

iREVIEW

STATE-OF-THE-ART PAPER

Imaging for Predicting and Assessing Prosthesis-Patient Mismatch After Aortic Valve Replacement



Philippe Pibarot, DVM, PhD,^a Julien Magne, PhD,^{b,c} Jonathon Leipsic, MD,^d Nancy Côté, PhD,^a Philippe Blanke, MD,^d Vinod H. Thourani, MD,^e Rebecca Hahn, MD^f

JACC: CARDIOVASCULAR IMAGING CME/MOC/ECME

CME/MOC/ECME Editor: Ragavendra R. Baliga, MD

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CME/MOC/ECME Objective for This Article: Upon completion, the reader should be able to: 1) predict the risk of PPM prior to AVR by measuring the native aortic annulus size by 3D imaging and by calculating the predicted indexed from the normal reference value of EOA of the prosthesis and patient's BSA; 2) to identify the most appropriate option to prevent or correct PPM using multi-modality imaging; 3) to differentiate PPM versus prosthetic valve stenosis versus normal prosthetic valve function using TTE and multi-modality imaging when appropriate; and 4) to determine in which cases, additional imaging modalities such as TEE, MDCT, or cinefluoroscopy are needed to complement the information by TTE and allows identification of PPM and/or prosthetic valve stenosis.

CME/MOC/ECME Editor Disclosure: *JACC: Cardiovascular Imaging* CME/MOC/ECME Editor Ragavendra R. Baliga, MD, has reported that he has no relationships to disclose.

Author Disclosures: Dr. Pibarot is the Canada Research Chair in Valvular Heart Disease, and is funded by a Foundation Grant (FDN-143225) from Canadian Institutes of Health research, Ottawa, Ontario, Canada. Drs. Pibarot and Hahn have received funding from Edwards Lifesciences and Medtronic for echocardiography core laboratory analyses in the context transcatheter valve therapy trials with no direct compensation. Dr. Leipsic has served as a consultant for and owns stock options in Circle Cardiovascular Imaging; and has worked in the core lab for Edwards Lifesciences and Medtronic. Drs. Leipsic and Blanke have received funding from Edwards Lifesciences for computed tomography laboratory analyses in the context transcatheter valve therapy trials with no direct compensation. Dr. Blanke has served as a consultant for Tendyne, Neovasc, and Circle Cardiovascular Imaging. Dr. Thourani is a consultant for Abbott Vascular, Boston Scientific, Edwards Lifesciences, Gore Vascular, and Jenavalve. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Medium of Participation: Print (article only); online (article and quiz).

CME/MOC/ECME Term of Approval

Issue Date: January 2019

Expiration Date: December 31, 2019

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Philippe Pibarot, DVM, PhD,^a Julien Magne, PhD,^{b,c} Jonathon Leipsic, MD,^d Nancy Côté, PhD,^a Philippe Blanke, MD,^d Vinod H. Thourani, MD,^e Rebecca Hahn, MD^f

ABSTRACT

Prosthesis-patient mismatch (PPM) occurs when the effective orifice area (EOA) of the prosthetic valve is too small in relation to a patient's body size, thus resulting in high residual postoperative pressure gradients across the prosthesis. Severe PPM occurs in 2% to 20% of patients undergoing surgical aortic valve replacement (AVR) and is associated with 1.5- to 2.0-fold increase in the risk of mortality and heart failure rehospitalization. The purpose of this article is to present an overview of the role of multimodality imaging in the assessment, prediction, prevention, and management of PPM following AVR. The risk of PPM can be anticipated at the time of AVR by calculating the predicted indexed from the normal reference value of EOA of the selected prosthesis and patient's body surface area. The strategies to prevent PPM at the time of surgical AVR include: 1) implanting a newer generation of prosthetic valve with better hemodynamic; 2) enlarging the aortic root or annulus to accommodate a larger prosthetic valve; or 3) performing TAVR rather than surgical AVR. The identification and quantitation of PPM as well as its distinction versus prosthetic valve stenosis is primarily based on transthoracic echocardiography, but important information may be obtained from other imaging modalities such as transesophageal echocardiography and multidetector computed tomography. PPM is characterized by high transprosthetic velocity and gradients, normal EOA, small indexed EOA, and normal leaflet morphology and mobility. Transesophageal echocardiography and multidetector computed tomography are particularly helpful to assess prosthetic valve leaflet morphology and mobility, which is a cornerstone of the differential diagnosis between PPM and pathologic valve obstruction. Severe symptomatic PPM following AVR with a bioprosthetic valve may be treated by redo surgery or the transcatheter valve-in-valve procedure with fracturing of the surgical valve stent.

(J Am Coll Cardiol Img 2019;12:149–62) © 2019 by the American College of Cardiology Foundation.

Approximately 300,000 prosthetic heart valves are implanted each year worldwide and with aging of the population, this number is estimated to triple to over 850,000 by 2050 (1). Despite major improvements in valve implantation techniques, hemodynamics, durability, and thrombogenicity, prosthetic valves are still subject

to inherent complications. These may include structural valve dysfunction, defined as permanent changes intrinsic to the prosthetic valve (i.e., wear and tear, leaflet disruption or calcific degeneration), or nonstructural valve dysfunction from abnormalities not intrinsic to the prosthesis (i.e., paravalvular regurgitation [PVR] or malpositioning) (2).

From the ^aDepartment of Cardiology, Quebec Heart & Lung Institute, Laval University, Quebec City, Canada; ^bService Cardiologie, Hôpital Dupuytren, CHU Limoges, Limoges, France; ^cINSERM 1094, Limoges, France; ^dDepartment of Radiology, University of British Columbia and St. Paul's Hospital, Vancouver, Canada; ^eDepartment of Cardiology, MedStar Heart and Vascular Institute and Georgetown University, Washington, DC; and the ^fDepartment of Cardiology, Columbia University Medical Center, New York, New York. Dr. Pibarot is the Canada Research Chair in Valvular Heart Disease, and is funded by a Foundation Grant (FDN-143225) from Canadian Institutes of Health research, Ottawa, Ontario, Canada. Drs. Pibarot and Hahn have received funding from Edwards Lifesciences and Medtronic for echocardiography core laboratory analyses in the context transcatheter valve therapy trials with no direct compensation. Dr. Leipsic has served as a consultant for and owns stock options in Circle Cardiovascular Imaging; and has worked in the core lab for Edwards Lifesciences and Medtronic. Drs. Leipsic and Blanke have received funding from Edwards Lifesciences for computed tomography laboratory analyses in the context transcatheter valve therapy trials with no direct compensation. Dr. Blanke has served as a consultant for Tendyne, Neovasc, and Circle Cardiovascular Imaging. Dr. Thourani is a consultant for Abbott Vascular, Boston Scientific, Edwards Lifesciences, Gore Vascular, and Jenavalve. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Prosthesis-patient mismatch (PPM) is considered nonstructural because it is not an intrinsic dysfunction of the prosthesis, per se. This problem indeed occurs when the size of a normally functioning prosthetic valve is too small in relation to the patient's body size and thus to the patient's cardiac output requirements, resulting in abnormally high transprosthetic gradients (3,4).

The prevalence of moderate PPM ranges from 20% to 70% and that of severe PPM from 2% to 20% following aortic valve replacement (AVR) (3,5–9). Transcatheter AVR (TAVR) is associated with a lower prevalence of PPM, especially severe PPM, compared with SAVR (5,9–15). Among transcatheter valves, self-expanding valves with supra-annular design are generally associated with a lower prevalence of PPM compared with balloon-expandable valves, but may be associated with somewhat higher rates of permanent pacemaker requirement and significant PVR (16,17).

Patients with PPM have worse functional class and exercise capacity, reduced regression of left ventricular (LV) hypertrophy, higher rate of heart failure rehospitalization, and reduced survival after SAVR when compared with patients with no PPM (5–9,18–20). Furthermore, PPM appears to have a more pronounced impact on outcomes in some specific subsets of patients such as those with pre-existing LV dysfunction or severe LV hypertrophy, concomitant mitral regurgitation, or classical or paradoxical low-flow, low-gradient aortic stenosis as well as in those <65 to 70 years of age (21–23). Meta-analyses report that severe and moderate PPM is associated with a 1.8- and 1.2-fold increase in mortality, respectively (6–9).

PPM is also associated with faster structural degeneration of bioprosthetic valves following SAVR (24,25). Furthermore, recent reports of transcatheter valve implantation in failed biological SAVR (valve-in-valve procedure) suggest that pre-existing severe PPM of the failed surgical bioprosthetic valves is associated with higher incidence of high residual gradient, less recovery of patients' functional capacity, and increased risk of mortality (26,27).

The identification and quantitation of PPM are primarily based on Doppler echocardiography. However, other imaging modalities, such as multi-detector computed tomography (MDCT), may provide important complementary information with regard to the prediction and assessment of PPM. The purpose of this paper is to present an overview of the role of multimodality imaging in the assessment, prediction, prevention, and management of PPM following AVR.

PREDICTION AND PREVENTION OF PPM

Because PPM results from an imbalance between the effective orifice area (EOA) of the prosthetic valve and the body surface area of the patient, the parameter that is generally used for identifying PPM is the indexed valve EOA (1,2). PPM is considered not clinically significant (i.e., absent or mild), moderate, or severe when the indexed EOA is $>0.85 \text{ cm}^2/\text{m}^2$, between 0.85 and $0.64 \text{ cm}^2/\text{m}^2$, and $\leq 0.65 \text{ cm}^2/\text{m}^2$, respectively. However, the indexed EOA may overestimate the severity of PPM in obese patients (body mass index $\geq 30 \text{ kg/m}^2$) (22,28) and the European Association of Cardiovascular Imaging and Valve Academic Research Consortium-2 therefore recommend using lower cutpoints of indexed EOA in obese patients (i.e., $<0.70 \text{ cm}^2/\text{m}^2$ for moderate PPM and $<0.55 \text{ cm}^2/\text{m}^2$ for severe PPM) (Table 1).

Given the significant impact of PPM on survival, functional recovery, heart failure hospitalization, and valve durability, pre-procedural planning to avoid PPM is of utmost importance. Severe PPM should ideally be avoided in every patient undergoing AVR, whereas moderate PPM should be avoided in vulnerable subsets such as patients with depressed LV systolic function; severe LV hypertrophy; low-flow, low-gradient aortic stenosis; or concomitant mitral regurgitation. To implement preventive strategies, it is first necessary to predict the required post-AVR indexed EOA, which minimizes the risk of clinically significant PPM, before prosthesis implantation (Figure 1).

SURGICAL AVR. To obtain the predicted indexed EOA of surgical prosthetic valves, one needs to: 1) know the model and size of the prosthesis that the surgeon plans to implant; 2) refer to the tables published in the 2016 recommendations of the European Association of Cardiovascular Imaging (4), which include the normal EOAs for the different models and label sizes of surgical prosthetic valves; and 3) divide the normal EOA by the patient's body surface area. This process can be done intraoperatively, once the debridement and sizing of the aortic annulus are accomplished or preoperatively by measuring the aortic annulus dimensions by MDCT or 3-dimensional transesophageal echocardiography (TEE) (Figure 1). Few studies have compared pre-procedural MDCT or 2-dimensional echocardiographic measurements to open surgical annular sizing (29–31). The prediction of valve size from the aortic annulus size measured by

ABBREVIATIONS AND ACRONYMS

AVR	= aortic valve replacement
EOA	= effective orifice area
LV	= left ventricular
LVOT	= left ventricular outflow tract
MDCT	= multidetector computed tomography
PPM	= prosthesis-patient mismatch
PVR	= paravalvular regurgitation
SAVR	= surgical aortic valve replacement
TAVR	= transcatheter aortic valve replacement
TEE	= transesophageal echocardiography
TTE	= transthoracic echocardiography

TABLE 1 Imaging Criteria for the Differential Diagnosis of Normal Prosthetic Valve Function vs. PPM vs. Valve Stenosis

	Normal	Moderate PPM	Severe PPM	Mild/Moderate Stenosis	Severe Stenosis
Leaflet morphology and mobility by TTE/TEE or MDCT*	Normal	Normal	Normal	Often abnormal	Abnormal
Doppler echo parameters					
Peak velocity, m/s	<3	3–3.5	≥3.5	3–4	≥4
Mean gradient, mm Hg	<20	20–30	≥30	20–35	≥35
Doppler velocity index	≥0.35	≥0.30	≥0.30	0.25–0.35	<0.25
EOA, cm ²	>1.00	>1.00	>1.00	Variable	<0.80
Indexed EOA, cm ² /m ²	>0.85	0.66–0.85	≤0.65	0.66–0.85	≤0.65
If BMI ≥30 kg/m ²	>0.70	0.56–0.70	≤0.55	0.56–0.70	≤0.55
Difference (normal EOA – measured EOA), cm ²	<0.30 (<1 SD)	<0.30 (<1 SD)	<0.30 (<1 SD)	0.30–0.60 (1–2 SD)	>0.60 (>2 SD)
Contour of the transprosthetic jet†	Triangular, early peaking	Triangular, early peaking	Triangular, early peaking	Triangular to intermediate	Rounded, symmetrical
Acceleration time, ms†	<80	<80	<80	80–100	>100
Acceleration time/LV ejection time ratio†	<0.32	<0.32	<0.32	0.32–0.37	>0.37
Changes in Doppler echo parameters during follow-up					
Increase in mean gradient, mm Hg	<10	<10	<10	10–19	≥20
Decrease in EOA, cm ²	<0.30	<0.30	<0.30	0.30–0.60	>0.60
Percent decrease in EOA, %	<25	<25	<25	25–49	≥50
Percent decrease in DVI, %	<20	<20	<20	20–39	≥40
Hybrid (Doppler CT) parameters					
Indexed hybrid EOA, cm ² /m ²	>1.00	0.81–1.00	≤0.80	0.81–1.00	≤0.80
If BMI ≥30 kg/m ²	>0.85	0.71–0.85	≤0.70	0.71–0.85	≤0.70

See Lancellotti et al. (4) and Hahn et al. (32) to obtain the normal reference values of effective orifice area for the different models and sizes of surgical and transcatheter prostheses. *Valve leaflet that is immobile or with restricted mobility, thrombus, or pannus; abnormal biologic valves; leaflet thickening/calciification, thrombus, or pannus. The mobility and morphology of the leaflet is assessed by transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), multidetector computed tomography (MDCT), or cinefluoroscopy (mechanical valves). †These parameters are affected by left ventricular (LV) function and chronotropy.

BMI = body mass index; CT = computed tomography; DVI = Doppler velocity index; EOA = effective orifice area.

imaging before SAVR will not take into account the excision of the valve and debridement of the annulus performed by the surgeon at the time of SAVR. Furthermore, despite recent efforts in the standardization of the labeling of prosthetic heart valve size, sizers, and sizing strategies, there are still some important discrepancies in the actual dimensions of the sizers provided by the manufacturers versus the label size of the prostheses. Once the model and size of the prosthesis to be implanted is determined, one can rapidly calculate the predicted indexed EOA and therefore estimate the risk of post-operative PPM. A predicted indexed EOA ≤0.65 cm²/m² (or ≤0.55 cm²/m² in obese patients) indicates a risk of severe PPM, whereas an indexed EOA ≤0.85 cm²/m² (or ≤0.70 cm²/m² in obese patients) is consistent with a risk of moderate PPM (Figure 1).

If severe or moderate PPM in vulnerable patients is anticipated from the calculation of the predicted indexed EOA, several preventive strategies can be considered (Figure 1):

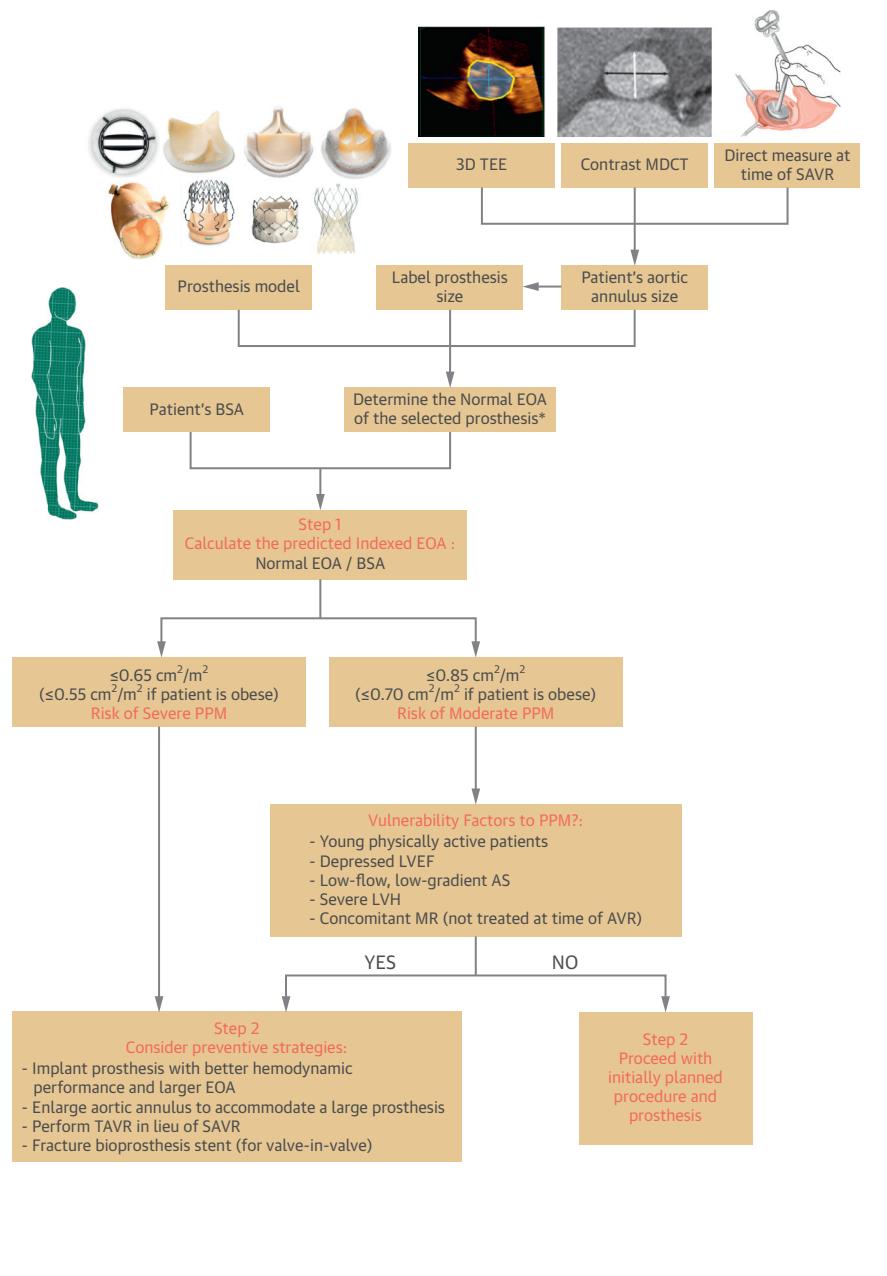
1. The surgeon may elect to implant another model of prosthetic valve providing a larger EOA for a given aortic annulus size (e.g., a stentless or sutureless prosthesis vs. a stented prosthesis).

2. The surgeon may perform an enlargement of the aortic root or annulus to accommodate a larger size of the stented bioprosthesis. This more invasive strategy should be contemplated only if the anatomy of the aortic root is favorable and the risk-benefit ratio of this concomitant procedure is considered reasonable.

3. TAVR may be considered in lieu of SAVR. For this strategy, it would be important to attempt prediction of PPM before operation. MDCT or 3-dimensional TEE is essential to identify patients with a small aortic annulus in whom it would be difficult to implant a medium or large size prosthetic valve during SAVR, even with extensive debridement of the annulus (Figure 1). In such patients, TAVR may be considered. A randomized trial is currently ongoing to compare these 2 types of AVR in patients with severe aortic stenosis and a small aortic annulus (NCT03383445).

TRANSCATHETER AVR. In the context of TAVR, the final size of the prosthesis is determined by the native annular size and not the transcatheter valve size. Importantly, a single-size transcatheter valve can be implanted in a range of annular sizes and is expanded to fill the annular space (32). Indeed, a given model

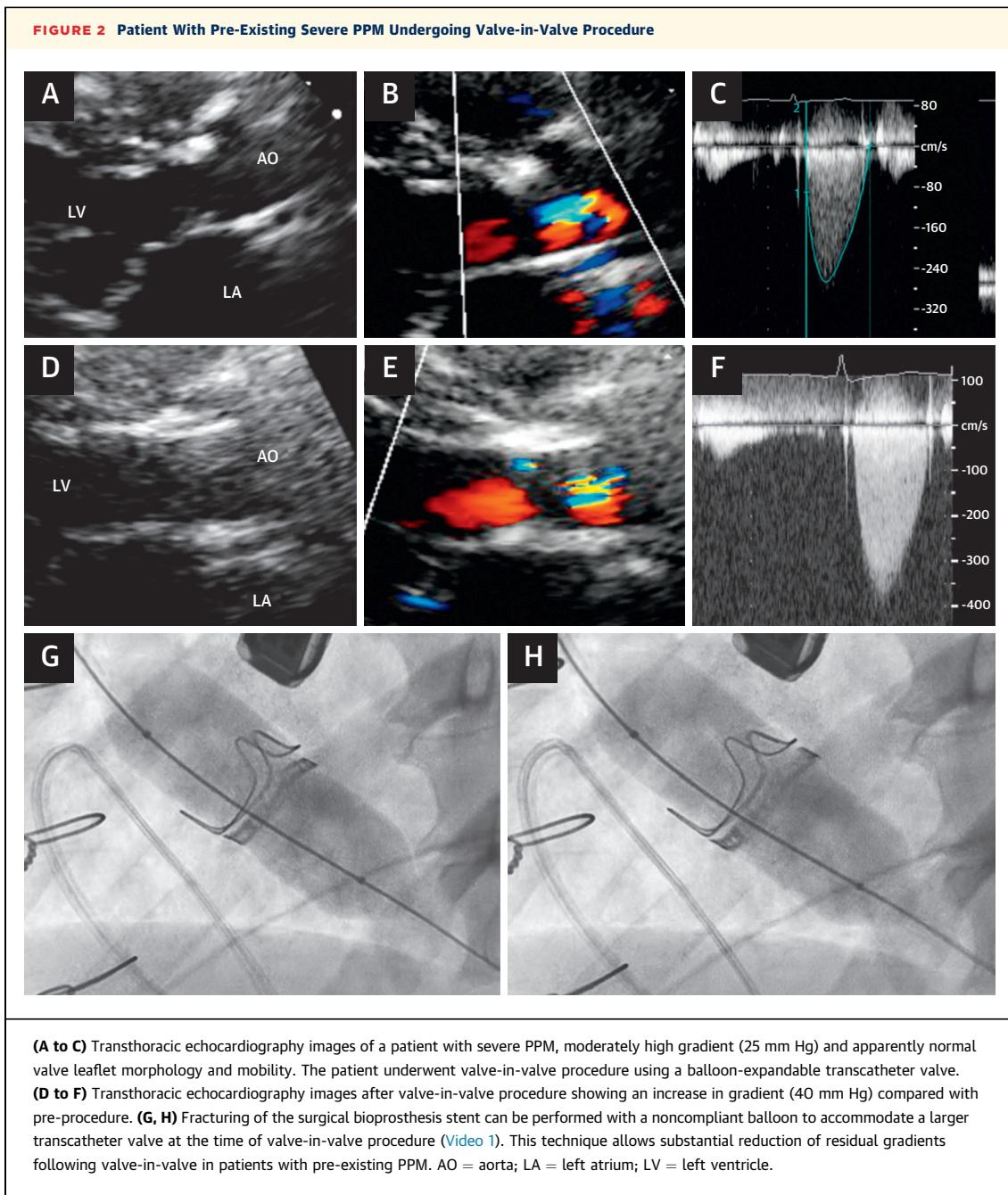
FIGURE 1 Algorithm for the Prediction and Prevention of PPM



This figure proposes an algorithm for the prediction and the prevention of prosthesis-patient mismatch (PPM). *The normal reference values of effective orifice area (EOA) can be obtained from Lancellotti et al. (4) in the case of surgical aortic valve replacement (SAVR) and Hahn et al. (32) in the case of transcatheter aortic valve replacement (TAVR). 3D = 3-dimensional; AS = aortic stenosis; AVR = aortic valve replacement; BSA = body surface area; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; MDCT = multidetector computed tomography; MR = mitral regurgitation; TEE = transesophageal echocardiography.

and label size of transcatheter aortic valve provides a larger EOA if fully deployed in a larger annulus than if somewhat underdeployed in a smaller annulus. It is thus preferable to determine the predicted

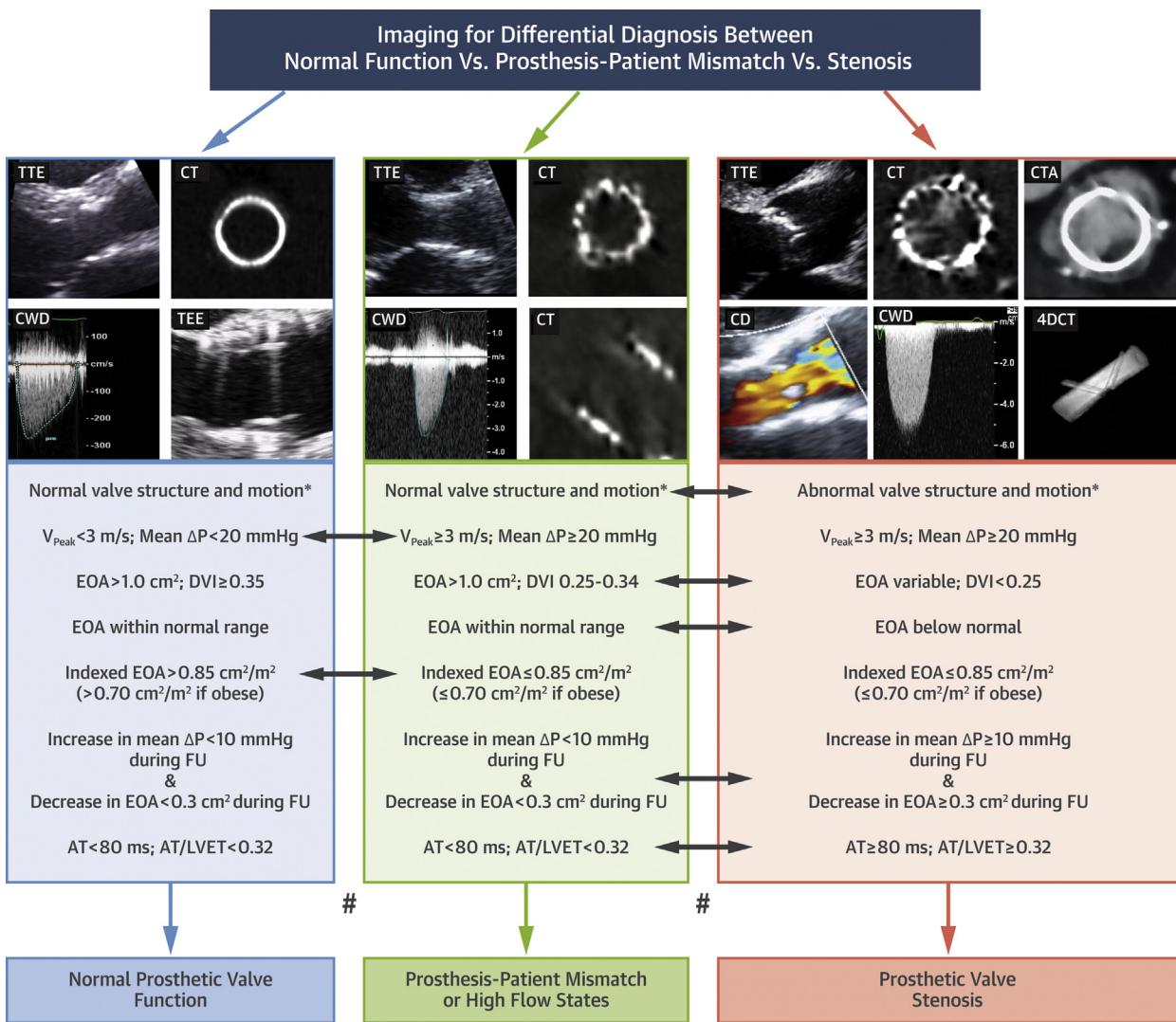
indexed EOA on the basis of the native aortic annulus size rather than label transcatheter valve size. Hahn et al. (32) recently published the normal values of EOA for the SAPIEN (Edwards Lifesciences, Irvine,



California), SAPIEN XT (Edwards Lifesciences), SAPIEN 3 (Edwards Lifesciences), CoreValve (Medtronic, Minneapolis, Minnesota), and Evolut R (Medtronic) according to label size and native aortic annulus size. If a risk of PPM, and especially severe PPM, is anticipated on the basis of the predicted indexed EOA, the options to prevent or reduce PPM are limited. One may use another model of transcatheter valve providing a larger EOA for a given annulus size, if available. In this regard, some studies suggest that, in a given aortic annulus size, the

self-expanding valves with a supra-annular design provide somewhat larger EOAs than balloon-expandable valves do. A high implant depth may also help to optimize the EOA for both self- and balloon-expandable valves. Intraprocedural balloon post-dilatation has been associated with larger EOA and could be considered (33,34). However, one should carefully weigh in the risk-benefit ratio of the PPM preventive strategies. For the same degree of severity, PPM likely has less impact on outcomes than PVR does. Hence, the prevention of PPM in the context of

CENTRAL ILLUSTRATION Role of Imaging for Differential Diagnosis Between Normal Valve Function, Prosthesis-Patient Mismatch, and Prosthetic Valve Stenosis



Pibarot, P. et al. J Am Coll Cardiol Img. 2019;12(1):149–62.

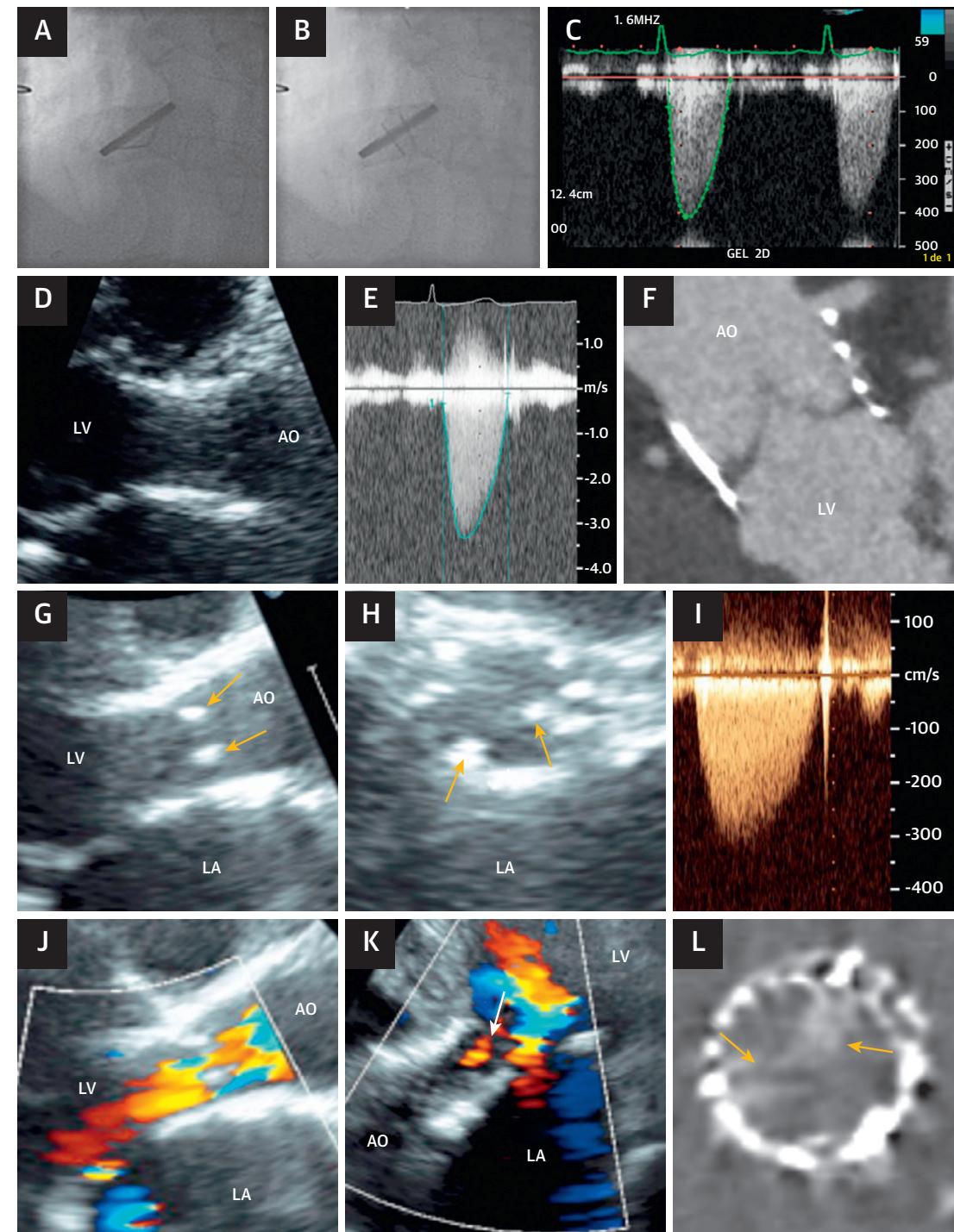
A multi-imaging modality, multiparameter integrative approach can help to make the differential diagnosis between normal prosthetic valve function versus prosthesis-patient mismatch versus prosthetic valve stenosis due to structural valve deterioration or SVD and double yellow arrows identify the parameters and criteria that allows differential diagnosis between normal function versus mismatch versus stenosis. ΔP = transprosthetic pressure gradient; 4DCT = 4-dimensional computed tomography; AT = acceleration time; CT = noncontrast computed tomography; CTA = computed tomography angiography (contrast computed tomography); CD = color Doppler; CWD = continuous-wave Doppler; DVI = Doppler velocity index; EOA = effective orifice area; FU = follow-up; LVET = left ventricular ejection time; MDCT = multidetector computed tomography; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography; V_{Peak} = peak transprosthetic aortic velocity.

TAVR should not be done at the cost of more PVR or more complications such as pacemaker implantation, annulus injury, or valve embolization. Several transcatheter heart valves can be used to minimize the risk of both PPM and PVR, including the SAPIEN 3, Evolut Pro, Accurate Neo, and Lotus valves.

TRANSCATHETER VALVE-IN-VALVE PROCEDURE

The valve-in-valve procedure is increasingly used for the treatment of patients with failed surgical bioprostheses. This procedure is associated with good hemodynamic, functional, and clinical outcomes in patients with acquired stenosis or transvalvular

FIGURE 3 Cases Illustrating the Role of Multimodality Imaging in the Differential Diagnosis Between PPM and Prosthetic Valve Stenosis



Continued on the next page

regurgitation related to fibrocalcific degeneration of valve leaflets. However, patients with high transprosthetic gradients related, in large part, to pre-existing PPM have worse outcomes following the valve-in-valve procedure. This context refers to the analogy of the Russian dolls, in which implanting a second valve within a first valve that is inherently too small for the patient's body size (and thus cardiac output requirements) can only worsen the hemodynamic status and thus the clinical status of the patient. **Figure 2** presents an illustrative case of such unfortunate scenario in which a symptomatic patient with high mean transprosthetic gradient (25 mm Hg) related to isolated severe PPM was treated by the valve-in-valve procedure. In this patient, the gradient increased to 40 mm Hg following the procedure because the implantation of the transcatheter valve further reduced the EOA of the surgical bioprosthetic valve with pre-existing severe PPM. It is thus essential to correctly identify and quantify PPM of the failed surgical bioprosthetic valve in patient candidates for the valve-in-valve procedure. Furthermore, in patients with high transprosthetic gradients, one should determine the etiology of the elevated gradient (i.e., PPM vs. stenosis vs. regurgitation vs. a combination of these etiologies), as discussed subsequently. To assess the presence and severity of pre-existing PPM of the surgical bioprosthetic valve before the valve-in-valve procedure, one can use a similar strategy as described previously for SAVR, in which the predicted indexed EOA is calculated from the normal value of EOA for the model and size of bioprosthetic valve implanted in the patient divided by his or her body surface area (4). Other imaging criteria to differentiate a pre-existing PPM versus an acquired stenosis of the bioprosthetic valve are presented in the following section. If a patient candidate for valve-in-valve procedure has

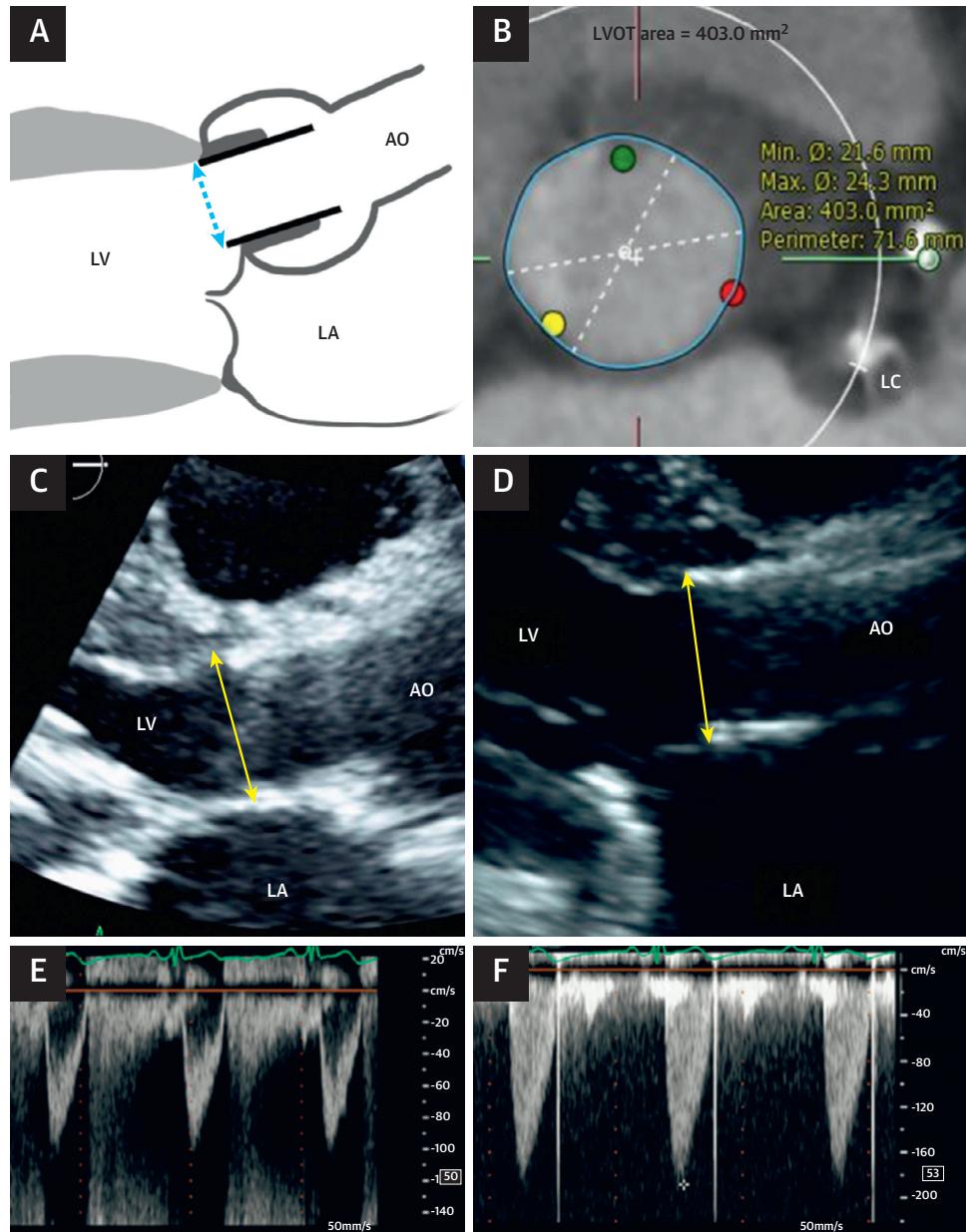
evidence of pre-existing PPM of the surgical bioprosthetic valve, the proceduralist may consider fracturing the bioprosthetic stent with an oversized non-compliant balloon (**Figure 2**, **Video 1**). This concomitant procedure indeed allows implantation of a larger transcatheter valve within the surgical bioprosthetic valve and therefore reduces the risk of severe PPM and high residual gradients after valve-in-valve procedure (35–37). Newer generations of surgical bioprostheses, such as the INSPIRIS Resilia aortic valve (Edwards Lifesciences) with expandable frame might allow the implantation of a larger transcatheter valve at the time of valve-in-valve procedure without the need of stent fracturing. However, the potential benefit of this new feature of the INSPIRIS bioprosthetic valve frame for future valve-in-valve procedures remains to be demonstrated. The implantation of a transcatheter valve with supra-annular design with a high implant depth (0 to 2 mm below the bioprosthetic stent) may also help to optimize the EOA and minimize residual gradients following the valve-in-valve procedure in patients with pre-existing PPM (27,38,39). The challenges raised by pre-existing PPM in the context of the valve-in-valve procedure also emphasize the importance of preventing PPM at the time of the initial SAVR and therefore providing the largest possible EOA “reserve” for future valve-in-valve procedures.

ASSESSMENT OF PPM AND DIFFERENTIAL DIAGNOSIS WITH PROSTHETIC VALVE STENOSIS

It is relatively frequent to measure a high gradient across a prosthetic aortic valve and the differential diagnosis is much more complex than for native aortic valve stenosis (**Central Illustration**). There are indeed several potential causes of an elevated

FIGURE 3 Continued

(A to C) A patient with 19-mm CarboMedics bileaflet mechanical valve (CarboMedics, Austin, Texas). **(C)** This patient has a high mean gradient (39 mm Hg) with an EOA of 1.06 cm² (which is close to the normal EOA for this prosthesis: 1.10 cm²) and indexed EOA of 0.51 cm²/m². **(A, B)** Cinefluoroscopy shows normal leaflet motion. This patient has severe PPM. **(D, E)** Transthoracic echocardiography images of a patient with a 20-mm SAPIEN XT (Edwards Lifesciences, Irvine, California) with a mean gradient of 26 mm Hg, an EOA of 1.20 cm², indexed EOA of 0.63 cm²/m², and normal leaflet morphology and mobility (**Video 2**). This patient has severe PPM. **Video 3** also shows an apical 5-chamber color Doppler view of a patient with a Carpentier-Edwards Perimount (Edwards Lifesciences, Irvine, California) valve with severe PPM: normal valve leaflet morphology and mobility with turbulent transvalvular flow. **(F)** Contrast MDCT can also be used to assess the morphology and mobility of surgical or transcatheter bioprosthetic valves. This image shows normal morphology and mobility in a SAPIEN XT transcatheter heart valve. **(G to K)** Patient with a SAPIEN 3 transcatheter heart valve implanted 3 years ago, **(I)** with a significant increase of peak/mean gradients (from 15/8 mm Hg at discharge to 41/24 mm Hg) and concomitant decrease in EOA (from 1.60 to 0.80 cm²). **(G, H)** Transthoracic echocardiography parasternal images showing hyperechogenic thickening of valve leaflets (**yellow arrows**) (**Video 4**). The echo density of leaflets is similar to that of the valve stent. **(J)** Narrowing of color Doppler transvalvular flow during systole and **(K)** a mild transvalvular aortic regurgitation during diastole (**white arrow**). These findings are consistent with calcific structural degeneration of valve leaflets associated with moderate valve stenosis and mild regurgitation. **(L)** Noncontrast MDCT can be used to detect and quantitate calcification of valve leaflets (**yellow arrows**) associated with structural valve degeneration. Abbreviations as in **Figures 1 and 2**.

FIGURE 4 Measurement of Prosthetic Valve EOA

(A) Schematic representation of the measurement of the LV outflow tract (LVOT) diameter in a patient with a transcatheter valve. **(C, D)** Transthoracic echocardiography parasternal long-axis images illustrating the measurement of the LVOT diameter in a **(C)** balloon-expandable SAPIEN XT valve and **(D)** self-expanding CoreValve. **(E)** LVOT flow velocity by pulsed-wave Doppler and **(F)** transprosthetic flow by continuous-wave Doppler. The prosthetic valve EOA is obtained by the continuity equation from the LVOT cross-sectional area, **(A, D)** calculated from LVOT diameter, and velocity-time integrals of **(E)** LVOT and **(F)** aortic flow. The EOA can also be obtained by fusion or hybrid imaging (i.e., by including in the continuity equation): **(B)** the LVOT area measured by contrast MDCT or by 3-dimensional TEE and **(E, F)** the velocities measured by Doppler. Abbreviations as in [Figures 1 and 2](#).

transprosthetic gradient. PPM is the most frequent cause of high gradient after AVR, the other potential causes being: 1) an acquired stenosis of the prosthetic valve due to thrombus, pannus, calcific leaflet

degeneration, or vegetations; 2) high flow states; or 3) technical errors. Transthoracic echocardiography (TTE) is the primary imaging modality to make the differential diagnosis between PPM versus acquired

stenosis of the prosthetic valve. However, other imaging modalities such as TEE, MDCT, or cinefluoroscopy may provide important complementary information, in particular on valve leaflets structural integrity and mobility (**Figure 3**). **Table 1** presents the parameters and criteria that may be used to differentiate normal prosthetic valve function versus PPM versus acquired prosthetic valve stenosis (**Central Illustration**).

VALVE LEAFLET MORPHOLOGY AND MOBILITY BY TTE, TEE, OR MDCT.

To differentiate between PPM versus prosthetic stenosis, imaging of valve leaflet morphology and mobility is key (**Figure 3**). With PPM, the valve structure and leaflet morphology and mobility are generally normal, whereas with bioprosthetic valve stenosis, the leaflets are thickened with reduced mobility (**Table 1**, **Figure 3**, **Videos 2, 3, and 4**). A leaflet thickness >2 mm is considered abnormal. However, visualization of valve leaflets is often suboptimal with TTE because of shadowing and reverberations caused by the prosthesis structure. TEE may improve the assessment of the leaflets morphology and mobility as well as the identification of other abnormalities such as pannus, thrombus, or vegetations that may also cause obstruction of the prosthetic valve. In case of bioprosthetic valve thrombosis, the leaflets generally harbor a diffuse hypoechogenic thickening, whereas calcific leaflet degeneration is often characterized by irregular hyperechogenic thickening (**Figure 3**, **Video 4**). With mechanical valves, the identification of reduced leaflet mobility may be difficult even with TEE, especially when the impairment of mobility is subtle and symmetric (bileaflet mechanical valves). Cinefluoroscopy is a simple, fast, and low-cost imaging modality to assess the mobility of mechanical valve leaflets (**Figure 3**). The opening and closing angles of the mechanical valve leaflets can be measured by cinefluoroscopy and compared with normal reference values for the different models of valves (**4**). Electrocardiography synchronized contrast enhanced MDCT is also clinically useful to: 1) assess the leaflet mobility in bioprosthetic or mechanical valves; 2) identify and provide an assessment of the extent of valve thrombus; and 3) allow modest capacity to differentiate thrombus versus pannus (**4**). Non-contrast MDCT is also increasingly utilized to detect the presence of leaflet mineralization a marker for calcific degeneration in bioprosthetic valves (**Figure 3**) (**4,25,40**). In a recent study, the presence of even a small amount of calcification within bioprosthetic valve leaflets on noncontrast MDCT was associated with a high risk of valve hemodynamic deterioration,

valve reintervention, and death following SAVR (**41**). Endocarditis may also cause obstruction of prosthetic valves. It should be noted that the mode of presentation of transcatheter valve endocarditis is often insidious and characterized by an obstructive pattern with heterogeneous thickening of valve leaflets, increase in gradients, and decrease in EOA (**42**). Vegetations and destruction of valve leaflets with transvalvular regurgitation are much less prevalent than in the endocarditis of surgical bioprostheses.

DOPPLER ECHOCARDIOGRAPHIC PARAMETERS.

With both PPM and valve stenosis, the peak aortic jet velocity and transprosthetic gradients are elevated, and these Doppler quantitative parameters are thus of limited utility to make the differential diagnosis between these 2 conditions (**Figure 3, Central Illustration**).

The valve EOA measured by the continuity equation and indexed for body surface area is the key parameter to diagnose and quantitate PPM following AVR. However, it does not allow the cardiologist to differentiate PPM versus valve stenosis given that the indexed EOA is small with both conditions (**Table 1**). **Figure 4** presents the method to measure the prosthetic valve EOA by the continuity equation method. To measure the stroke volume (i.e., numerator of the equation) in surgical and transcatheter valves, the LV outflow tract (LVOT) diameter and velocity should be measured just below the apical border of the stent or ring. The LVOT diameter is measured from outer border to outer border of the stent or ring (**Figure 4**). For measurement of LVOT flow velocity, the pulsed-wave Doppler sample should be placed immediately below the apical border of the stent with no valve opening or closing clicks visible. The transprosthetic flow velocity is obtained by continuous-wave Doppler with careful multiwindow interrogation including the apical and right parasternal windows.

The determination of the LVOT area by TTE is challenging and subject to measurement error. To overcome this limitation, one can use the LVOT diameter measured at the end of the AVR procedure by TEE and use this value for all subsequent calculations of the stroke volume and EOA during follow-up. Three-dimensional imaging using 3-dimensional TEE or contrast MDCT may also be used to directly measure the LVOT area (**Figure 4**) (**43**). However, it is important to underline that the “hybrid” EOA calculated using the LVOT area measured by MDCT (before or after AVR) and the flow velocities measured by Doppler yields large values of EOA compared with the echocardiography-derived EOA (**43**). Hence, larger cutpoint values of indexed EOA should be applied to

identify PPM when hybrid MDCT-Doppler EOA is utilized (43): 0.81 to 1.00 cm²/m² for moderate PPM and ≤ 0.80 cm²/m² for severe PPM (**Table 1**). Importantly, hybrid MDCT-Doppler EOA did not allow for better discrimination of downstream clinical risk from PPM in an intermediate risk TAVR population, suggesting that it may not be an incremental measure.

In patients with PPM, the EOA measured by the continuity equation (**Figure 4**) is within the normal range but the indexed EOA is small, whereas in patients with stenosis, the measured EOA is smaller than the normal reference value (**Table 1, Central Illustration**). Hence, it is essential to compare the measured EOA to the normal reference value of EOA for the prosthesis model, label size, or patient's annulus size (see previous section). If the EOA measured in the patient is within ± 0.30 cm² (or ± 1 SD) of the normal value of EOA, the valve function is considered normal. However, if the EOA is < 0.30 cm² (or 1 SD) from the normal value, one should suspect stenosis. A difference between normal EOA versus measured EOA > 0.60 cm² (or 2 SD) suggests a significant stenosis. A recommendation document from the European Association of Cardiovascular Imaging (4) and Hahn et al. (32) report the normal mean and SD values for the surgical and transcatheter aortic valves, respectively. The Doppler velocity index is the ratio of the velocity time integral of LVOT flow to velocity time integral of transprosthetic flow. In patients with isolated PPM, it is generally > 0.30 to 0.35, whereas in those with valve stenosis it is < 0.35 (mild or moderate stenosis) or < 0.25 (severe stenosis) (**Table 1**).

Semiquantitative parameters describing the timing of peak transprosthetic velocity may also be useful to assess valve function. In patients with normal prosthetic valve function or PPM, the timing of the peak velocity generally occurs early in systole and the ratio of acceleration time to LV ejection time is < 0.32 , whereas in patients with prosthetic valve stenosis, the peaking of velocity is delayed in systole and the ratio is increased (**Table 1, Central Illustration**) (44). The advantage of these indices is that they are independent of Doppler beam angulation in relation to flow direction and they are less subject to measurement errors than EOA is. However, they are influenced by LV systolic function. For example, a patient with normally functioning aortic prosthesis and concomitant depressed myocardial contractility may nonetheless exhibit a rounded velocity contour with late velocity peaking, as we have also witnessed the same in patients with severe PPM.

CHANGES IN ECHOCARDIOGRAPHIC PARAMETERS

DURING FOLLOW-UP. Another key feature of prosthetic valve stenosis is deterioration in valve hemodynamics: the increase in transprosthetic velocity and gradients with concomitant decrease in EOA and Doppler velocity index from baseline (early post-AVR) to follow-up echocardiograms (**Table 1, Central Illustration**). This is one of the reasons why it is important to assess the baseline valve hemodynamic performance, ideally at 1-month post-AVR. The quality of the pre-discharge echocardiogram is indeed often suboptimal, especially following SAVR. PPM occurs at the time of AVR, whereas stenosis develops after AVR. Hence, in a patient with isolated PPM, the gradient is already elevated at baseline echocardiogram performed early post-AVR and it will remain stable over time. On the other hand, an increase in mean gradient ≥ 10 mm Hg with concomitant decrease in EOA (> 0.30 cm²) during follow-up suggests prosthetic valve stenosis. An increase in gradient during follow-up associated with stable or increase in EOA and Doppler velocity index is generally related to an improvement in LV ejection fraction and an increase in LV outflow and should not be misinterpreted as a prosthetic valve stenosis. An increase in mean gradient ≥ 20 mm Hg with marked decrease in EOA (> 0.60 cm² or $> 50\%$) and Doppler velocity index ($> 40\%$) compared with early post AVR echocardiogram is consistent with severe prosthetic valve stenosis (**Table 1, Central Illustration**) (4). PPM and prosthetic valve stenosis are not mutually exclusive and many patients with high transprosthetic gradient harbor both PPM and valve stenosis.

MANAGEMENT OF PPM

Patients with evidence of PPM, especially severe PPM, should receive close clinical and imaging follow-up, as they are at higher risk for accelerated structural valve deterioration (bioprosthetic valves), heart failure, and death. Valve reintervention may be considered if: 1) PPM is severe or associated with greater than or equal to moderate valve stenosis; 2) mean transprosthetic gradient is high (≥ 30 to 35 mm Hg); or 3) the patient develops heart failure symptoms or LV systolic dysfunction (45). In patients with surgical prosthetic valves, the following options may be considered for valve reintervention: 1) a redo surgery with replacement of the severely mismatched prosthesis by a new prosthetic valve with larger size or better hemodynamic performance (and thus with larger EOA); or 2) transcatheter valve-in-valve procedure using a self-expanding valve with supra-annular design and fracturing of

the stent of the surgical bioprosthetic valve (**Figure 2**). In patients with transcatheter valves, PPM is less frequent and less severe and the options to correct PPM are more limited. A “transcatheter valve in transcatheter valve” procedure using a larger valve and overexpansion of the first valve may be considered (40), but this approach needs further validation. The transcatheter valve-in-valve procedure is not an option in patients having surgical mechanical prosthetic valves with severe PPM. The only option in such case is a redo surgery, but the risk-benefit ratio of reintervention should be carefully assessed.

CONCLUSIONS

PPM is a frequent sequela of AVR, which is associated with increased risk of structural valve degeneration, heart failure hospitalization, and mortality. PPM is less frequent and less severe following transcatheter versus SAVR. The risk of PPM can be anticipated before AVR by calculating the predicted indexed from the normal reference value of EOA of the prosthesis and patient's body surface area. The strategies to prevent PPM at the time of SAVR include: 1)

implanting a newer generation of prosthetic valve with better hemodynamic; 2) enlarging the aortic annulus or root to accommodate a larger prosthetic valve; or 3) performing TAVR rather than SAVR. The identification and quantitation of PPM as well as its distinction versus prosthetic valve stenosis is primarily based on TTE, but important information may be obtained from other imaging modalities such as TEE and MDCT (**Central Illustration**). PPM is characterized by high transprosthetic velocity and gradients, normal EOA, small indexed EOA, and normal leaflet morphology and mobility. Severe symptomatic PPM following AVR with a bioprosthetic valve may be treated by redo surgery or transcatheter valve-in-valve procedure with cracking of the surgical valve stent.

ACKNOWLEDGMENT The authors thank Mia Pibarot for the assistance in the preparation of the figures.

ADDRESS FOR CORRESPONDENCE: Dr. Philippe Pibarot, Institut Universitaire de Cardiologie et de Pneumologie de Québec, 2725 Chemin Sainte-Foy, Québec City, Québec G1V 4G5, Canada. E-mail: philippe.pibarot@med.ulaval.ca.

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KEY WORDS aortic valve replacement, bioprostheses, Doppler echocardiography, multidetector computed tomography, prosthesis-patient mismatch

APPENDIX For supplemental videos, please see the online version of this paper.



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