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Incidence, Predictors, and Prognostic Impact of Late Bleeding Complications After Transcatheter Aortic Valve Replacement

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ABSTRACT

BACKGROUND The incidence and prognostic impact of late bleeding complications after transcatheter aortic valve replacement (TAVR) are unknown.

OBJECTIVES The aim of this study was to identify the incidence, predictors, and prognostic impact of major late bleeding complications (MLBCs) (≥30 days) after TAVR.

METHODS Clinical and echocardiographic outcomes of patients who underwent TAVR within the randomized cohorts and continued access registries in the PARTNER (Placement of Aortic Transcatheter Valves) trial were analyzed after stratifying by the occurrence of MLBCs. Predictors of MLBCs and their association with 30-day to 1-year mortality were assessed.

RESULTS Among 2,401 patients who underwent TAVR and survived to 30 days, MLBCs occurred in 142 (5.9%) at a median time of 132 days (interquartile range: 71 to 230 days) after the index procedure. Gastrointestinal complications (n = 58 [40.8%]), neurological complications (n = 22 [15.5%]), and traumatic falls (n = 11 [7.8%]) were identified as the most frequent types of MLBCs. Independent predictors of MLBCs were the presence of low hemoglobin at baseline, atrial fibrillation or flutter at baseline or 30 days, the presence of moderate or severe paravalvular leak at 30 days, and greater left ventricular mass at 30 days. MLBCs were identified as a strong independent predictor of mortality between 30 days and 1 year (adjusted hazard ratio: 3.91; 95% confidence interval: 2.67 to 5.71; $p < 0.001$).

CONCLUSIONS MLBCs after TAVR were frequent and associated with increased mortality. Better individualized and risk-adjusted antithrombotic therapy after TAVR is urgently needed in this high-risk population. (THE PARTNER TRIAL: Placement of AoRTic TraNscathetER Valve Trial; NCT00530894) (J Am Coll Cardiol 2014;64:2605–15) © 2014 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

BARC = Bleeding Academic Research Consortium

GI = gastrointestinal

MLBC = major late bleeding complication

PVL = paravalvular leak

TAVR = transcatheter aortic valve replacement

Periprocedural bleeding events after transcatheter aortic valve replacement (TAVR) are frequent and have been shown to be associated with worse prognosis (1-6). Although early bleeding complications after TAVR are related mainly to procedural or technical factors (e.g., vascular complications) (7-9), the cause, nature, and impact of late bleeding (after 30 days) in this population remain unknown. Given the advanced age and the presence of multiple comorbidities, including atrial fibrillation (AF) or coronary artery disease, among the currently treated TAVR population (10-20), it is to be expected that late bleeding events, especially in the context of routine dual-antiplatelet therapy and/or anticoagulation, will be frequent and will adversely affect long-term prognosis (21). As a first

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step to better define and individualize antithrombotic therapy after TAVR (3,21,22) and to inform future trials for this population, we sought to characterize the incidence, predictors, and impact of major late bleeding complications (MLBCs; ≥30 days) on long-term prognosis after TAVR using pooled data from the multicenter, randomized PARTNER (Placement of Aortic Transcatheter Valves)-1 trial, the randomized continued-access PARTNER trial, and the nonrandomized continued-access PARTNER registry.

METHODS

STUDY POPULATION. The PARTNER-1 trial was a multicenter, randomized clinical trial comparing TAVR with surgical aortic valve replacement for high-risk patients (cohort A) and TAVR with medical therapy for inoperable patients (cohort B) (14,15). After completion of the randomized trial and before commercial approval of the transcatheter heart valve (SAPIEN, Edwards Lifesciences, Irvine, California), additional patients were treated in a randomized continued-access trial as well as in a nonrandomized continued-access registry, with the same inclusion and exclusion criteria as in the randomized trial. All patients had severe native aortic stenosis documented on screening transthoracic echocardiography within 30 days of enrollment and were evaluated by 2 surgeons for assessment of risk with surgical aortic valve replacement. Important exclusion criteria included bicuspid aortic valve disease, ejection fraction <20%, renal failure, severe mitral regurgitation, severe aortic regurgitation, recent gastrointestinal (GI) bleeding, or a recent neurological event. Complete inclusion and exclusion criteria have been presented in the supplementary appendices to previous publications (14,15).

All patients undergoing TAVR received either a 23- or a 26-mm balloon-expandable transcatheter heart valve delivered via either the transfemoral or transapical approach on the basis of vascular access. Annular assessments to determine valve size required were site determined using transthoracic echocardiography, transesophageal echocardiography, or multislice computed tomography. All patients underwent transthoracic echocardiography before discharge and at clinical follow-up assessments, including 1 month, 6 months, and 1 year. The present analysis included all patients who actually underwent TAVR and survived up to 30 days. The institutional review board at each participating site approved the study, and all patients provided written informed consent.

STUDY ENDPOINTS. Bleeding complications were defined according to a modified version of the Valve Academic Research Consortium criteria as described in the PARTNER trial protocol and were restricted to those events that occurred at or after 30 days (14,15,23,24). Bleeding events were classified as either major or minor. MLBCs were defined as a clear site of bleeding that met any 1 of the following criteria: bleeding that caused death; bleeding that caused a new hospitalization or prolonged hospitalization ≥24 h because of treatment, bleeding that required pericardiocentesis or an open and/or endovascular procedure for repair or hemostasis, bleeding that caused permanent disability (e.g., blindness, paralysis, hearing loss), and bleeding that required transfusion of >3 U of blood within a 24-h period. Minor bleeding had to meet all of the following criteria: a bleeding event that did not meet criteria for major bleeding, clear site for bleeding, and loss of hemoglobin >3 g/dl or loss of hematocrit >9%. Adjustment for transfusions was included at 1 g/dl or 3% for each unit of blood. Only major bleeding events are reported in the present analysis.

member of the PARTNER Executive Committee. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Sanjay Kaul, MD, MPH, served as Guest Editor for this paper.
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