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Standardized Definitions for Bioprosthetic Valve Dysfunction Following Aortic or Mitral Valve Replacement

JACC State-of-the-Art Review

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ABSTRACT

Bioprosthetic valve dysfunction (BVD) and bioprosthetic valve failure (BVF) may be caused by structural or nonstructural valve dysfunction. Both surgical and transcatheter bioprosthetic valves have limited durability because of structural valve deterioration. The main objective of this summary of experts participating in a virtual workshop was to propose standardized definitions for nonstructural and structural BVD and BVF following aortic or mitral biological valve replacement with the goal of facilitating research reporting and implementation of these terms in clinical practice. Definitions of structural BVF, based on valve reintervention or death, underestimate the true incidence of BVF. However, definitions solely based on the presence of high transprosthetic gradient at a given echocardiogram during follow-up overestimate the incidence of structural BVD and BVF. Definitions of aortic or mitral structural BVD must therefore include the confirmation by imaging of permanent structural changes to the leaflets alongside evidence of deterioration in valve hemodynamic function at echocardiography follow-up. (J Am Coll Cardiol 2022;80:545-561)

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ABBREVIATIONS AND ACRONYMS

BVD = bioprosthetic valve dysfunction

BVF = bioprosthetic valve failure

DVI = Doppler velocity index

HALT = hypo-attenuated leaflet thickening

LV = left ventricle

PPM = prosthesis-patient mismatch

RLM = restricted leaflet motion

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

Bioprosthetic valve dysfunction (BVD) and bioprosthetic valve failure (BVF) may be caused by structural or nonstructural reasons. Bioprosthetic valves have limited durability because of structural valve deterioration. It is unknown whether transcatheter valves will have long-term durability that is similar to surgical valves. There are challenges to accurate delineation of the prevalence and consequences of BVD and BVF. Historical definitions of structural BVF, based on valve reintervention or death, underestimate the true incidence and timing of BVF because they only capture the most severe cases.[1] Furthermore, many patients with severe BVD may not undergo valve reintervention because they refuse or are considered too high risk. Deaths may not be classified as valve-related despite structural BVD directly or indirectly contributing to the death. For all of these reasons it is important to define BVD using imaging rather than intervention. However, earlier definitions solely based on the presence of high transprosthetic gradient overestimate the incidence of structural BVD and BVF because they also include nonstructural dysfunction, such as prosthesis-patient mismatch (PPM).

Recent statements, including European Association of Cardio-Thoracic Surgery/European Association of Percutaneous Coronary Intervention, VIVID (Valve-in-Valve International Database), and VARC 3 (Valve Academic Research Consortium-3) redefined structural BVD based on identification of morphologic and hemodynamic valve deterioration of aortic bioprosthetic valves at echocardiographic follow-up.[2-4] There are currently no standardized definitions of morphologic and hemodynamic valve deterioration of mitral bioprosthetic valves. In October 2021, the Heart Valve Collaboratory[5] convened a virtual workshop to discuss and address these issues and propose standardized definitions of BVD and BVF.

HIGHLIGHTS

- Both surgical and transcatheter aortic and mitral bioprosthetic valves have limited durability and are prone to structural valve deterioration.
- Consideration only of valve-related reintervention or death underestimates the incidence of structural BVD.
- Definition of structural BVD requires confirmation by imaging of permanent structural changes in the leaflets, struts, or stent and hemodynamic deterioration.

The main objective of this expert consensus document is to propose or complement standardized definitions and measurement methods of: nonstructural and structural BVD and BVF following aortic or mitral biological valve replacement. These definitions should support standardized reporting in research and help guide clinical practice.

1. DEFINITIONS AND ASSESSMENT OF BVD AND BVF

1.1. ASSESSMENT OF AORTIC BVD. Imaging of the structure and function of the prosthetic valve is essential in the assessment of the presence, stage, and category of BVD, and transthoracic echocardiography (TTE) is the primary modality used for this purpose. However, computed tomography (CT) may provide important incremental information regarding the etiology of BVD. Although American guidelines

and Tel-Aviv University, Tel-Aviv, Israel; [t]University of Michigan Health, Ann Arbor, Michigan, USA; [u]Heart Valve Voice US, Washington, DC, USA; [v]Department of Cardiovascular Surgery, Houston Methodist Hospital, Houston, Texas, USA; [w]Cardiovascular Center, Bad Oeynhausen, Germany; [x]Baylor Scott and White, The Heart Hospital, Plano, Texas, USA; [y]CHU Stat Tilman, Liège, Belgium; [z]Department of Cardiovascular Surgery, Marcus Valve Center, Piedmont Heart Institute, Atlanta, Georgia, USA; and the [aa]Hart Long Centrum Leiden, Leiden University, Leiden, the Netherlands. *This paper reflects the views of the authors and does not necessarily represent the practices, policies, requirements, or recommendations of the U.S. Food and Drug Administration. The mention of commercial products, their sources, or their use in connection with material reported here is not to be construed as either an actual or implied endorsement of such products by the Department of Health and Human Services. Furthermore, the use of the word "required," "must," or "should" in the document is not intended to indicate a U.S. Food and Drug Administration requirement. †More details about the Heart Valve Collaboratory can be found at https://www.heartvalvecollaboratory.org/. This paper is a summary of a virtual workshop organized by the Heart Valve Collaboratory and held on October 1-2, 2021.

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recommend TTE follow-up following biological surgical aortic valve replacement (SAVR) at baseline, 5 years, 10 years, and annually thereafter, recent appropriate use recommendations state that it may be appropriate to perform follow-up TTE imaging <3 years following SAVR, particularly in the setting of small prostheses and elevated transvalvular gradients.[6] It is the opinion of the writing group that following SAVR or transcatheter aortic valve replacement (TAVR) with a bioprosthetic valve, it is recommended to perform a TTE at baseline, ideally between 1 and 3 months postprocedure, at 1 year, and annually thereafter, or at any time if any new symptoms occur or if complications are suspected.[7,8] **Table 1** summarizes the key recommendations for the measurements of the echocardiographic parameters of bioprosthetic valve hemodynamic function. Particular attention should be paid to the measurements of the left ventricular (LV) outflow tract diameter and velocity, which are often challenging in the presence of a surgical or transcatheter prosthetic valves.

Figure 1 describes the 4-step algorithm for the detection, staging, and categorization of aortic BVD and BVF. The presence of any of the clinical or echocardiographic abnormalities described in Step 1 of **Figure 1** should raise the suspicion of BVD and trigger further TTE assessment and other confirmatory examinations if necessary (transesophageal echocardiography [TEE], multidetector CT, or cardiac catheterization), to confirm the presence of BVD (**Table 2**). In Step 2, the assessment of valve leaflet morphology and mobility by TTE and other imaging modalities is key to differentiate between the possible etiologies of BVD: ie, nonstructural BVD, structural BVD, valve thrombosis, and valve endocarditis (**Figure 1, Table 3**).

Step 3 consists of the assessment of any change, from baseline to follow-up TTEs, in the morphology or function of the bioprosthetic valve during follow-up to confirm the presence of BVD and determine the stage of BVD progression: Stage 1: morphologic valve deterioration without significant hemodynamic changes; Stage 2: moderate hemodynamic valve deterioration; Stage 3: severe hemodynamic valve deterioration (**Figure 1, Table 4**). The absence of morphologic or hemodynamic valve deterioration (Stage 1, 2, or 3) does not exclude the presence of nonstructural BVD, whereas presence of Stage 2 or 3 implies that morphologic valve changes are present (Stage 1) (**Central Illustration**).

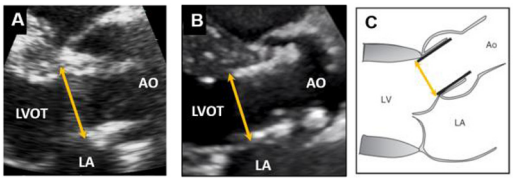
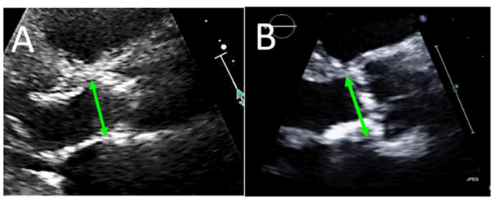
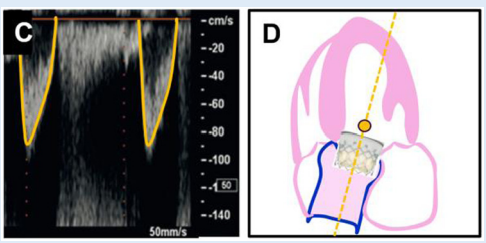
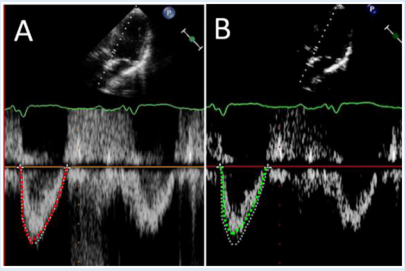
1.2. NONSTRUCTURAL BVD. Nonstructural BVD is defined as any abnormality, not intrinsic to the valve device, resulting in hemodynamic valve dysfunction (**Figure 1, Table 2**). Examples include paravalvular regurgitation; subvalvular pannus overgrowth; inappropriate positioning (including procedural malposition and postdeployment migration) or sizing (undersizing or oversizing); and PPM. Pannus has been classified as nonstructural BVD in VARC-3 because it is not related to a deterioration of the structure of the bioprosthetic valve per se. However, the development of a pannus may lead to acquired and irreversible BVD that may ultimately require reintervention.

Paravalvular regurgitation and PPM are 2 important causes of nonstructural BVD with no morphologic abnormalities of the bioprosthetic valve leaflets themselves (**Central Illustration**). TEE may be helpful to differentiate a paravalvular regurgitation (nonstructural BVD) vs a transvalvular regurgitation (ie, structural BVD). These nonstructural BVDs are already present at the outset of the initial valve replacement procedure and they generally remain stable during follow-up. However, in some rare cases, paravalvular regurgitation may improve or worsen during follow-up or may not be present at the time of implantation but develop during follow-up, generally as a consequence of valve endocarditis. Hence, PPM as well as the vast majority of paravalvular regurgitation cases cannot be classified as Stage 1, 2, or 3 BVD: ie, no evidence of morphologic or hemodynamic valve deterioration during follow-up (**Figure 1, Table 4**). Nonstructural BVD can, nonetheless, lead to BVF and eventually require reintervention (**Central Illustration**).

Aortic PPM is defined as an indexed effective orifice area (EOA) $\leq$0.85 cm^2/m^2; and severe PPM as an indexed EOA $\leq$0.65 cm^2/m^2 (**Figure 1**). Lower cutoff values of indexed EOA (ie, $\leq$0.70 and $\leq$0.55 cm^2/m^2 for moderate and severe PPM, respectively) should be applied to identify aortic PPM in obese patients (body mass index $\geq$30 kg/m^2). More details on the methods used to define aortic PPM are described in the companion paper.[6]

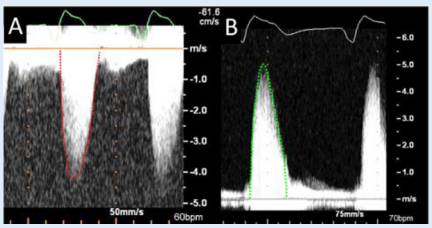
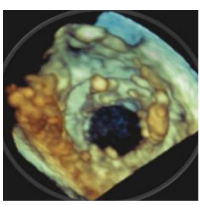
1.3. STRUCTURAL BVD. Structural BVD is defined as permanent changes intrinsic to the valve, including the bioprosthetic valve leaflets, stent, sewing ring or struts (**Figure 1, Tables 2 and 4**). Examples of structural BVD include leaflet wear and tear, disruption, flail leaflet, leaflet fibrosis, and/or calcification and thickening, as well as strut or stent fracture or deformation compromising valve hemodynamic performance. Hence, the diagnosis of structural BVD requires that criteria for Stage 1 BVD are met with documentation by TTE or other imaging modalities (ie, TEE or CT) of irreversible structural changes to

TABLE 1 Recommendations for Doppler Echocardiographic Measurements and Calculations Required to Assess Bioprosthetic Valve Hemodynamic Function

Echocardiographic Parameter	Measurement and Calculation	Caveats and Recommendations
Timing of TTE examinations	Aortic and mitral bioprostheses • Prehospital discharge • Baseline: between 1 and 3 mo • 1 y • Annually beyond 1 y	The assessment of the changes in structure and function of the bioprosthetic valves between the baseline and follow-up TTE is key to allow early detection of BVD. Such assessment requires a comprehensive baseline TTE between 1 and 3 mo postprocedure and routine annual TTE follow-up thereafter.
LVOT diameter by 2D echocardiography for calculation of left ventricular stroke volume: The LVOT diameter is measured from outer to outer edge of the stent or ring just below the sewing ring for surgical bioprostheses (A) or the stent for transcatheter bioprostheses (B and C).	Aortic bioprostheses 	Because the native aortic annulus and prosthetic aortic valve sewing ring remain relatively stable, to reduce interexamination variability in the measurement of AVA and MVA, it is recommended to use as standard whichever of the first FU visit or the baseline postprocedural echocardiogram gives the clearer LV outflow diameter.
The LVOT diameter is measured from inner to inner edge of native structures at or just below the level of the native aortic annulus (A). In the setting of ectopic calcification in the LVOT, annulus, or anterior mitral leaflet, the diameter measurement should ignore this calcium and measure to the base of the anterior mitral valve leaflet (B).	Mitral bioprostheses (native aortic valve)  LVOT Area = 0.785 × (LVOT diameter)^2	
LVOT flow velocity by pulsed wave Doppler for calculation of left ventricular stroke volume: The LVOT velocity is measured by placing the pulsed-wave Doppler sample just apical (ie, proximal) to the ventricular aspect of the prosthesis sewing ring or stent (C and D) in systole.	Aortic bioprostheses 	The pulsed wave sample volume should remain apical (or proximal) to the sewing ring or stent frame in systole. Thus, depending on LV function, the diastolic position of the sample volume may appear as much as 1-1.5 cm apical to the systolic position. Unlike in the setting of a native aortic valve, a closure click is not typically seen because the sample volume remains apical to the bioprosthetic leaflets.
Pulsed wave Doppler of laminar flow just proximal to flow acceleration. The modal velocity should be traced to measure LVOT VTI and not the faint higher velocity profile. (A) (red line) An incorrectly traced Doppler signal. Reducing the gain or increasing the reject will result in a modal velocity profile (green tracing, B).	Aortic and mitral bioprostheses 	
Calculation of Stroke volume The stroke volume across the aortic valve is calculated by multiplying the LVOT area by the velocity-time integral of the LVOT flow measured by pulsed-wave Doppler.	LVOT SV = LVOT Area × LVOT VTI	

Continued on the next page

TABLE 1 Continued

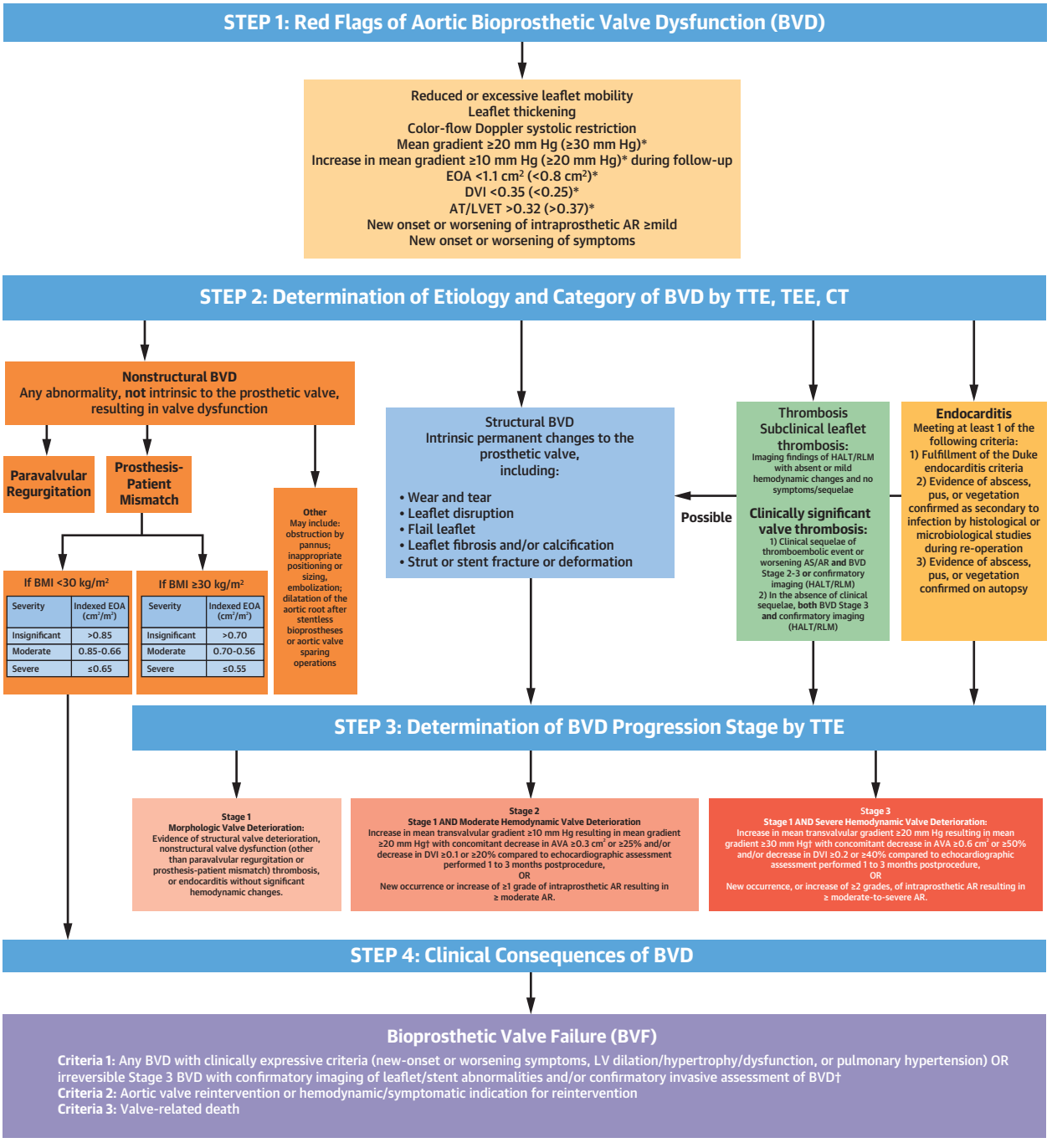
Echocardiographic Parameter	Measurement and Calculation	Caveats and Recommendations
Bioprosthetic valve flow velocity by continuous wave Doppler Continuous wave Doppler performed from any imaging window that obtains the highest velocity, with the densest, most uniform continuous wave spectral profile. Apical windows (A) may not yield a higher velocity than a nonapical window (B, right parasternal window). Peak velocity, mean gradient and aortic VTI are measured. From these measurements, effective AVA and DVI are calculated.	Aortic bioprostheses  Aortic Valve Area = LVOT SV ÷ Aortic VTI Doppler Velocity Index = LVOT VTI ÷ Aortic VTI	Aortic bioprostheses The probe position for acquisition of the peak velocity is most often dependent on patient-specific anatomy; thus, it will not often change unless the position of the prosthesis changes the direction of the main transaortic flow. To reduce interexamination variability in the measurement of AVA, DVI, and mean gradient, it is recommended to use the same window for continuous-wave Doppler interrogation of aortic bioprosthetic valve flow for all baseline and follow-up echocardiograms in a given patient. The aortic DVI decreases with hemodynamic deterioration of aortic bioprosthetic valves.
Continuous wave Doppler derived from the apical 4-chamber view. Peak velocity, mean gradient, and mitral VTI are measured. From these measurements, effective MVA and DVI are calculated.	Mitral bioprostheses  Mitral Valve Area = LVOT SV ÷ Mitral VTI Doppler Velocity Index = Mitral VTI ÷ LVOT VTI	Mitral bioprostheses The LVOT SV can be used as a substitute for mitral SV in the absence of ≥ moderate AR or MR. However peak and mean gradient (as well as velocity time integral) may be affected both by the construct of the valve as well as by the assumptions of the modified Bernoulli equation and thus may reduce the accuracy of the continuity equation in this setting. The mitral DVI increases (vs decreases for aortic DVI) with hemodynamic deterioration of mitral bioprosthetic valves. Both stenosis and regurgitation of mitral bioprostheses result in increase in mitral DVI.
Anatomic mitral valve area by 3-dimensional echocardiography and planimetry	Mitral bioprostheses 	The measurement of the anatomic MVA of mitral bioprosthesis by planimetry is challenging. The "anatomic" MVA is often larger than the "effective" area measured by the continuity equation because of the flow contraction that occurs downstream of the valve orifice.

AO = aorta; AVA = aortic valve area; DVI = Doppler velocity index; FU = follow-up; LA = left atrium; LV = left ventricle; LVOT = left ventricular outflow tract; MVA = mitral valve area; SV = stroke volume; VTI = velocity time integral.

the bioprosthetic valve (**Table 3, Central Illustration**). The process of structural valve deterioration typically starts with Stage 1: ie, structural changes with no deterioration in valve hemodynamic function; then progresses to Stage 2 with moderate hemodynamic valve deterioration; then to Stage 3 with severe hemodynamic valve deterioration; and ultimately BVF (**Table 4**). However, there are exceptions; eg, major and acute structural changes to the valve leaflets, such as leaflet prolapse, tear, or perforation, may lead to severe hemodynamic valve deterioration (ie, Stage 3) and BVF immediately. Hence, the stages are not necessarily sequential in all patients.

The finding of a high transprosthetic gradient (>20 mm Hg) and/or small valve effective orifice area (EOA) (<1.2 cm^2) or low Doppler velocity index (DVI) (<0.35) at a given TTE during follow-up are red flags but are not sufficient to confirm the presence and etiology of BVD. Indeed, an elevated transprosthetic gradient may be caused by a severe PPM in the absence of any acquired prosthetic valve stenosis because of thrombosis or structural valve deterioration. This is why a change in morphology and hemodynamic deterioration are necessary for the definition of structural BVD (**Figure 2, Table 4**). The key hemodynamic changes that support the diagnosis of structural BVD are a significant increase in gradient with concomitant decrease in EOA or DVI and/or new-onset or worsening of transvalvular aortic regurgitation (**Table 4**). Hence, unless the gradient is very high (≥50 mm Hg) and valve structure is clearly abnormal, a diagnosis of structural BVD or BVF should not be established and reintervention should

FIGURE 1 **Detection, Staging, and Categorization of Aortic Bioprosthetic Valve Dysfunction and Failure**



This figure presents a 4-step algorithm for detection, staging, and categorization of aortic BVD. *Red flags with higher level of suspicion of BVD. †Invasive measurement of mean gradient and valve effective orifice area can be performed by using cardiac catheterization, when clinical and/or echocardiographic red flags of BVD (Step 1) are present but permanent structural abnormalities of leaflet/stent cannot be confirmed by TTE or other imaging modalities (TEE or CT). Adapted with permission from Généreux et al.[4] AR = aortic regurgitation; AS = aortic stenosis; AT = acceleration time; BMI = body mass index; BVD = bioprosthetic valve dysfunction; CT = computed tomography; DVI = Doppler velocity index; EOA = effective orifice area; FU = follow-up; HALT = hypo-attenuated leaflet thickening; LVET = left ventricular ejection time; RLM = reduced leaflet motion; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

TABLE 2 Standardized Definitions of Bioprosthetic Valve Dysfunction and Failure

Categories of BVD
Structural BVD
• Intrinsic permanent changes to the prosthetic valve leaflets or stent, including leaflet wear and tear, disruption, flail leaflet, leaflet fibrosis and/or calcification, stent fracture, or deformation.
• See Tables 4 and 5 for definitions of Stages 1, 2, and 3 BVD.
• Subclinical: Imaging findings of permanent changes to the leaflets or stent with absent or mild hemodynamic changes AND no symptoms/sequelae.
• Clinically significant: 1) Stage 2 or 3 BVD with clinically expressive criteria (new-onset or worsening symptoms, LV dilation/hypertrophy/dysfunction, or pulmonary hypertension); 2) in the absence of symptoms or sequelae, both hemodynamic valve deterioration Stage 2 or 3 and confirmatory imaging of morphologic leaflet/stent abnormalities and/or confirmatory invasive hemodynamic assessment of valve hemodynamic dysfunction.
Nonstructural BVD
• Any abnormality, not intrinsic to the prosthetic valve, resulting in valve dysfunction. Examples include residual intraprosthetic or paraprosthetic regurgitation; pannus, tissue, or suture; inappropriate positioning or sizing; prosthesis-patient mismatch; and valve embolization.
Valve thrombosis
• Subclinical leaflet thrombosis: Imaging findings of hypo-attenuated (CT) or hypo-echogenic (echocardiography) leaflet thickening and/or reduced leaflet motion with absent or mild hemodynamic changes AND no symptoms/sequelae.
• Clinically significant valve thrombosis: 1) symptoms or clinical sequelae of thrombo-embolic event with imaging findings of leaflet thickening and/or reduced leaflet motion; 2) in the absence of symptoms and clinical sequelae, both hemodynamic valve deterioration Stage 2 or 3 and confirmatory imaging (leaflet thickening and/or reduced leaflet motion).
Valve endocarditis
• Meeting at least 1 of the following criteria: 1) fulfillment of the Duke endocarditis criteria; 2) evidence of abscess, pus, or vegetation confirmed as secondary to infection by histological or microbiological studies during reoperation; 3) evidence of abscess, pus, or vegetation confirmed on autopsy.
Criteria of BVF
Criteria 1: Any significant bioprosthetic valve dysfunction with clinically expressive criteria (new-onset or worsening symptoms, LV and/or RV dilation/hypertrophy/dysfunction, or pulmonary hypertension) OR Stage 3 hemodynamic valve deterioration related to permanent changes to the prosthetic valve with confirmatory imaging of morphologic leaflet/stent abnormalities and/or confirmatory invasive assessment of valve hemodynamic dysfunction.
Criteria 2: Valve reintervention or hemodynamic/symptomatic indication for valve intervention.
Criteria 3: Valve-related death.[a]

[a]Cardiovascular mortality presumed to be associated with bioprosthetic valve dysfunction. This Table is adapted with permission from Généreux et al.[4]

BVD = bioprosthetic valve dysfunction; BVF = bioprosthetic valve failure; CT = computed tomography.

not be considered on the sole basis of a high gradient and/or a small aortic valve area (AVA) or DVI at a single TTE during follow-up.

1.4. VALVE THROMBOSIS. Valve thrombosis may be divided into subclinical thrombosis and clinically significant thrombosis (Table 2). If leaflet thrombus is suspected, either by TTE (increase in gradient or reduced leaflet motion) or because of a clinical event (thromboembolic events, heart failure), further investigation by contrast-enhanced CT or TEE should be performed to confirm the diagnosis (Table 3). On CT, the definition of clinical leaflet thrombosis currently requires the presence of both hypo-attenuated leaflet thickening (HALT) and reduced leaflet motion (RLM).[9] Hypo-attenuation affecting leaflet motion is considered synonymous with leaflet thrombus.[4] Subclinical leaflet thrombosis is considered when imaging findings of HALT/RLM or hypoattenuation affecting leaflet motion are present but with no or mild valve hemodynamic deterioration and no symptoms/sequelae (Figure 1, Table 2). Subclinical thrombosis may resolve spontaneously without any treatment in up to 50% of cases (Tables 2 and 4).[10] At the present time, there is no evidence that subclinical leaflet thrombosis has significant impact on clinical outcome, and there is thus no rationale for anticoagulation therapy in the presence of this abnormality. Clinically significant valve thrombosis requires the following: 1) clinical sequelae of a thromboembolic event or worsening stenosis or regurgitation, and hemodynamic valve dysfunction or confirmatory imaging (HALT/RLM); and 2) in the absence of clinical sequelae, both BVD Stage 3 (ie, severe hemodynamic valve deterioration) and confirmatory imaging (HALT/RLM) (Figure 1, Tables 2 and 4). BVD related to clinical valve thrombosis generally resolves with anticoagulation therapy with a vitamin K antagonist, but it may recur following the end of treatment. In some cases, it may evolve to valve leaflet fibrosis and calcification and thus become irreversible (ie, structural BVD), eventually leading to BVF and reintervention (Figure 1, Central Illustration). Further studies and guidelines are needed to determine which type and duration of anticoagulation regimen is required for the prevention and treatment of valve leaflet thrombosis following TAVR or SAVR.

TABLE 3 Multimodality Imaging of Morphological Abnormalities of Valve Leaflets or Stent for Determination of the Type of Bioprosthetic Valve Dysfunction

	Prosthesis-Patient Mismatch	Valve Thrombosis	Pannus	Valve Endocarditis	Structural Valve Deterioration
TTE/TEE	Normal valve leaflet morphology and mobility	Diffuse or focal hypo-echogenic leaflet thickening (>2 mm) of at least 1 leaflet	Dense fixed hyper-echogenic tissue involving periannular region or sewing ring	Presence of vegetation(s)	Diffuse or focal hyper-echogenic leaflet thickening (>2 mm) of at least 1 leaflet
		Normal or reduced leaflet mobility	Normal leaflet morphology	Valve leaflet thickening	Reduced mobility and/or torn/avulsed/perforated leaflets
		Paucity (restriction) of color Doppler transvalvular flow	Leaflet mobility may be normal or abnormal	Possible torn/avulsed/perforated leaflets or reduced leaflet mobility	Paucity (restriction) of color Doppler transvalvular flow
				Paravalvular complications: abscess, pseudo-aneurysm, fistula, dehiscence	
Multidetector CT					
Noncontrast CT	No leaflet calcification	No leaflet calcification	No leaflet calcification	No leaflet calcification	Leaflet calcification
Contrast-enhanced CT	Normal leaflet morphology and mobility	Hypo-attenuated leaflet thickening (HALT)	Hypodense semicircular or circular structure along and beneath the valve ring/stent	Paravalvular complications: vegetations, abscess, pseudo-aneurysm, fistula, dehiscence	Calcific or noncalcific hyper-dense leaflet thickening affecting leaflet motion
		Hypo-attenuation affecting leaflet motion (HAM) (possible)			
		Reduced leaflet motion (RLM) (possible)			Reduced leaflet motion (RLM) (possible)
Nuclear imaging					
^{18}F-NaF PET/CT	No ^{18}F-NaF uptake at the level of the bioprosthetic valve leaflets [a]	Increased ^{18}F-NaF uptake at the level of the bioprosthetic valve leaflets (possible)[a]	Unknown	Increased ^{18}F-NaF uptake at the level of the bioprosthetic valve leaflets (possible)	Increased ^{18}F-NaF uptake at the level of the bioprosthetic valve leaflets (possible)[a]
^{18}F-FDG PET/CT	No increased ^{18}F-FDG uptake at the level of the valve or paravalvular region[a]	Unknown	Unknown	Increased ^{18}F-FDG uptake at the level of the bioprosthetic valve and paravalvular region	No increased ^{18}F-FDG uptake at the level of the bioprosthetic valve or paravalvular region[a]

[a]For research use.
^{18}F-FDG = 18F-fluorodeoxyglucose; CT = computed tomography; PET = positron emission tomography; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

1.5. VALVE ENDOCARDITIS. Bioprosthetic valve endocarditis is defined by at least 1 of the following criteria: 1) fulfillment of the Duke endocarditis criteria; 2) evidence of abscess, pus, or vegetation confirmed as secondary to infection by histological or microbiological studies during reoperation; and 3) evidence of abscess, pus, or vegetation confirmed on autopsy (**Figure 1, Tables 2 and 3**). Endocarditis is often associated with morphologic and hemodynamic valve deterioration, and may thus lead to Stage 2 or 3 BVD (stenosis and/or regurgitation) (**Table 4**). CT and positron emission tomography (PET)-CT may provide important incremental information for the diagnosis of endocarditis and of complications such as abscess (**Table 4**). Endocarditis-related BVD may resolve with intravenous antibiotics or may lead to BVF and require reintervention (**Figure 1, Central Illustration, Table 2**).

1.6. BIOPROSTHETIC VALVE FAILURE. All categories of BVD (ie, nonstructural, structural, thrombosis, or endocarditis) may cause symptoms, heart failure, or death, and/or require valve reintervention. Thus, defining criteria of BVF remains an important clinical metric of valve durability and a trigger for reintervention (Step 4 in **Figure 1**). However, compared with redo surgery, transcatheter valve-in-valve (ViV) procedures are often relatively straightforward with favorable anatomy; thus, the threshold for reintervention is another important consideration in defining the clinical impact of BVD. **Table 2** shows the definitions of the 3 criteria of BVF previously proposed by EACPI/European Association of Cardio-Thoracic Surgery and VARC-3.[2,4] Criteria 1 BVF includes the following: 1) any BVD (nonstructural, structural, thrombosis, or endocarditis) associated

TABLE 4 Standardized Definitions of the Stages of BVD Following Biological Aortic Valve Replacement

Stage 1: Morphological Valve Deterioration • Evidence of structural valve deterioration, nonstructural valve dysfunction (other than paravalvular regurgitation or prosthesis-patient mismatch), thrombosis, or endocarditis without significant hemodynamic changes (see Table 3)
Stage 2: Moderate Hemodynamic Valve Deterioration[a] • Morphological valve deterioration (Stage 1) AND • Increase in mean transvalvular gradient ≥10 mm Hg resulting in mean gradient ≥20 mm Hg[b] with concomitant decrease in AVA ≥0.3 cm^2 or ≥25% and/or decrease in DVI ≥0.1 or ≥20% compared with echocardiographic assessment performed 1 to 3 mo postprocedure (or discharge if not available) OR New occurrence or increase of ≥1 grade of intraprosthetic AR resulting in ≥ moderate AR
Stage 3: Severe Hemodynamic Valve Deterioration[a] • Morphological valve deterioration (Stage 1) AND • Increase in mean transvalvular gradient ≥20 mm Hg resulting in mean gradient ≥30 mm Hg[b] with concomitant decrease in AVA ≥0.6 cm^2 or ≥50% and/or decrease in DVI ≥0.2 or ≥40% compared with echocardiographic assessment performed 1 to 3 mo postprocedure (or discharge if not available) OR New occurrence, or increase of ≥2 grades, of transvalvular AR resulting in severe AR

[a]When assessing the presence and severity of hemodynamic valve deterioration, it is important to differentiate true hemodynamic changes vs interechocardiography variability in the measurement of gradient, AVA, DVI, or AR (see Table 1). In particular, one should use the same window for continuous-wave Doppler interrogation when comparing gradients in early (1 to 3 months) postprocedural echocardiography vs follow-up echocardiography. Each case with potential hemodynamic valve deterioration should be individually adjudicated to confirm presence, stage, and etiology. Hemodynamic valve deterioration may be caused by structural valve deterioration but also by nonstructural dysfunction including valve thrombosis and endocarditis. The assessment of valve leaflet morphology and structure as well as clinical features (fever, blood culture, and so on) and change in valve and clinical status over time are key to make differential diagnosis between the different etiologies of hemodynamic valve deterioration: structural valve deterioration vs valve thrombosis or endocarditis vs nonstructural dysfunction (prosthesis-patient mismatch or paravalvular regurgitation) (see Table 3). [b]This criteria for hemodynamic dysfunction assumes normal flow. Adapted with permission from Généreux et al.[4]

BVD = bioprosthetic valve dysfunction; other abbreviations as in Table 1.

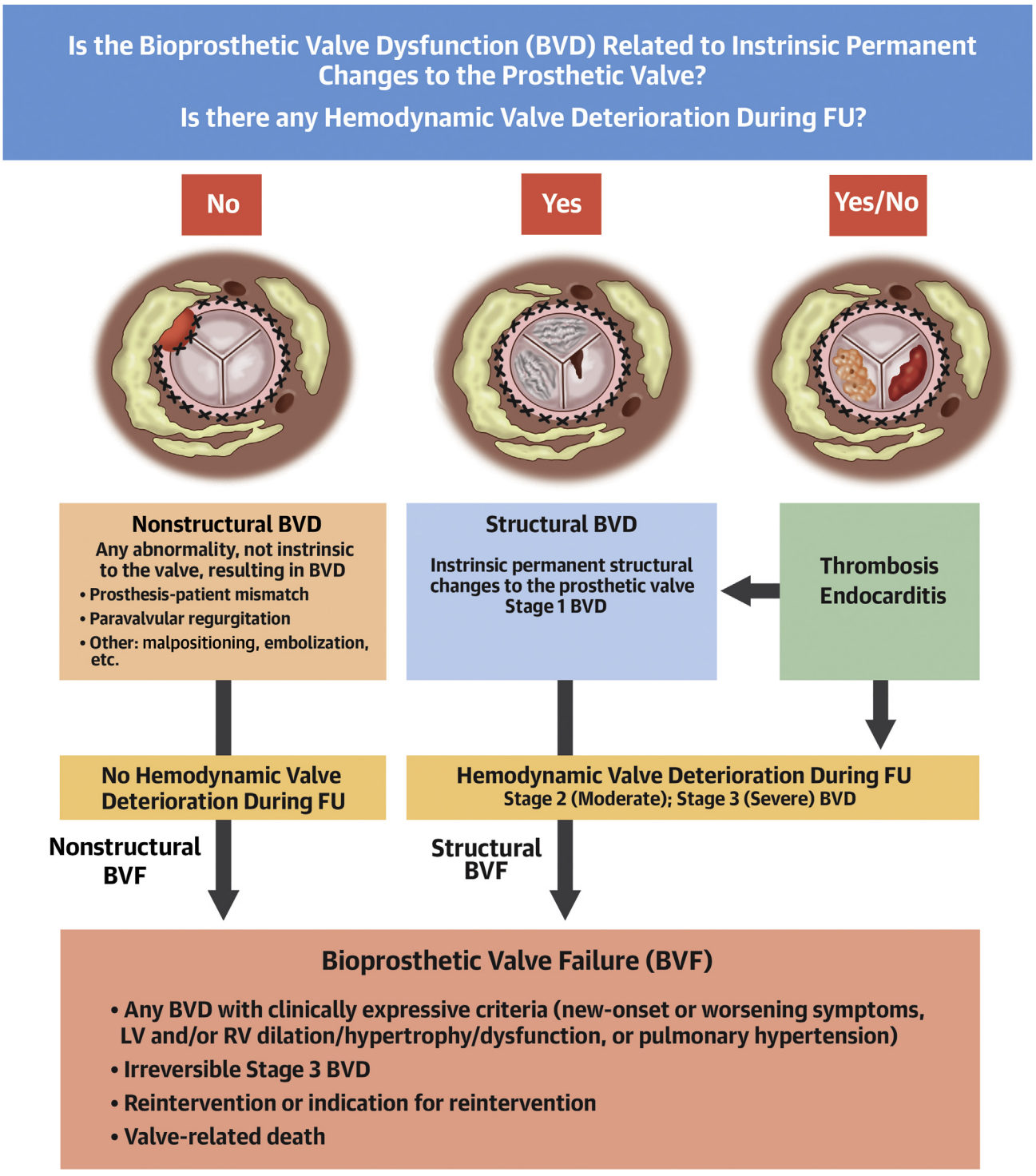
with clinically expressive criteria (ie, new-onset or worsening symptoms, LV dilation/hypertrophy/dysfunction, or pulmonary hypertension); or 2) irreversible Stage 3 BVD in the absence of clinically expressive criteria (Figure 1, Table 2). Criteria 2 consists of valve reintervention or indication of reintervention and implies that criteria for Stage 1 BVF are met. Criteria 3 consists of valve-related death.

2. DEFINITIONS OF MITRAL BVD AND BVF

2.1. ASSESSMENT OF MITRAL BVD. As with aortic bioprostheses, the detection, staging, and categorization of mitral BVD and BVF are primarily based on follow-up of bioprosthetic valve structure and function by TTE (Figure 2, Tables 2 and 5). Other imaging modalities, including CT, may provide important complementary information, especially for the differential diagnosis of the category of mitral BVD (Table 3). Table 5 describes the proposed classification and criteria for the staging of mitral BVD. The transmitral pressure gradient is highly flow- and chronotropy-dependent, and transmitral flow and diastolic filling time may vary extensively from one patient to the other and, for a given patient, from one TTE visit to the other. We therefore do not support the use of an increase in gradient during follow-up (Figure 2, Table 5), but rather the change in DVI during follow-up as the main criterion to suspect the presence of hemodynamic valve deterioration and determine the progression stage of mitral BVD. For mitral bioprostheses, DVI is defined as the ratio of the velocity-time integral of transmitral flow by continuous-wave Doppler to the velocity-time integral in the LV outflow tract by pulsed wave Doppler, and so this parameter increases in the presence of mitral bioprosthetic valve stenosis (Figure 2, Table 5). An increase in DVI >0.6 and/or decrease in mitral valve EOA (measured by continuity equation method), generally associated with a concomitant increase in mean gradient >5 mm Hg during follow-up, is consistent with Stage 2 BVD (ie, moderate hemodynamic valve deterioration). Like aortic bioprosthetic valves, mitral BVD can be categorized into nonstructural and structural dysfunction, thrombosis, and endocarditis (Figure 2, Tables 2 and 3).

2.2. CATEGORIES OF MITRAL BVD. Nonstructural BVD is defined as any abnormality, not intrinsic to the valve device, resulting in mitral valve dysfunction (Figure 2, Central Illustration, Table 2). Examples include paravalvular mitral regurgitation; leaflet entrapment by pannus, chordae, or suture; inappropriate positioning or sizing, and PPM. Mitral PPM is defined as an indexed EOA ≤1.2 cm^2/m^2, and severe PPM refers to an indexed EOA ≤0.9 cm^2/m^2 (Figure 2). As for aortic PPM, lower cutoff values of indexed EOA (≤1.0 and ≤0.75 cm^2/m^2 for moderate and severe PPM, respectively) should be used in obese (body mass index ≥30 kg/m^2) patients. Moderate PPM may occur in 20%-70% of mitral valve replacements, with

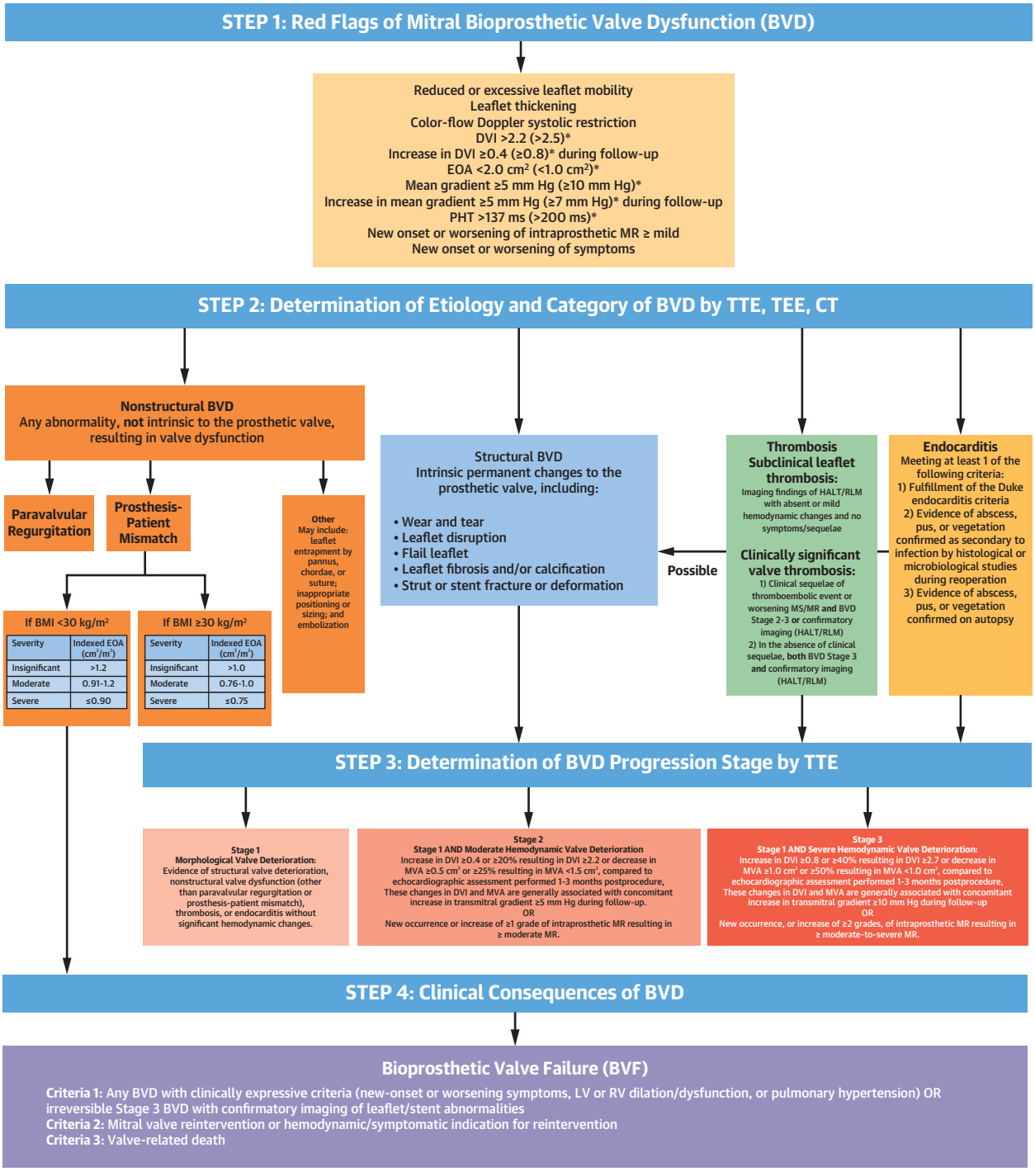
CENTRAL ILLUSTRATION **Classification and Definitions of Bioprosthetic Valve Dysfunction and Failure**



Pibarot P, et al. J Am Coll Cardiol. 2022;80(5):545-561.

This figure presents the classification and main criteria for definition of (aortic or mitral) bioprosthetic valve dysfunction and failure. BVD = bioprosthetic valve dysfunction; BVF = bioprosthetic valve failure; FU = follow-up.

FIGURE 2 **Detection, Staging, and Categorization of Mitral Bioprosthetic Valve Dysfunction and Failure**



This figure presents a 4-step algorithm for detection, staging, and categorization of mitral BVD. *Red flags with higher level of suspicion of BVD. MR = mitral regurgitation; MS = mitral stenosis; other abbreviations as in Figure 1.

TABLE 5 Standardized Definitions of the Stages of BVD following Biological Mitral Valve Replacement

Stage 1: Morphological Valve Deterioration

- Evidence of structural valve device deterioration, nonstructural valve dysfunction (other than paravalvular regurgitation or device/prosthesis-patient mismatch), thrombosis, or endocarditis without significant hemodynamic changes (see Table 3)

Stage 2: Moderate Hemodynamic Valve Deterioration[a]

- Morphological valve device deterioration (Stage 1)

AND

- Increase in DVI ≥0.4 or ≥20% resulting in DVI ≥2.2 or decrease in MVA ≥0.5 cm^2 or ≥25% resulting in MVA <1.5 cm^2, compared with echocardiographic assessment performed 1 to 3 mo postprocedure (or discharge if not available). These changes in DVI and MVA are generally associated with concomitant increase in transmitral gradient ≥5 mm Hg during follow-up[b]

OR

New occurrence or increase of ≥1 grade of MR resulting in ≥ moderate MR

Stage 3: Severe Hemodynamic Valve Deterioration[a]

- Morphological valve deterioration (Stage 1)

AND

- Increase in DVI ≥0.8 or ≥40% resulting in DVI ≥2.5 or decrease in MVA ≥1.0 cm^2 or ≥50% resulting in MVA <1.0 cm^2, compared to echocardiographic assessment performed 1 to 3 mo postprocedure (or discharge if not available). These changes in DVI and MVA are generally associated with concomitant increase in transmitral gradient ≥10 mm Hg during follow-up[b]

OR

New occurrence, or increase of ≥2 grades, of MR resulting in ≥ moderately severe MR

[a]When assessing the presence and severity of hemodynamic valve deterioration, it is important to differentiate true-hemodynamic changes versus inter-echo variability in the measurement of Doppler velocity index, MVA, gradient, or MR (see Table 1). Each case with potential hemodynamic valve deterioration should be individually adjudicated to confirm presence, stage, and etiology. Hemodynamic valve deterioration may be caused by structural valve device deterioration but also by nonstructural dysfunction including thrombosis and endocarditis. The assessment of valve leaflet morphology and structure as well as clinical features (fever, blood culture, and so on) and change in valve and clinical status over time are key to make differential diagnosis between the different etiologies of hemodynamic valve deterioration: structural valve deterioration vs valve thrombosis or endocarditis vs nonstructural dysfunction (prosthesis-patient mismatch or paravalvular regurgitation) (see Table 3). [b]The transmitral gradient is highly flow and chronotropy dependent. Mitral Valve Academic Research Consortium (MVARC) thus recommend to primarily rely on changes in DVI and MVA to identify hemodynamic valve deterioration. Changes in peak E velocity and mean gradient during follow-up are corroborating. It is important to note that, as opposed to aortic valve DVI, mitral DVI increases with hemodynamic valve deterioration.

Abbreviations as in Table 4.

severe PPM seen in 2%-10%.[11] Severe mitral PPM is associated with reduced survival following mitral valve replacement and failure of pulmonary hypertension to regress.[12,13]

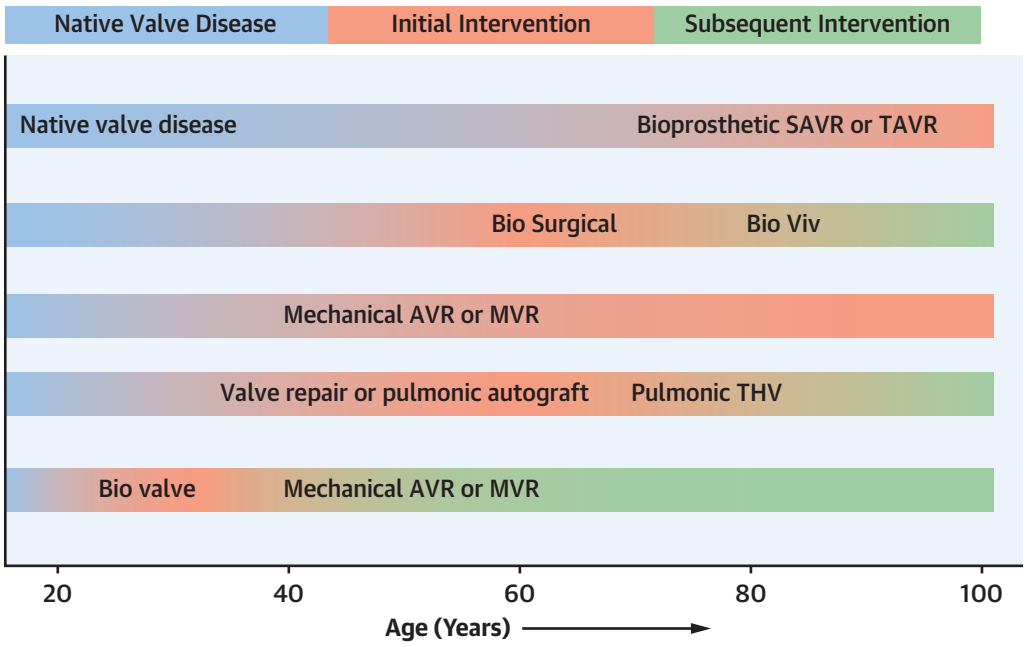
The parameters and criteria for the definition of structural BVD, valve thrombosis, and endocarditis are similar for mitral versus aortic bioprosthetic valves (Figure 2, Tables 2 and 5). The measurement of a high peak E velocity or mean gradient and/or of a high DVI or small mitral valve area at any TTE during follow-up should therefore not be necessarily interpreted as the confirmation of structural BVD and used as a trigger for reintervention. As for aortic bioprostheses, the diagnosis of structural BVD requires the visualization by TTE or other imaging modalities of permanent structural changes to the mitral valve leaflets or stent, and the diagnosis of Stage 2 or 3 structural BVD also required the documentation of significant deterioration of hemodynamic valve function (stenosis and/or transvalvular mitral regurgitation) during follow-up (Tables 3 and 5). TEE is particularly helpful to assess leaflet morphology and the mobility of mitral bioprosthetic valves and to determine the localization and severity of valve regurgitation if any.

2.3. MITRAL BVF. The criteria for defining the presence and stage of mitral BVF are similar to those for aortic BVF (Figure 2, Table 2). Patients with mitral BVF may undergo either surgical or transcatheter reintervention.

3. COMPLEMENTARY METHODS AND FUTURE DIRECTIONS FOR ASSESSING BIOPROSTHETIC VALVE DYSFUNCTION

3.1. CARDIAC CATHETERIZATION FOR ASSESSMENT OF AORTIC BVD. Echocardiographic assessment of native aortic valve stenosis has demonstrated excellent correlation with invasive hemodynamics. Coupled with the ease of assessment and ability to perform multiple studies, echocardiography has become the standard of care for hemodynamic evaluation of native mitral and aortic valve functions with only a limited role for invasive hemodynamics that is reserved for situations with discrepancy between clinical and echocardiographic findings. However, echocardiography was found to be discordant to and overestimate invasive gradients following SAVR and TAVR.[14-17] This overestimation was noted to be more significant in normal prosthetic valves with better correlation with invasive measurements in the presence of prosthetic valve stenosis. The phenomenon has been noted to occur in all valve designs, independent of the aortic dimension and pressure recovery. A recent study of degenerated SAVR valves before ViV TAVR with concomitant echocardiographic and invasive gradients demonstrated no discordance

FIGURE 3 **Potential Trajectories for Valve Disease over a Patient's Lifetime**



The choice of initial and subsequent valve interventions depends on many factors with a key consideration being the durability of the intervention vs the patient's life expectancy, and thus the risk of adverse outcomes or need for repeat intervention. For example, younger patients might need repeat interventions over their lifetime because of bioprosthetic valve deterioration and failure, especially given the limited data on transcatheter aortic valve durability. Of course, patient age serves only as a surrogate for life expectancy; it is crucial to consider other factors affecting remaining life-years, as well as the feasibility of different types of repeat intervention. In addition, other factors important to patients may affect the sequence of interventions. For example, the choice of a mechanical valve precludes a subsequent transcatheter valve-in-valve (ViV) procedure (a transcatheter bioprosthetic valve placed within a previous surgical or transcatheter bioprosthetic valve). On the other hand, a bioprosthetic valve might be chosen in a young patient planning pregnancy or high-impact sports, switching to a mechanical valve later in life. Additional research on potential lifetime trajectories is needed to support some of these potential pathways. AVR = aortic valve replacement; Bio = biological prosthetic valve; MVR = mitral valve replacement; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement; THV = transcatheter heart valve.

in the absence of primary prosthetic valve stenosis with increasing discordance in mixed and primary prosthetic valve regurgitation.[18]

Similarly, when obtained concomitantly under similar hemodynamic conditions immediately post-TAVR, discordance between echocardiography and catheterization was found to occur in both balloon-expandable and self-expanding valve platforms, and to a larger extent in ViV TAVR.[16,17] Immediately after TAVR, discordance >10 mm Hg between echocardiography and catheterization was noted in 9% of patients following native TAVR and in 25% of patients following ViV TAVR.[16] This brings into question the role of balloon valve stent fracture after valve implantation based solely on echocardiographic assessment without invasive corroboration. A study in a small series of patients with increasing echocardiographic gradients to ≥20 mm Hg at midterm post-TAVR follow-up following TAVR, and with no evidence of structural valve deterioration on CT, undergoing concomitant echocardiographic and invasive assessment of aortic valve hemodynamics demonstrated invasive gradients <20 mm Hg in 70% of patients.[19] Discordance at midterm follow-up may suggest a role for invasive confirmation before consideration for aortic valve reinterventions.

The recommendations for the invasive assessment of aortic prosthetic valve hemodynamics by cardiac catheterization as well as the advantages and limitations of this technique are described in details in the companion paper.[6] The main advantages of cardiac catheterization are as follows: 1) it directly measures the blood pressures and pressure gradients vs the velocity-derived pressure gradient obtained by the Bernoulli formula by Doppler echocardiography, and hence is not subjected to the limitations of the simplified Bernoulli equation; and 2) it accounts for the pressure recovery phenomenon and therefore

measures the net transvalvular pressure gradient across the prosthetic valve, which is generally lower than the pressure gradient measured at the level of the vena contracta by Doppler. The main limitation is that the gradients are flow-dependent and may underestimate the presence and severity of BVD in the context of low-flow state. This is a major issue given that ~70% of patients are in low-flow state during the TAVR procedure. It is possible to also measure the EOA by cardiac catheterization, but this requires left and right heart catheterization and is often not done in practice. We thus recommend that invasive measurement of both mean gradient and valve EOA (using Gorlin formula) could be considered to confirm the presence and severity of aortic BVD and before consideration of aortic valve reintervention if high mean gradient (≥30 mm Hg) with DVI <0.35 is present at TTE and any of following situations: 1) no evidence or no adequate visualization of morphologic abnormalities of valve leaflets by TTE, TEE, or CT; and/or 2) presence of symptoms, LV dilation/hypertrophy/dysfunction, pulmonary hypertension, or presence of ambiguous clinical symptoms such as shortness of breath or exercise intolerance (**Figure 1, Tables 3 and 4**).

Limited data is available for the correlation of invasive and echocardiographic mitral valve gradients immediately after mitral valve replacement or on long-term follow-up, and their impact on clinical outcomes following transcatheter and surgical mitral valve replacement is unknown. Hence, for now, we recommend confirming diagnosis, stage, and category of mitral BVD by TTE and other imaging modalities such as TEE and CT. The role of cardiac catheterization for this purpose remains to be demonstrated.

3.2. COMPUTED TOMOGRAPHY. Current detection of BVD relies on echocardiographic or invasive identification of hemodynamic valve dysfunction: a very late finding in the natural history of the disease. The development and application of structural imaging modalities that can detect BVD earlier is therefore a critical clinical need. Calcification is the common final pathway of bioprosthetic valve degeneration. Noncontrast CT calcium scoring scans can detect valve leaflet calcification providing an objective maker of valve degeneration[20]; however, it can frequently be challenging on these scans to differentiate valve leaflet calcium from metallic artefact related to the valve stents struts. Contrast CT angiography provides higher spatial resolution and improved detection of both valve leaflet calcification as well as the detection of pannus and the characteristic appearance of HALT as a marker of valve thrombus formation. 4-dimensional CT allows visualization of leaflet motion and additional information regarding the functional consequences of HALT. Subclinical leaflet thrombosis was reported in 4% of surgical and 13% of transcatheter valves.[10,21] Further work is required to assess the association between these structural abnormalities assessed by multimodality imaging and valve hemodynamics in both the short- and longer-terms. However, assessment of valve structural abnormalities by noncontrast and contrast-enhanced CT may be useful in current clinical practice to identify the etiology of BVD: ie, valve leaflet thrombosis vs pannus vs structural valve deterioration caused by fibrocalcific remodeling of valves leaflets (**Table 3**).

3.3. POSITRON EMISSION TOMOGRAPHY. Molecular PET has also been used to investigate bioprosthetic valve degeneration (**Table 3**). 18F-NaF PET images calcification activity with the valve leaflets and provides an early marker of valve degeneration. In 2 recent multicenter observational studies in patients with both surgical and transcatheter bioprosthetic valves, 18F-NaF PET identified evidence of valve degeneration that was not evident on echocardiography or contrast-enhanced CT and was the most powerful predictor of subsequent deterioration in valve hemodynamics and the development of overt valve failure.[22,23] Further work is required to investigate the more widespread clinical utility of these molecular imaging approaches for the assessment of BVD (**Table 3**). PET-CT is particularly useful when prosthetic valve endocarditis is suspected but TTE and TEE imaging is normal (**Table 3**).

4. IMPLICATIONS FOR LIFETIME MANAGEMENT OF PATIENTS WITH AORTIC OR MITRAL VALVE DISEASE

4.1. SHARED DECISION MAKING IN CHOOSING THE RIGHT VALVE FOR THE RIGHT PATIENT. The intent of surgical or transcatheter intervention is to reduce the hemodynamic burden imposed by native heart valve disease, alleviate symptoms, improve quality of life, and in some instances, extend survival. The choice of valve repair vs replacement hinges on several factors including the patient's expected remaining years of life; the expected durability of the repair or prosthetic valve; imaging (echo and CT) evaluation of valve anatomy; the risk of PPM; the risk of complications; concurrent valve, aortic, or LV disease; vascular access; and patient preferences.[7,8] Thus, the Heart Valve Collaboratory strongly supports an individualized approach by a multidisciplinary heart team, with shared patient decision making.

At the time of the index treatment decision, the following issues should be reviewed: 1) the durability

advantage of a mechanical valve, particularly in younger patients, vs the risks, inconvenience, and lifestyle limitations of lifelong anticoagulation; 2) the possibility of valve repair for mitral disease or a pulmonic autograft procedure (Ross procedure) for aortic disease in younger patients; 3) the risk and time course of bioprosthetic valve deterioration; and 4) options for and feasibility of a repeat procedure if needed.

4.2. PATIENT TRANSITION FROM NATIVE VALVE DISEASE TO PROSTHETIC VALVE DISEASE. Valve replacement palliates but does not completely resolve heart valve disease; something that is not always clear to the patient. The question of how to reconcile patient expectations for management of their valve disease versus actual clinical options is complex (**Figure 3**). Shared decision making can be challenging depending on patient education and clinician's limited understanding of patient preferences.[7] For example, there is wide variation in patient preferences regarding the risk of a repeat valve procedure (eg, durability).[8] Further research to capture patient preferences around this issue would be helpful, along with improved patient education resources and decision aids for both patients and clinicians.

4.3. PREVENTION OF PROSTHETIC VALVE COMPLICATIONS. Patient follow-up does not end with valve replacement, but rather requires establishing a new schedule of surveillance of prosthetic valve performance, ventricular function, and cardiac symptoms, underscoring the importance of a longitudinal relationship between patients and their clinical care team (**Figure 3**). Periodic echocardiographic imaging is a fundamental component of this process. Issues regarding anticoagulation when indicated and antibiotic prophylaxis before dental procedures are reviewed on an ongoing basis. Guidelines recommend routine anticoagulation for 3 months following SAVR or surgical mitral valve replacement, but it is still unclear whether this this treatment is beneficial or harmful after TAVR.[7,8] Bioprosthetic valve durability and the competing risks of thromboembolism and bleeding with mechanical heart valve substitutes are overarching concerns. Other key issues in the long-term management of patients with a prosthetic valve include: 1) optimal dental care and antibiotic prophylaxis for prevention of endocarditis; 2) encouraging healthy lifestyle behaviors (regular exercise, a healthy diet, not smoking, maintaining a normal body size); and 3) primary and secondary cardiovascular risk factor reduction (statin therapy, blood pressure and diabetes management).

4.4. SHARED DECISION MAKING IF VALVE FAILURE OCCURS. Many patients with valvular heart disease are likely to require repeat interventions over their lifetime because of progressive disease after repair or BVF. Early detection of valve hemodynamic deterioration by echocardiography with subsequent intervention before the development of significant structural valve failure may be beneficial for some patients. The type and timing of reintervention is centered on a patient's values and preferences with the goal of improving quality of life and reaching projected life expectancy based on age and medical status (**Figure 3**). This discussion should include all of the therapeutic options, valve types, and durability with risk/benefit ratios that will provide the lowest cumulative risk, best quality of life, and minimal number of subsequent procedures.

5. SUMMARY AND CONCLUSIONS

BVD and BVF following surgical or transcatheter aortic or mitral valve replacement may be caused by structural or nonstructural valve dysfunction (**Central Illustration**). Bioprosthetic valves have limited durability because of structural valve deterioration. Definitions of structural BVF, based on valve reintervention or death, underestimate the true incidence of BVF. However, definitions solely based on the presence of high transprosthetic gradient at a given echocardiogram during follow-up overestimate the incidence of structural BVD and BVF. A high gradient may be caused by severe PPM, which corresponds to nonstructural BVD. Definitions of aortic or mitral structural BVD must thus include the confirmation by TTE, TEE, and/or CT of permanent structural changes to the leaflets (or stent) (ie, Stage 1 BVD) alongside evidence of deterioration in valve hemodynamic function at TTE follow-up (ie, Stage 2 or 3 BVD) (**Central Illustration**).

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Navigate. Dr Abbas has received research grants and consulting fees from Edwards Lifesciences. Dr Dweck has served as a consultant to Edwards Lifesciences and Medtronic; has received research funding from Edwards Lifesciences and Medtronic; and has received speaking fees from NVT. Dr Leipsic has served as a consultant for Circle CVI and MVRX; and has received institutional funding for CT core laboratory analyses from Edwards Lifesciences, Neovasc, Abbott, Medtronic, Boston Scientific, PI Cardia, and Conformal. Dr Rogers has served as a consultant and physician proctor for Edwards Lifesciences and Medtronic; has served as an advisory board member for Medtronic; and holds equity interest in Transmural Systems. Dr Sathananthan has served as a consultant to Edwards Lifesciences and Medtronic; has received research funding from Edwards Lifesciences and Medtronic; and has received speaking fees from NVT. Dr Guerrero has received institutional research grant support from Edwards Lifesciences. Dr Ternacle has served as a consultant for Philips Healthcare and Abbott Medical. Dr Barbanti has served as a consultant for Edwards Lifesciences and Boston Scientific. Dr Généreux has served as a consultant and advisor for and received speaker fees from Abbott Vascular, Abiomed, BioTrace Medical, and Medtronic; has served as a consultant for Boston Scientific, GE Healthcare, iRhythm Technologies, Opsens, Siemens, and Teleflex; has served as a consultant, PI Eclipse Trial, for Cardiovascular System Inc; has served as a consultant, advisor, and proctor for and received speaker fees and research grant from Edwards LifeSciences for the PI EARLY-TAVR and PI PROGRESS trials; has served as a consultant for and has equity in Pi-Cardia, Puzzle Medical, Saranas, and Soundbite Medical Inc; has served as a consultant for and received speaker fees from Shockwave; and has served as a consultant for the PI Feasibility study for 4C Medical. Dr Kaneko has served as a consultant for Edwards Lifesciences, Medtronic, and Abbott Structural. Dr Wood has served as a consultant to and his institution (CCI-CIC) receives grant support from Edwards Lifesciences, Abbott Vascular, and Medtronic. Dr Gillam has served as a consultant to Philips and Bracco; is an advisory board member for Edwards Lifesciences; and has core lab contracts with Edwards Lifesciences, Medtronic, and Abbott for which she receives no direct compensation. Dr Reardon has served as a consultant for Medtronic, Boston Scientific, Abbott Medical, and Gore Medical; all fees for such are to his department. Dr Rodes-Cabau has received institutional research grants from Edwards Lifesciences, Medtronic, and Boston Scientific. Dr Thourani has performed consulting/research for Abbott Vascular, Boston Scientific, Cryolife, Edwards Lifesciences, Medtronic, and Shockwave. Dr Bax's institution (Department of Cardiology, LUMC, the Netherlands) has received research grants from Medtronic, Biotronik, Edwards Lifesciences, and Boston Scientific. Dr Mack has served as a co-principal investigator for clinical trials for Abbott and Edwards Lifesciences; and has served as study chair for a trial for Medtronic; all roles were uncompensated. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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