JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 72, NO. 3, 2018

PUBLISHED BY ELSEVIER

ORIGINAL INVESTIGATIONS

Hemodynamic Deterioration of Surgically Implanted Bioprosthetic Aortic Valves

Erwan Salaun, MD,[a,b] Haïfa Mahjoub, MD, PhD,[a] Abdellaziz Dahou, MD, PhD,[a] Patrick Mathieu, MD, MSc,[a] Éric Larose, MD, MSc,[a] Jean-Pierre Després, PhD,[a] Josep Rodés-Cabau, MD,[a] Benoit J. Arsenault, PhD,[a] Rishi Puri, MBBS, PhD,[c] Marie-Annick Clavel, DVM, PhD,[a] Philippe Pibarot, DVM, PhD[a]

ABSTRACT

BACKGROUND Dysmetabolic profile has been associated with native aortic valve stenosis. However, there are limited data on the effects of an atherogenic milieu and its potential implications on the structural and hemodynamic deterioration of aortic bioprosthetic valves.

OBJECTIVES This prospective longitudinal study sought to determine the predictors and impact on outcomes of hemodynamic valve deterioration (HVD) of surgically implanted aortic bioprostheses.

METHODS A total of 137 patients with an aortic bioprosthesis implanted for a median time of 6.7 (interquartile range: 5.1 to 9.1) years prospectively underwent a first (baseline) assessment with complete Doppler echocardiography, quantitation of bioprosthesis leaflet calcification by multidetector computed tomography (CT), and a fasting blood sample to assess cardiometabolic risk profile. All patients underwent a second (follow-up) Doppler echocardiography examination at 3 (interquartile range: 2.9 to 3.3) years post-baseline visit. HVD was defined by an annualized change in mean transprosthetic gradient ≥3 mm Hg/year and/or worsening or transprosthetic regurgitation by ≥1/3 class. The primary endpoint was a nonhierarchical composite of death from any cause or aortic reintervention procedure (redo surgical valve replacement or transcatheter valve-in-valve implantation) for bioprosthesis failure.

RESULTS Thirty-four patients (25.6%) had leaflet calcification on baseline CT, and 18 patients (13.1%) developed an HVD between baseline and follow-up echocardiography. Fifty-two patients (38.0%) met the primary endpoint during subsequent follow-up after the second echocardiographic examination. Leaflet calcification (hazard ratio [HR]: 2.58; 95% confidence interval [CI]: 1.35 to 4.82; $p = 0.005$) and HVD (HR: 5.12; 95% CI: 2.57 to 9.71; $p < 0.001$) were independent predictors of the primary endpoint. Leaflet calcification, insulin resistance (homeostatic model assessment index ≥2.7), lipoprotein-associated phospholipase A2 activity (Lp-PLA2 per 0.1 nmol/min/ml increase), and high level of proprotein convertase subtilisin/kexin 9 (PCSK9) (≥305 ng/ml) were associated with the development of HVD after adjusting for age, sex, and time interval since aortic valve replacement.

CONCLUSIONS HVD identified by Doppler echocardiography is independently associated with a marked increase in the risk of valve reintervention or mortality in patients with a surgical aortic bioprosthesis. A dysmetabolic profile characterized by elevated plasma Lp-PLA2, PCSK9, and homeostatic model assessment index was associated with increased risk of HVD. The presence of leaflet calcification as detected by CT was a strong predictor of HVD, providing incremental risk-predictive capacity. (J Am Coll Cardiol 2018;72:241–51) © 2018 by the American College of Cardiology Foundation.

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Institut Universitaire de Cardiologie et de Pneumologie de Québec/Québec Heart & Lung Institute, Laval University, Quebec City, Québec, Canada; [b]Centre de Résonance Magnétique Biologique et Médicale (CRMBM), UMR 7339, Centre National de la Recherche Scientifique, Aix-Marseille Université, Marseille, France; and the [c]Cleveland Clinic Coordinating Center for Clinical Research (C5R), Cleveland, Ohio. Dr. Pibarot has received research grants from Edwards Lifesciences and Medtronic for echocardiography core lab analyses in transcatheter aortic valve replacement. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Blase Carabello, MD, served as Guest Editor for this paper.

Manuscript received December 15, 2017; revised manuscript received March 18, 2018, accepted April 17, 2018.

ISSN 0735-1097/$36.00
https://doi.org/10.1016/j.jacc.2018.04.064

ABBREVIATIONS AND ACRONYMS

AVR = aortic valve replacement

CI = confidence interval

CT = computed tomography

HDL = high-density lipoprotein

HOMA = homeostatic model assessment

HR = hazard ratio

HVD = hemodynamic valve deterioration

LDL = low-density lipoprotein

LDLR = low-density lipoprotein receptor

Lp-PLA2 = lipoprotein-associated phospholipase A2

PCSK9 = proprotein convertase subtilisin/kexin 9

Aortic valve disease is the most frequent valvular heart disease and the most frequent cause of valve procedure in high-income countries (1). The prevalence of this disease is expected to increase dramatically in the coming decades due to the aging of the population and increase in the rates of cardiometabolic diseases such as type 2 diabetes (2). Aortic valve replacement (AVR) is indicated when aortic stenosis is severe and symptoms and/or left ventricle systolic dysfunction occur (3). The ratio of bioprostheses versus mechanical valves used for AVR has increased markedly in the past decade. This temporal change is in large part related to: 1) the low thrombogenicity of bioprostheses and the fact that they do not require lifetime anticoagulation; 2) the improvement in valve hemodynamics, particularly in the small bioprosthetic sizes; and 3) the introduction of transcatheter AVR (4,5). However, compared with mechanical prostheses, bioprostheses have a shorter durability with quasi-systematic deterioration within 20 years of implantation (5–7). Most studies have established the rate of bioprosthesis deterioration on the basis of valve reintervention due to bioprosthesis failure (8–10). However, reintervention may underestimate the rate of bioprosthesis degeneration, given that older patients with severe comorbidities may not undergo reintervention despite significant valve deterioration. Several recent studies, recommendations, and position statements propose to define bioprosthesis degeneration upon the basis of valve structural and hemodynamic deterioration assessed by Doppler echocardiography and other imaging modalities (7,11–13).

SEE PAGE 252

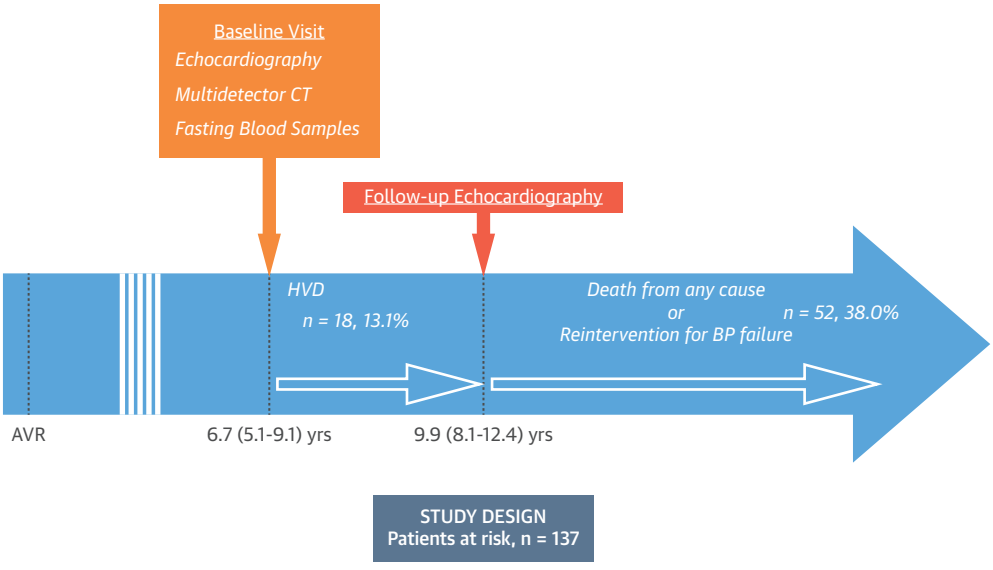
Some retrospective or cross-sectional studies reported that metabolic syndrome (14), lipid-mediated inflammation (11,15,16), and leaflet mineralization assessed by computed tomography (CT) (17,18) were associated with hemodynamic valve deterioration (HVD).

The aim of this prospective longitudinal study was to determine the predictors and impact on outcomes of bioprosthesis HVD following surgical AVR.

METHODS

STUDY POPULATION. Two hundred and three patients who underwent isolated (except coronary artery bypass grafting) bioprosthetic AVR with at least 3 years of follow-up were prospectively recruited in the study. The population characteristics and methods of this study have been previously reported (11). Briefly, Doppler echocardiography, multislice CT examination, and blood sample analyses were

FIGURE 1 Study Design and Follow-Up



AVR = aortic valve replacement; BP = bioprosthetic; CT = computed tomography; HVD = hemodynamic valve deterioration.