Patient Prosthesis Mismatch

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Abstract

Concept of patient prosthesis mismatch came into existence from 1978 onward when Rahimtoola first defined it as "mismatch can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve." Patient prosthesis mismatch produces higher than expected pressure gradient through normally functioning valve. Since insertion of first ball caged mechanical valve in descending aorta by Dr. Charles Hufnagel in 1952, prosthetic valve had undergone tremendous improvement in terms of valve design, hemodynamics, durability, and thrombogenicity. Despite these marked changes in valve design, prosthetic valves are still subjected to inherent complications.

Keywords
- paravalvular regurgitation
- prosthesis mismatch
- prosthetic valve

Introduction

Concept of patient prosthesis mismatch (PPM) came into existence from 1978 onward when Rahimtoola first defined it as "mismatch can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve."[1] PPM produces higher than expected pressure gradient through normally functioning valve.

Since insertion of first ball caged mechanical valve in descending aorta by Dr. Charles Hufnagel in 1952,[2] prosthetic valve had undergone tremendous improvement in terms of valve design, hemodynamics, durability, and thrombogenicity. Despite these marked changes in valve design, prosthetic valves are still subjected to inherent complications.

Pathophysiology

Pathophysiology of PPM can be explained by the Hydraulic equation which states,

$$TPG = Q2 \ / \ [k \ 6EOA2]$$

where TPG is trans prosthetic gradient, Q is transvalvular flow, k is the constant, and EOA is effective orifice area.

Equation implies that the smaller the expected effective orifice area in relation to body surface area (BSA), the higher will be transprosthetic gradient. Conversely, for transvalvular gradient to remain low, effective orifice area must be proportional to the flow required.

Definition of Patient Prosthesis Mismatch

Most widely accepted parameters for defining PPM is indexed EOA which is EOA divided by patients BSA.[3,4] Gradients increase exponentially when indexed EOA is 0.8 to 0.9 cm^2/m^2 (►**Fig. 1**).

Obese patients tend to have lower cardiac output requirements for similar BSA. Indexed EOA may overestimate severity of PPM in obese patients (body mass index [BMI] = 30 kg/m^2).

European Association of Cardiovascular Imaging and Valve Academics recommend using lower cut-off points of indexed EOA in obese patients. EOA less than 0.70 cm^2/m^2

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	Mild or Not Clinically Significant, cm²/m²	Moderate, cm²/m²	Severe, cm²/m²
Aortic position	>0.85 (0.8–0.9)	≤0.85 (0.8–0.9)	≤0.65 (0.6–0.7)
Mitral position	>1.2 (1.2–1.3)	≤1.2 (1.2–1.3)	≤0.9 (0.9)

Fig. 1 Exponential increase of gradients with indexed effective orifice area (EOA).

reflects moderate PPM and <0.55 cm²/m² reflects severe PPM.[5,6]

Incidence

Although concept of PPM is applicable in all the four valves, it is mainly reported in left-sided valves. Aortic PPM is most prevalent, followed by mitral PPM. Incidence of moderate PPM in aortic position is found to be 20 to 70%, whereas that in mitral position is 30 to 70%. Severe PPM occurs in 2 to 20% of patients undergoing surgical aortic valve replacement (AVR).[7,8] Transcatheter AVR (TAVR) is associated with a lower prevalence of PPM, especially severe PPM, compared with surgical AVR.[9,10] Among transcatheter valves, self-expanding valves with supra-annular design are generally associated with a lower prevalence of PPM compared with balloon-expandable valves.[11,12]

Parameters Used to Define Patient Prosthesis Mismatch

Indexed Effective Orifice Area

Indexed EOA = EOA of prosthesis/patient's BSA

Indexed EOA is only a parameter that has been found to consistently correlate with postoperative gradients.[1]

Internal Geometric Area

Internal geometric area (IGA) is based on the ex vivo measurement of the internal diameter of the prosthesis. As IGA is more reproducible, some authors recommend to use IGA for defining PPM (►**Fig. 2**).

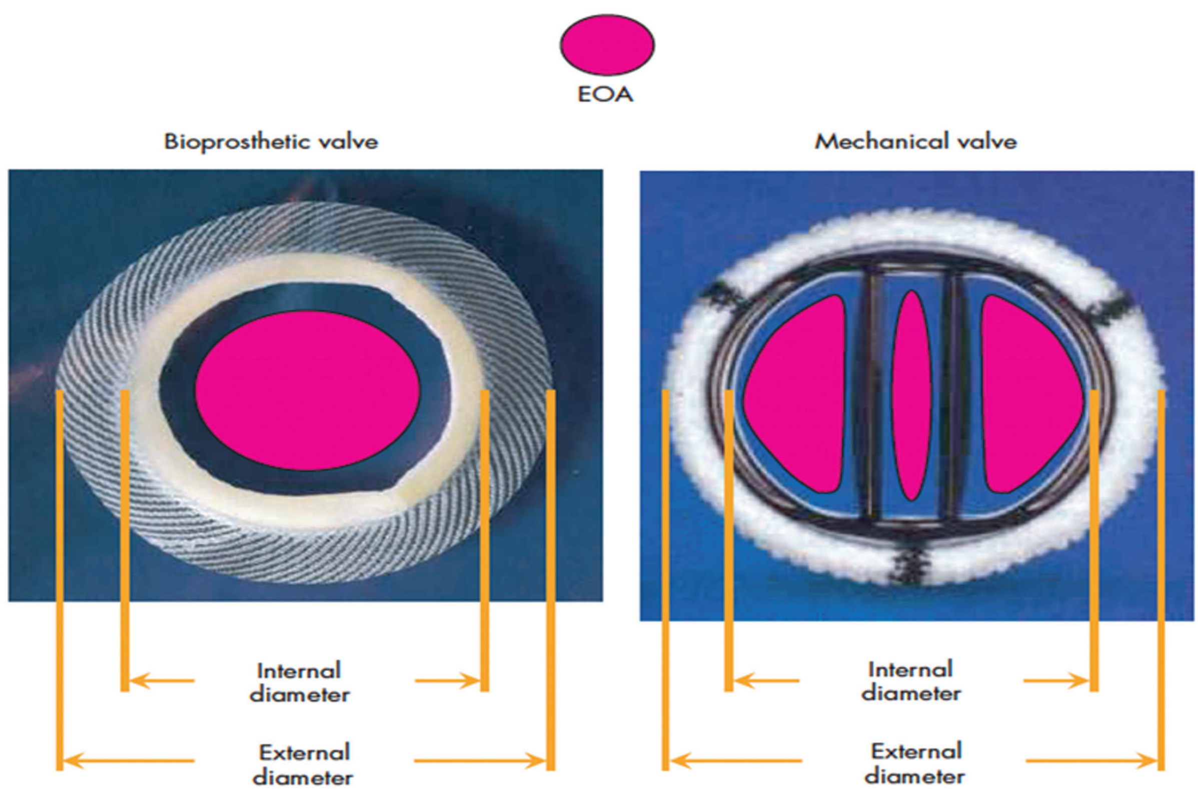

Fig. 2 Comparison of bioprosthetic valve and a bileaflet mechanical valve in fully opened leaflet position. Pink color is effective orifice area (EOA), clearly it is lesser than internal geometric area (IGA).

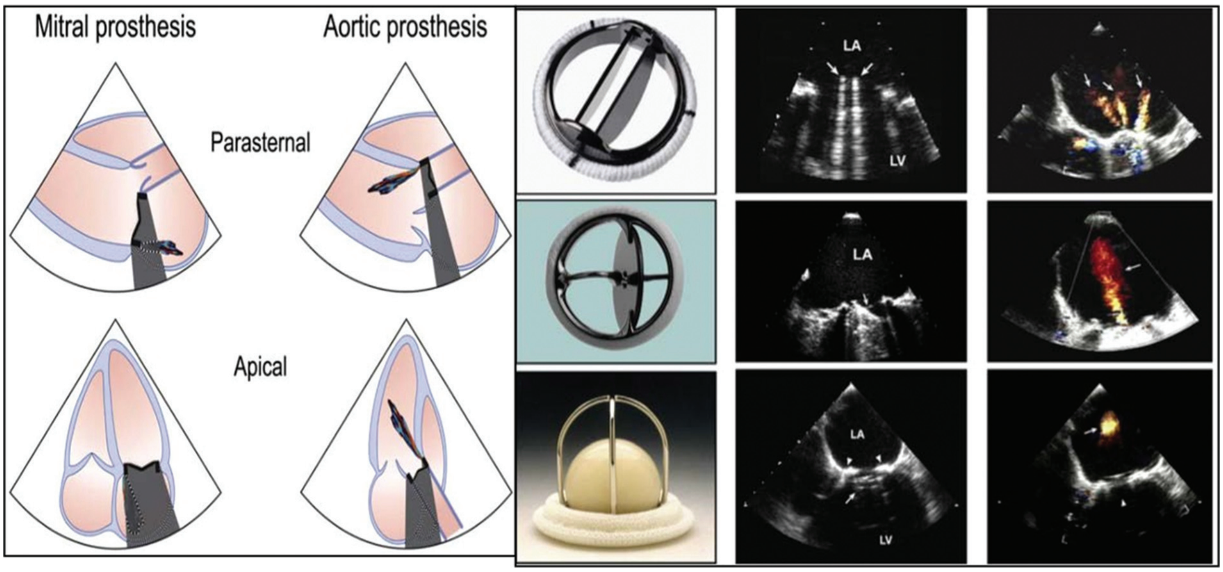

Fig. 3 Types of prosthetic shadow seen on TEE, with a particular valve.

Echocardiography

Echocardiography of prosthetic valve is way more challenging than that of native valve. Almost all the prosthetic valves are obstructive by their design, and it requires expertise to differentiate mild obstruction inherent to their design from that of pathological obstruction and PPM.

A full transthoracic echocardiographic study requires multiple angulations of probe and use of multiple views. To rule out intermittent obstruction, prolonged Doppler examination may then be required for diagnosis. transesophageal echocardiography (TEE) is more likely to be needed for evaluation of prosthetic valve and associated complications (►**Fig. 3**; ►**Table 1**).

Velocity and Gradients on Echocardiography Post–Valve Replacement

Doppler velocity recordings across normal prosthetic valves usually resemble those of mild native aortic stenosis. Maximal velocity across valve is usually <3 m/s with triangular shape of the velocity contour. As stenosis increases, velocity and gradient across valve will increase as well. High gradients may be seen with normally functioning valves with small sized valve or PPM or due to increased stroke volume or because of valve obstruction. Conversely, a mildly elevated gradient in severe left ventricular (LV) dysfunction may indicate significant stenosis. Thus, ability to distinguish malfunctioning from normal prosthetic valves in high flow states on the basis of gradients is very unreliable.

Table 1 Doppler parameters for evaluation of aortic valve

A complete examination includes the following:
• Estimation of pressure gradients
• Effective orifice area
• Doppler velocity index
• Assessment of regurgitation if present
• Left ventricular size and function

Contour of the velocity through prosthesis is a qualitative index, and it should be used in conjunction with other quantitative indices. In a normal valve, even during high flow, there is a triangular shape to the velocity with early peaking of the velocity and short acceleration time (AT; AT time from the onset of flow to maximal velocity). With prosthetic valve obstruction, a more rounded velocity contour is seen with velocity peaking almost in midejection with prolonged AT, prolonged ejection time (ET), and prolonged AT-to-ET ratio. These parameters contributes to overall assessment of valve function, particularly in high gradients. A cut-off AT value of 100 ms has been attributed to differentiate between normal and stenotic prosthetic valves. An AT-to-ET ratio of >0.4 is also consistent with prosthetic valve obstruction. One thing to emphasize here that these indices are independent of Doppler angulation with jet direction (►**Figs. 4** and **5**).

Effective Orifice Area

Aortic EOA is most often derived with continuity equation

$$EOA_{PrAV} - CSA_{LVO} \times VTI_{LVO} / VTI_{PrAV}$$

CSA_{LVO} is the cross-sectional area of the outflow tract, derived from diameter measurement just underneath the prosthesis from the parasternal long-axis view.

$$CSA_{LVO} = \pi (D / 2)^2$$

VTI_{LVO} is the VTI proximal to the leaflets or occluder as recorded from an apical five-chamber or long-axis view using PW Doppler (►**Fig. 6**).

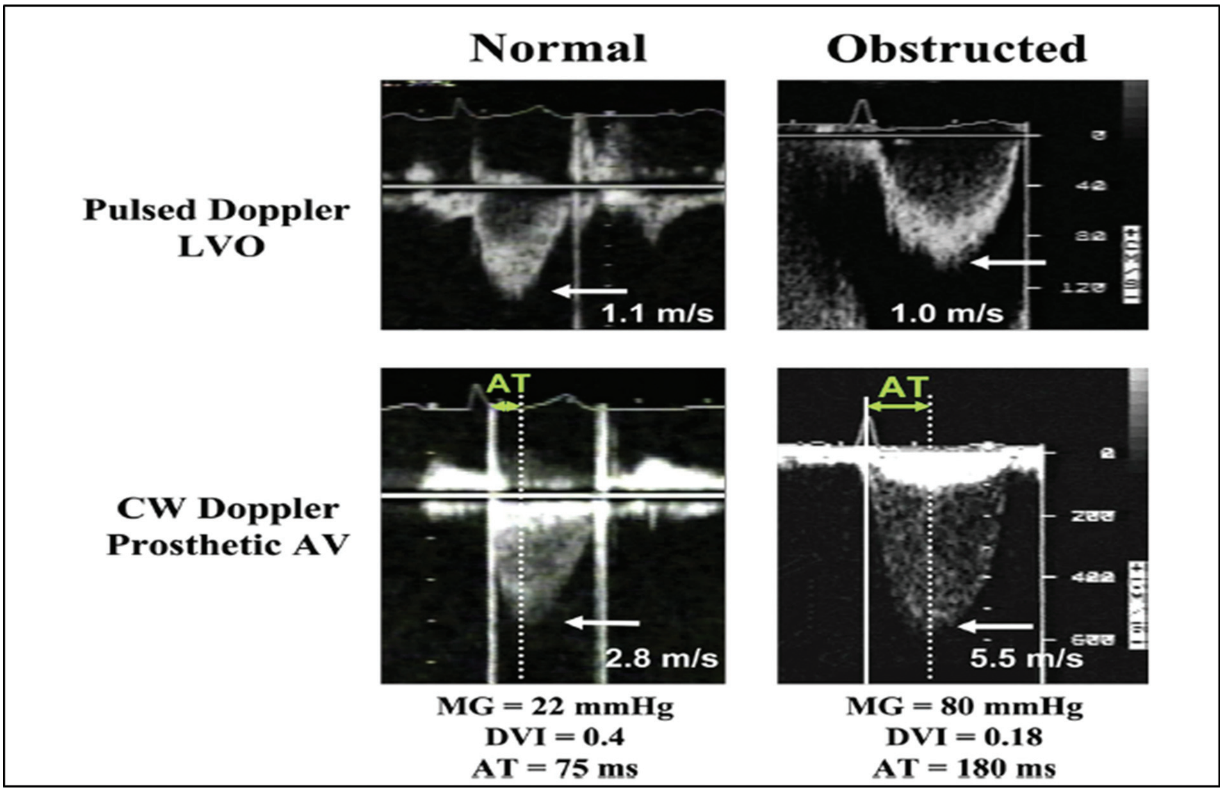

Fig. 4 Pulse wave and continuous wave doppler across LVOT and prosthetic valve showing comparison of normal and obstructed prosthetic aortic valve.

Doppler velocity index: The Doppler velocity index (DVI) is a dimensionless ratio of the proximal velocity in LVO tract to that of flow velocity through the prosthesis:

$DVI = V_{LVO} / V_{prAV}$

DVI does not take into account the diameter of LVOT and is much less dependent on valve size. So considered as better indicator of valve functioning. A DVI of <0.25 is highly suggestive of significant valve obstruction (►**Tables 2** and **3**).

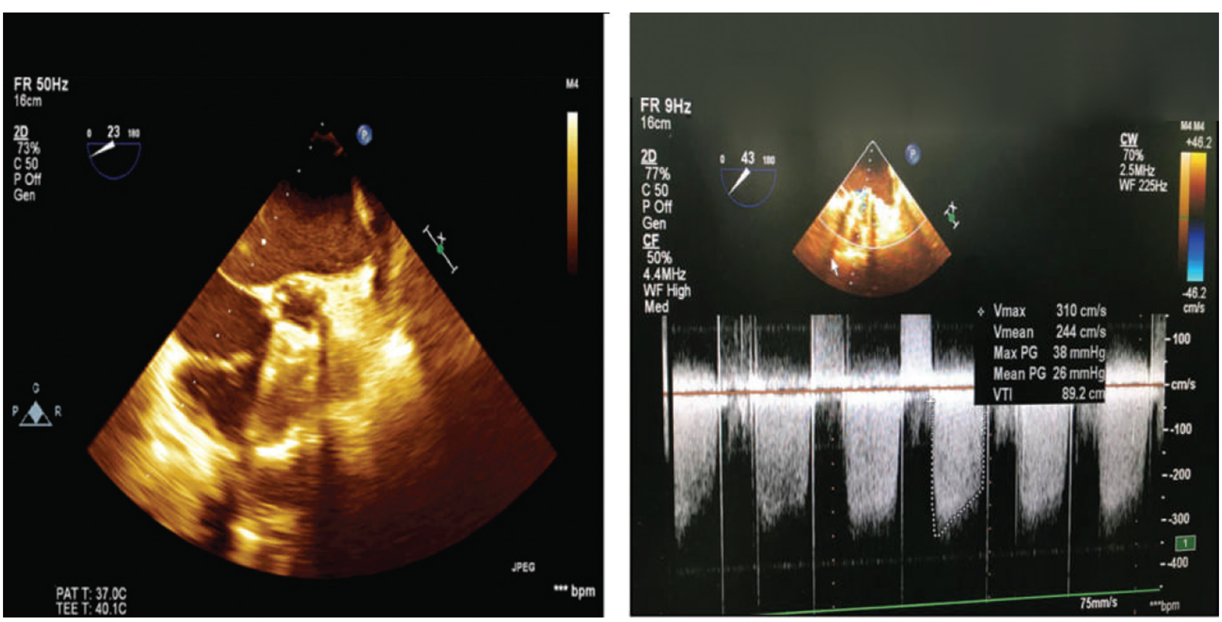

Fig. 5 CW Doppler across aortic valve showing high mean gradient across aortic valve. CW: Continuous Wave.

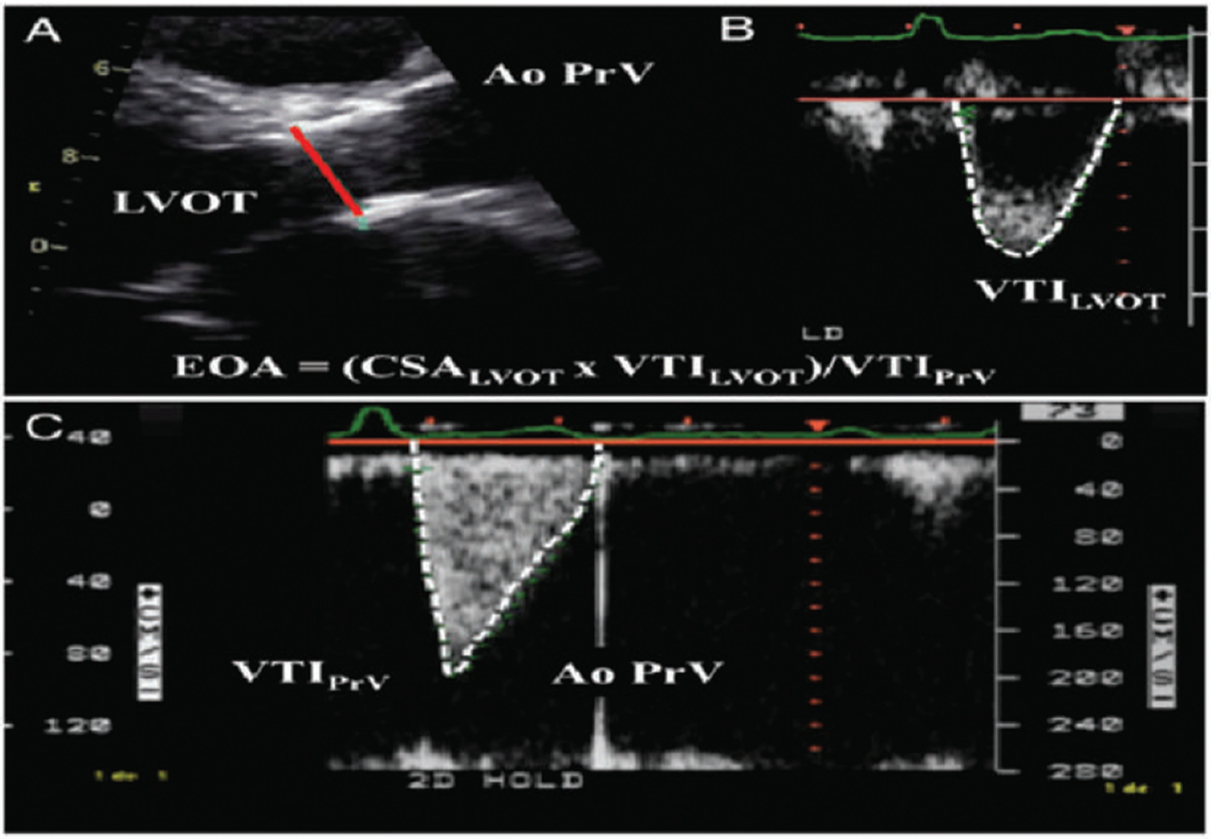

Fig. 6 Parasternal long-axis view for derivation of LVOT diameter and subsequently.

Table 2 Summarizing parameters of Doppler echocardiography

• Pressure gradient – Simplified Bernoulli's equation: $4V^2$
• Effective orifice area – Continuity equation: effective orifice area = stroke volume / VTI_{PrV} – Better index of valve function than gradient alone
• Dimensionless Index (DVI) = ratio of velocity proximal to the valve, to the velocity through the valve

Table 3 Doppler parameters of prosthetic aortic valve function

	Normal	Suggests stenosis
Peak velocity (m/s)	<3	>4
Mean gradient (mm Hg)	<20	>35
Doppler velocity index	≥0.3	<0.25
Effective orifice area (cm^2)	>1.2	<0.8
Contour of jet	Triangular Early peaking	Rounded Symmetrical contour
Acceleration time (ms)	<80	>100

Table 4 showing parameters required for mitral valve examination

Mean pressure gradient
Pressure half time
Effective orifice area
Doppler velocity index
Valvular or paravalvular regurgitation

Mitral Patient Prosthesis Mismatch: Diagnosis

Doppler Echocardiography is the gold standard for diagnosing mitral PPM (►**Table 4**).

Mean Gradient

Normal gradient across mitral valve is less than 5 to 6 mm Hg. High mean gradients may be due to hyperdynamic states, tachycardia, PPM, regurgitation, or stenosis. Since mean gradient is affected by tachycardia, heart rate at which gradient is obtained should always be noted (►**Table 5**; ►**Figs. 7** and **8**).

Pressure Half Time

Pressure half-time seldom exceeds 130 ms across a normally functioning mitral valve prosthesis. Gradual increase in pressure half-time over serial measurement or markedly prolonged single measurement (>200 ms) indicates

Table 5 Outpatient department to operation theatre: A 41-year-old female

Example of 41 year old female patient coming with high gradient across mitral valve . thrombolysis was planned and post procedure normal functioning valve seen
Height: 149 cm, weight: 53 kg, BSA: 1.46 m^2
Concentric LVH LVMI = 119 g/2, RWT = 0.53, LVEF 74%
Aortic root = 2.8 cm, LVOT diameter = 2.1 cm, LVOT VTI = 26.7
Ao VTI = 98.1
DVI = 0.27
EOA = 0.94 cm^2, iEOA = 0.64
MVG = 42 mm Hg
PIG = 89 mm Hg
SPAP = 33 mm Hg

Abbreviations: Ao VTI, Aortic velocity time interval; BSA, body surface area; DVI, Doppler velocity index; EOA, effective orifice area; MVG, mitral valve gradient; PG, peak gradient, SPAP, systolic pulmonary artery pressure; VTI, velocity time interval.

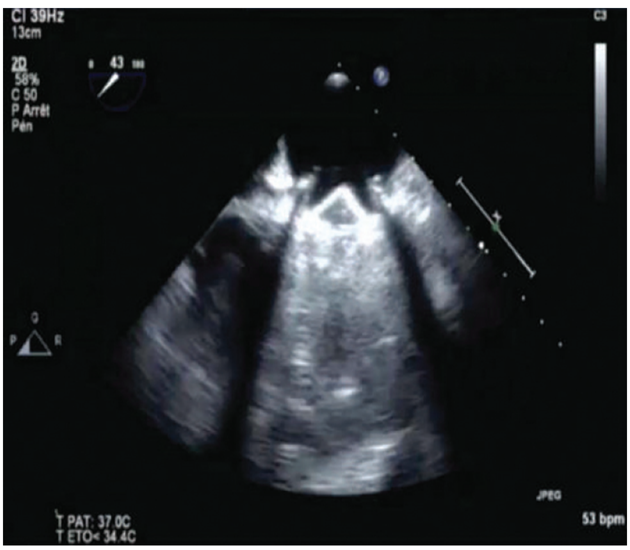

Fig. 7 Preprocedure stuck mitral valve.

prosthetic valve obstruction. However, minor changes in pressure half-time may occur due altered loading conditions or aortic insufficiency (►**Fig. 9**).

Effective Orifice Area

EOA is derived as stroke volume through the prosthesis divided by the VTI of the mitral jet velocity.

EOA calculation by the continuity equation is preferable to that measured by pressure half-time in mitral prostheses.

In leaflet valves, the smaller central orifice has a higher velocity than larger outside orifices which may lead to underestimation of EOA by continuity equation. Thus, EOA by the continuity equation is more accurate for bioprosthetic valves and single tilting disc mechanical valves.

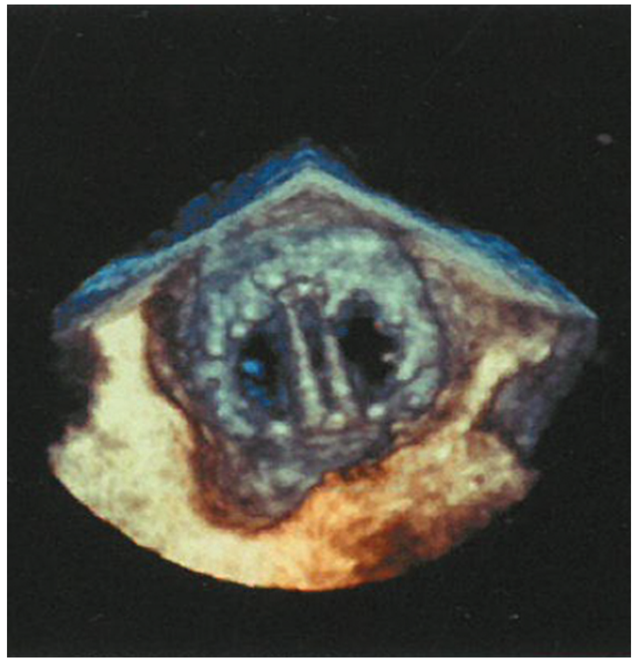

Fig. 8 A 3D TEE still frame image from the LA viewpoint imaging, demonstrating a normal bileaflet mechanical valve in the mitral position. 3D, three-dimensional; LA, left atrium.

$$EOA = SV / VTI\ mitral$$

Stroke volume through mitral valve is equated with that through LVOT when there is no significant MR or AR. Normative information on EOA and EOA indexed to BSA is available for several types of prostheses in the mitral position. So far, effective areas are usually applied when there is discrepancy between pressure gradients and pressure half-time (►**Fig. 10**).

Doppler Velocity Index

Ratio of the VTIs of the mitral prosthesis to the LVO tract:

$$DVI = VTI_{PrMV} / VTI_{LVOT}$$

It is an index of prosthetic mitral valve mechanical function. In high output states, there will be increase in velocity across both the valves, thus nullifying the effect of high flow on DVI. However, DVI would be elevated either in mitral stenosis (increased velocity across the mitral valve) or in mitral regurgitation (increased velocity across mitral valve and decreased velocity in LVOT). In mechanical valves, DVI < 2.2 is considered as normal.

Clinical Sequalae of Patient Prosthesis Mismatch

Left Ventricular Function

Postoperative occurrence of PPM is associated with less regression of LV mass, thus associated with depressed LV function. In a study of 1,103 patients with a porcine bioprosthetic valve, Del Rizzo et al found strong and independent relation between indexed EOA and extent of LV mass regression after AVR.[13] Tasca et al in a smaller series of patients also demonstrated that normalization of LV mass is

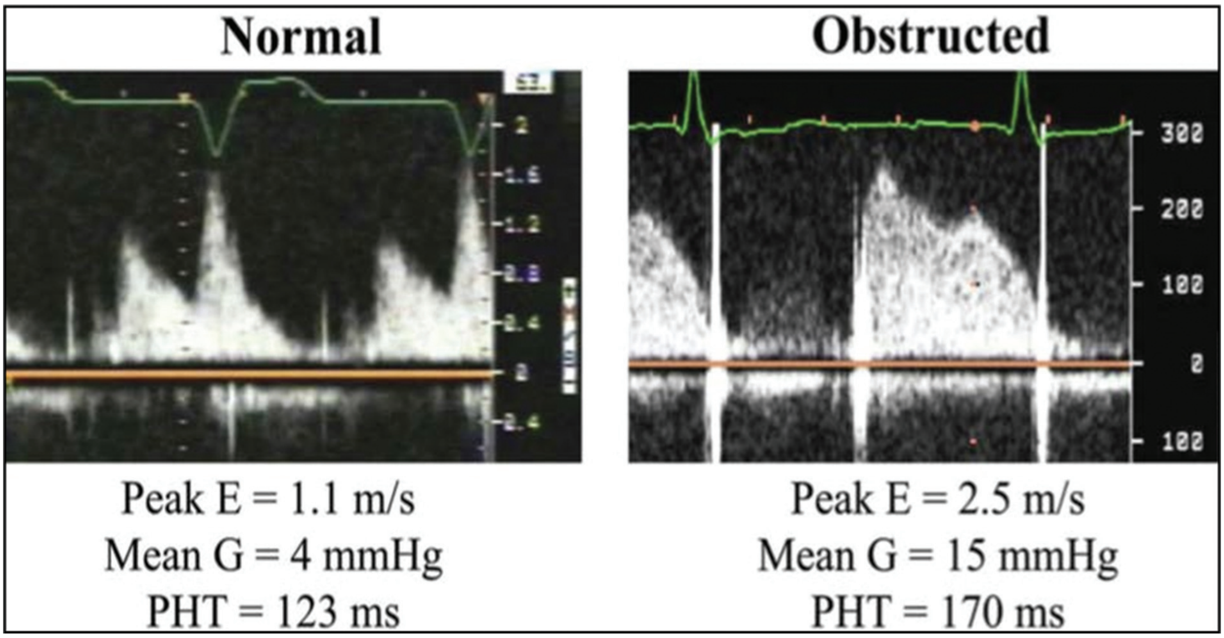

Fig. 9 Continuous wave interrogation across mitral valve showing indices of obstruction across mitral valve

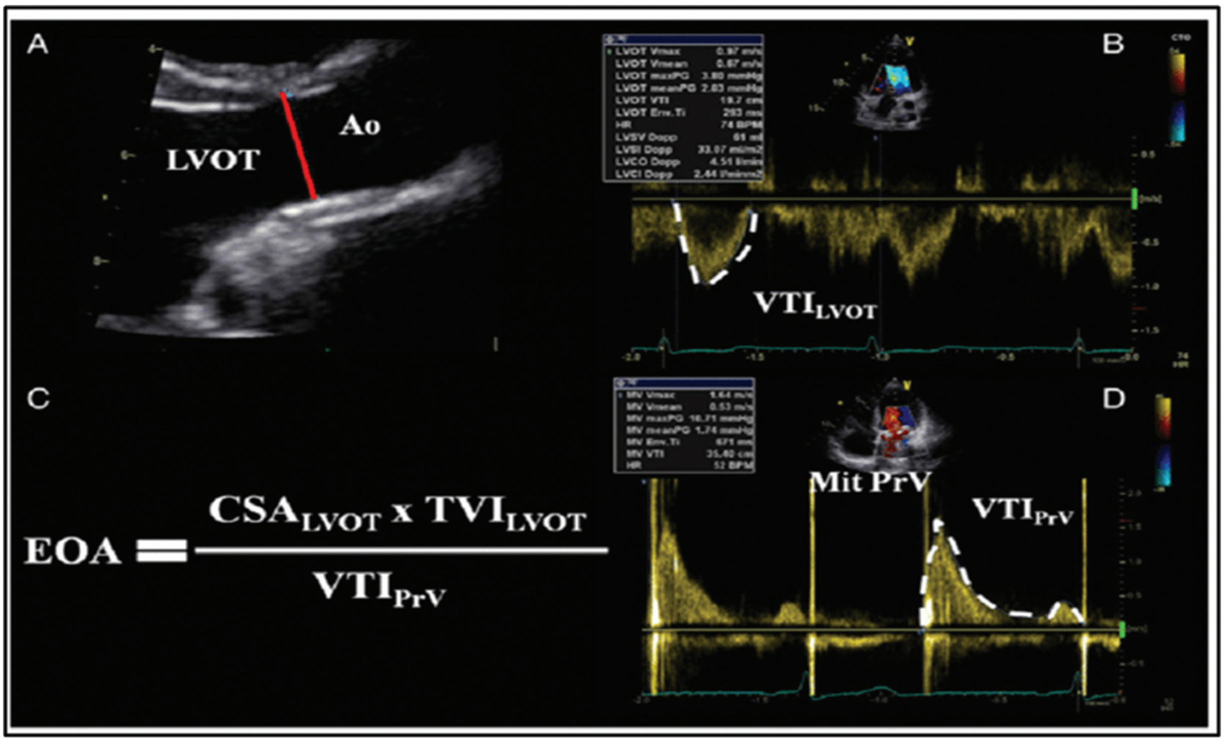

Fig. 10 Doppler evaluation of mitral prosthesis.

negatively and independently influenced by PPM.[14] Usually after AVR, there occur normalization of coronary flow reserve. PPM compromises normalization of flow reserve and thus have detrimental impact on LV function. Consistently, PPM is associated with a significant reduction in cardiac index during postoperative course.[15] Patients with severe PPM or with preoperative severe LV dysfunction face the greatest burnt. Incidence of congestive heart failure was significantly higher in patients with PPM.[16] PPM become more hazardous in patients with low flow low gradient AS or patient with concomitant mitral regurgitation or those with severe LV hypertrophy.

Bleeding Complication

Vincentelli et al reported that abnormalities of the von Willebrand factor are common in patients with severe

	EOAi by Prosthesis size (mm)					
Prosthesis size (mm)	**19**	**21**	**23**	**25**	**27**	**29**
Average EOA (cm^2)	1.1	1.3	1.5	1.8	2.3	2.7
BSA (m^2)						
0.6	1.83	2.17	2.50	3.00	3.83	4.50
0.7	1.57	1.86	2.14	2.57	3.29	3.86
0.8	1.38	1.63	1.88	2.25	2.88	3.38
0.9	1.22	1.44	1.67	2.00	2.56	3.00
1	1.10	1.30	1.50	1.80	2.30	2.70
1.1	1.00	1.18	1.36	1.64	2.09	2.45
1.2	0.92	1.08	1.25	1.50	1.92	2.25
1.3	0.85	1.00	1.15	1.38	1.77	2.08
1.4	0.79	0.93	1.07	1.29	1.64	1.93
1.5	0.73	0.87	1.00	1.20	1.53	1.80
1.6	0.49	0.88	0.88	0.88	0.88	1.69
1.7	0.65	0.76	0.88	1.06	1.35	1.59
1.8	0.61	0.72	0.83	1.00	1.28	1.50
1.9	0.58	0.68	0.79	0.95	1.21	1.42
2	0.55	0.65	0.75	0.90	1.15	1.35
2.1	0.52	0.62	0.71	0.86	1.10	1.29
2.2	0.50	0.59	0.68	0.82	1.05	1.23
2.3	0.48	0.57	0.65	0.78	1.00	1.17
2.4	0.46	0.54	0.63	0.75	0.96	1.13
2.5	0.44	0.52	0.60	0.72	0.92	1.08

Fig. 11 Appropriate-sized valve for patient. BSA, body surface area.

aortic stenosis.[17] They also stated that the von Willebrand abnormalities are directly related to transvalvular gradient, and stenosis induced shear stress. These abnormalities are supposed to improve after AVR but patients with PPM, they have shown to have persistent factor abnormalities contributing to hemolysis and increased bleeding problem.

Early Mortality

Due to surgery-induced myocardial edema, cardiopulmonary bypass induces myocardial injury, left ventricle is more vulnerable in early postoperative course. Left ventricle becomes more sensitive to increased hemodynamic burden imposed by PPM. Several studies reported that early mortality is significantly increased in patients with PPM.[18,19]

Late Mortality

PPM has been shown to be directly related to occurrence of late mortality.[18] Patient undergoing long-term valve degeneration and pannus formation have less-effective orifice area reserve and occurrence of PPM in such patient can be catastrophic.

Prevention of Mismatch

PPM is modifiable and can be avoided by following simple algorithm

Calculate patient's BSA from weight and height

Ø BSA $\times$ 0.85 cm^2/m^2

The result is being the minimum EOA that the prosthesis to be implanted should have to avoid PPM. For example, if patient's BSA is 1.80 m^2, then 1.53 cm^2 is the minimum EOA that choose the prosthesis in light of result obtained and the reference values for different types and sizes of prosthesis.

Manufactures Chart for Prediction of Patient Prosthesis Mismatch Used at the All India Institute of Medical Sciences

Different manufactures provide color coded charts for use of appropriate-sized valve for patient (►**Fig. 11**).

Management of Patient Prosthesis Mismatch

Patients with evidence of PPM, especially severe PPM, should receive close clinical and imaging follow-up.

Valve reintervention may be considered if

- PPM is severe or associated with greater than or equal to moderate valve stenosis.
- Mean transprosthetic gradient is high (30–35 mm Hg).
- Patient develops heart failure symptoms or LV systolic dysfunction.

If PPM is projected with type of prosthesis that was originally intended to be implanted, following options can be considered:

- Option 1: implant another type of prosthesis with larger EOA, such as a stent-less bioprosthesis, a new generation mechanical prosthesis or an aortic homograft.
- Option 2: enlarge the aortic root to accommodate a larger prosthesis of the same type.
- Option 3: can do TVAR rather than surgical AVR.

Conclusion

PPM is common but modifiable risk factor that provided simple steps of calculating BSA and EOA has been done and manufacture's chart has been referred timely. Echocardiography plays a pivotal role in diagnosis of PPM. No single Doppler parameter is considered superior, and combination of different doppler parameters is sufficient to make the diagnosis. Hemodynamics of patients, valve types and size, and previous echocardiography records should be taken into account while making the diagnosis. It can lead to worsening of hemodynamic function, less regression of LV mass, more cardiac events, and lower survival post–valve replacement. Once diagnosis of PPM confirmed, whether to replace the valve or not, it should be considered in the light of present clinical scenario.

There are various methods to calculate PPM as follows:

- It is a nonstructural dysfunction, a composite category that includes any abnormality that results in stenosis or regurgitation of the operated valve that is not intrinsic to the valve itself, exclusive of thrombosis and infection.
- This includes inappropriate sizing which is called valve prosthesis – patient mismatch (VP – PM).
- When the effective prosthetic valve area after insertion into the patient is less than that of a normal valve.
- Patients with aortic prosthetic heart valve (PHV) have obstruction to left ventricular outflow (similar to aortic stenosis), and patients with mitral PHV have obstruction to left atrial emptying (similar to mitral stenosis).
- Various methods to calculate PPM.
- Echocardiography-derived EOA index (EOAI) is dependent on accurate measurements.
- Severe PPM may impact survival.
- Patients with low EF are most vulnerable.
- Avoidance of PPM is the best treatment.

Conflict of Interest
None declared.

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