, TAVR with early-generation balloon-expandable valves has been shown to have comparable outcomes to surgical aortic valve replacement (SAVR) for patients at intermediate risk (5). When using third-generation balloon-expandable valves, TAVR may have superior results as compared with SAVR in intermediate-risk patients (6).

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Female sex has been demonstrated as an independent risk factor for adverse outcomes after SAVR (7–11). A comprehensive analysis of sex-specific differences among inoperable and high-risk patients undergoing TAVR within the clinical trial structure of the PARTNER (Placement of Aortic Transcatheter Valves) trial, which used the balloon-expandable SAPIEN transcatheter valve (Edwards Lifesciences, Irvine, California), clearly demonstrated that women had lower mortality than men did at 1 year following TAVR despite a higher incidence of vascular and bleeding complications (12). Similarly, an analysis of intermediate-risk patients randomized to TAVR in the PARTNER IIA trial, which used the second-generation SAPIEN XT transcatheter valve (Edwards Lifesciences), demonstrated a trend toward lower 2-year mortality in women as compared with men despite a higher incidence of vascular complications in women (13). Recently, an analysis of the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) registry confirmed a mortality difference for women undergoing TAVR in a large, "real-world" cohort of patients with an earlier-generation SAPIEN valve (14). The mortality difference in these studies was felt in part to be due to the comorbid differences between women and men.

As compared with the SAPIEN and SAPIEN XT valves, the newer-generation SAPIEN 3 (S3) (Edwards Lifesciences) valve has a reduced profile and an additional outer cuff to enhance paravalvular sealing (15). The PARTNER II S3 observational study was implemented to evaluate the safety and efficacy of the S3 valve in both intermediate-risk (S3i) and high-risk or inoperable (S3HR) patients (6). We sought to perform a comprehensive analysis of sex-specific differences in patients undergoing TAVR in the S3i and S3HR cohorts to determine whether the difference associated with female sex after TAVR using earlier generation valves persists. We report the baseline demographic characteristics and core laboratory-assessed echocardiographic parameters of women and men treated with S3 TAVR, as well as adjudicated 30-day and 1-year outcomes stratified by sex.

METHODS

STUDY DESIGN AND PATIENTS. The PARTNER II S3 trial incorporated 2 parallel prospective, multicenter, active treatment cohorts of patients with

consultant for Edwards Lifesciences. Dr. Williams has served as a consultant for and received research funding from Edwards Lifesciences. Dr. Hahn has had echocardiographic core lab contracts with Edwards Lifesciences (no direct compensation). Dr. Webb has served as a consultant for Edwards Lifesciences; and a member of the PARTNER trial executive committee (no direct compensation). Dr. Svensson owns equity in Cardiosolution and Valvexchange as well as intellectual property with Postthorax; has served as a member of the PARTNER trial executive committee (no direct compensation); and has served as the chairman of the PARTNER trial publications office. Dr. Kirtane has received institutional research grant support from Boston Scientific, Abbott Vascular, Medtronic, Abiomed, Eli Lilly, CathWorks, Philips, Siemens, and Spectranetics. Dr. Douglas has received institutional grant support from Edwards Lifesciences and has had echocardiographic core lab contracts with Edwards Lifesciences (no direct compensation). Dr. Cohen has received research grant support from Edwards Lifesciences, Medtronic, Abbott Vascular, and Boston Scientific; and has served as a consultant for Edwards Lifesciences and Medtronic. Ms. Alu has served as a consultant for Claret Medical. Dr. Tuzcu has served as a member of the PARTNER Trial Executive Committee (no direct compensation). Dr. Makkar has received grants from Edwards Lifesciences and has served as a consultant for Abbott Vascular, Cordis, and Medtronic. Dr. Herrmann has received institutional grant support from Edwards Lifesciences, Medtronic, St. Jude Medical, Boston Scientific, Bayer, and Abbott Vascular; and has served as a consultant for Edwards Lifesciences. Dr. Babaliaros has served as a consultant for Abbott Vascular and Edwards Lifesciences. Dr. Thourani has served as a consultant for Edwards Lifesciences. Dr. Leon has served as a member of the PARTNER trial executive committee (no direct compensation). Dr. Kodali has served as a consultant and on the steering committee for Edwards Lifesciences; has served on the scientific advisory board for Thubrikar Aortic Valve, Inc., and Dura Biotech; and owns equity in Thubrikar Aortic Valve, Inc. Dr. Mack has served as a member of the PARTNER trial executive committee (no direct compensation) and as the co-principal investigator of the Edwards Lifesciences PARTNER III trial. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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