Accepted Manuscript

Title: Usefulness of Mitral Valve Prosthetic or Bioprosthetic Time Velocity Index Ratio to Detect Prosthetic or Bioprosthetic Mitral Valve Dysfunction

Author: Sushil Allen Luis, Lori A. Blauwet, Himabindu Samardhi, Cathy West, Ramila A. Mehta, Chris R. Luis, Gregory M. Scalia, Fletcher A. Miller Jr, Darryl J. Burstow

PII: S0002-9149(17)31191-8
DOI: http://dx.doi.org/doi: 10.1016/j.amjcard.2017.07.026
Reference: AJC 22773

To appear in: *The American Journal of Cardiology*

Received date: 24-4-2017
Accepted date: 12-7-2017

Please cite this article as: Sushil Allen Luis, Lori A. Blauwet, Himabindu Samardhi, Cathy West, Ramila A. Mehta, Chris R. Luis, Gregory M. Scalia, Fletcher A. Miller Jr, Darryl J. Burstow, Usefulness of Mitral Valve Prosthetic or Bioprosthetic Time Velocity Index Ratio to Detect Prosthetic or Bioprosthetic Mitral Valve Dysfunction, *The American Journal of Cardiology* (2017), http://dx.doi.org/doi: 10.1016/j.amjcard.2017.07.026.

Usefulness Of Mitral Valve Prosthetic Or Bioprosthetic Time Velocity Index Ratio To Detect Prosthetic Or Bioprosthetic Mitral Valve Dysfunction

Sushil Allen Luis, MBBS*; Lori A. Blauwet, MD*; Himabindu Samardhi, MBBS; Cathy West, DMU; Ramila A. Mehta; Chris R. Luis, MBBS; Gregory M. Scalia, MBBS; Fletcher A. Miller Jr, MD; Darryl J. Burstow, MBBS

* Drs S. A. Luis and L. A. Blauwet contributed equally to this work.

Author Affiliations: Department of Cardiovascular Diseases (Drs S. A. Luis, Blauwet, and Miller) and Division of Biomedical Statistics and Informatics (Ms Mehta), Mayo Clinic, Rochester, Minnesota; The Prince Charles Hospital (Drs Samardhi, West, C. R. Luis, Scalia, and Burstow), Brisbane, Australia; and School of Medicine (Drs Luis, Scalia, and Burstow), The University of Queensland, Brisbane, Australia. Dr S. A. Luis is formerly of The Prince Charles Hospital, Brisbane, Australia.

Reprints: Sushil Allen Luis, MBBS, Department of Cardiovascular Diseases, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (Luis.S@mayo.edu Phone: 507-266-3089 Fax: 507-266-7929).

Text word count: 2,525

Abstract word count: 247

No. of tables: 5

No. of online supplemental tables: 2

No. of figures: 5

Running title: Mitral Valve Prosthesis Ratio

Publisher: To expedite proof approval, send proof via email to scipubs@mayo.edu.

Abstract

The present study aimed to investigate the utility of transthoracic echocardiographic (TTE) Doppler-derived parameters in detection of mitral prosthetic valve dysfunction and to define optimal cutoff values for identification of such dysfunction by valve type. In total, 971 TTE studies (647 mechanical prostheses; 324 bioprostheses) were compared with transesophageal echocardiography for evaluation of mitral prosthesis function. Among all prostheses, mitral valve prosthesis (MVP) ratio (ratio of time velocity integral of MVP to that of left ventricular outflow tract; odds ratio [OR] [95% CI], 10.34 [6.43-16.61]; *P*<.001), E velocity (OR [95% CI], 3.23 [1.61-6.47]; *P*<.001), and mean gradient (OR [95% CI], 1.13 [1.02-1.25]; *P*=.02) provided good discrimination of clinically normal and clinically abnormal prostheses. Optimal cutoff values by receiver operating characteristic analysis for differentiating clinically normal and abnormal prostheses varied by prosthesis type. Combining MVP ratio and E velocity improved specificity (92%) and positive predictive value (65%) compared with either parameter alone, with minimal decline in negative predictive value (92%). Pressure half-time (OR [95% CI], 0.99 [0.98-1.00]; *P*=.04) did not differentiate between clinically normal and clinically abnormal prostheses but was useful in discriminating obstructed from normal and regurgitant prostheses. In conclusion, cutoff values for TTE-derived Doppler parameters of MVP function were specific to prosthesis type and carried high sensitivity and specificity for identifying prosthetic valve dysfunction. MVP ratio was the best predictor of prosthetic dysfunction and, combined with E velocity, provided a clinically useful parameter for determining likelihood of dysfunction and need for further assessment with transesophageal echocardiography.

Keywords: Doppler echocardiography; echocardiography; mitral valve prosthesis; transthoracic echocardiography

Introduction

Assessment of mitral prosthetic valve function by transthoracic echocardiography (TTE) poses considerable challenges in patients with mechanical and bioprosthetic valves. Acoustic shadowing related to prosthetic material frequently obscures valve components and the adjacent left atrium, impairing TTE detection of prosthetic valve dysfunction, particularly regurgitation (1,2), often necessitating additional imaging with transesophageal echocardiography (TEE). Despite these limitations, TTE is the recommended modality for routine monitoring of prosthetic valve function because of its safety, widespread availability, and noninvasive nature (1). We aimed to investigate the utility of Doppler-derived parameters of mitral valve prosthesis (MVP) function obtained with TTE for the detection of prosthetic valve dysfunction in a large cohort of mechanical and bioprosthetic MVPs. We also aimed to define optimal cutoff values for identification of prosthetic valvular dysfunction by valve type.

Methods

A retrospective review was performed of consecutive patients with MVPs undergoing both comprehensive TTE and TEE within 30 days, at Mayo Clinic in Rochester, Minnesota, United States of America, and The Prince Charles Hospital in Brisbane, Australia, between January 1, 2004, and December 31, 2012. Patients were identified through searches of echocardiography databases at both institutions. Demographic and clinical data were abstracted from echocardiographic and operative reports. The study was reviewed and approved by the Mayo Clinic Institutional Review Board and The Prince Charles Hospital Research Ethics Committee and complies with the Declaration of Helsinki. Inclusion and exclusion criteria are listed in Figure 1.

TEE was defined as the gold standard for evaluation of MVP function. All TEE studies were performed using standard, commercially available systems with multiplane TEE probes. Prosthetic mitral valve function was assessed in multiple planes and acoustic windows with 2-dimensional color flow Doppler and continuous-wave Doppler assessments as defined by current guidelines (3). All TEE studies were performed for routine clinical indications and reviewed by experienced echocardiologists, with specific evaluation of prosthetic valve function, including assessment of possible prosthetic valve obstruction and the presence or absence of prosthetic and/or periprosthetic mitral valve regurgitation. Severity of mitral regurgitation was classified semiquantitatively in accordance with current guidelines (4).

TTE studies were performed using standard commercially available systems. Standard TTE parameters were assessed with 2-dimensional pulse-wave Doppler and continuous-wave Doppler in accordance with current guidelines (1,5). The TEE findings were masked to investigators. Doppler measurements from 5 cardiac cycles were averaged in atrial fibrillation (6). Mitral prosthetic effective orifice area and indexed effective orifice area were calculated using the continuity equation. The MVP ratio was calculated as the ratio of the time velocity integral of transprosthetic mitral flow by continuous-wave Doppler to time velocity integral of the left ventricular outflow tract by pulse-wave Doppler.

With use of TEE, normal prostheses were defined as prostheses with normal leaflet motion, trivial or less prosthetic regurgitation, and no evidence of periprosthetic regurgitation.

Mitral regurgitation was defined as the presence of prosthetic or periprosthetic regurgitation without evidence of leaflet restriction. Mitral stenosis was defined as the presence of restricted prosthetic leaflet opening. Combined mitral stenosis and regurgitation was defined as concomitant presence of mitral stenosis and at least moderate mitral regurgitation. Prostheses

were then divided into 2 functional categories for statistical analysis: clinically normal and clinically abnormal. Clinically normal prostheses included all valve prostheses with less than moderate mitral regurgitation. Clinically abnormal prostheses included valve prostheses classified with significant mitral regurgitation (moderate or greater mitral regurgitation), mitral stenosis, or combined mitral stenosis and regurgitation as defined above.

Continuous variables are expressed as mean (SD) and categorical variables as percentages. Receiver operating characteristic curves were computed to determine optimal cutoff values to detect MVP dysfunction. Doppler-derived parameters of clinically normal prostheses were compared with those of clinically abnormal prostheses by receiver operator curve analysis. Subgroup analysis by valve type was also performed, comparing both groups. Optimal cutoff values by the receiver operator curve analysis were chosen to optimize sensitivity over specificity, which was defined as the point where sensitivity equals 1 and 1 – specificity equals 0. The predictive ability of each variable was compared with area under the receiver operator curve using the trapezoidal rule. Statistical significance was defined as $P<.05$. Statistical analysis was performed with SAS version 9.4 (SAS Institute Inc).

Results

We reviewed 1,228 TTE studies, of which 971 met study criteria (Figure 1), including 647 mechanical prostheses (67%) and 324 bioprostheses (33%) (Online Supplemental Tables 1 and 2). Prosthesis size ranged between 21 and 35 mm. Mean (SD) age of the study population was 63.4 (14.6) years, and 557 patients (57%) were female. Mean (SD) hemoglobin was 108 (19) g/L; mean (SD) heart rate at TTE was 75 (12) beats per minute. Heart rhythm was identified in 949 patients: sinus rhythm in 564 patients (59%), atrial arrhythmias in 298 (31%), paced rhythms in 85 (9%), and junctional arrhythmia or complete heart block in 2 (0.2%). Mean

(SD) left ventricular ejection fraction was 54% (13%) (range, 8%-80%), with 331 patients (34%) having left ventricular systolic dysfunction as defined by an ejection fraction <52% (5).

Doppler-derived parameters of normally functioning MVPs obtained during TTE examination are listed in Table 1. Significant differences in Doppler parameters were found between valve types (*P*<.001). Compared with porcine bioprostheses, bileaflet mechanical and pericardial prostheses had a lower mean gradient and MVP ratio and larger effective orifice area—suggestive that these prostheses have a more physiologic hemodynamic profile.

Smaller prosthesis size was associated with significantly higher E velocity (*P*<.001), mean gradient (*P*<.001), time velocity integral of the MVP (*P*=.001), and time velocity integral of the left ventricular outflow tract (*P*<.001). MVP ratio was not significantly affected by prosthesis size (*P*=.19), suggestive that time velocity integral of the MVP and time velocity integral of the left ventricular outflow tract were both proportionately altered by clinical factors. Pressure half-time was unaffected by prosthesis size (*P*=.59).

Abnormal MVPs as defined by TEE were associated with increased E velocity, mean gradient, time velocity integral of MVP, and MVP ratio (Table 2). Pressure half-time among prostheses with mitral regurgitation was similar to normal prostheses, regardless of mitral regurgitation severity.

Prosthetic stenosis was associated with greater E velocity, mean gradient, and MVP ratio than both normal prostheses and those with moderate or greater mitral regurgitation. These parameters were most markedly increased in the combined mitral stenosis and mitral regurgitation group. Pressure half-time was significantly prolonged in the mitral stenosis and combined mitral stenosis and mitral regurgitation groups but not in the other groups.

Table 3 and Figure 2 present the results of the receiver operator curve analysis with cutoff values optimized for sensitivity. Across all prostheses, MVP ratio, E velocity, and mean gradient provided good discrimination of clinically normal and clinically abnormal prostheses, in rank order by odds ratio (Table 4). Pressure half-time did not differentiate clinically normal from clinically abnormal prostheses.

Differences existed in the optimal cutoff values by receiver operator curve analysis among prosthesis types (Table 3). Results of subgroup receiver operator curve analysis for tilting disk prostheses are not reported because of small sample size. An increased MVP ratio was proven to be the strongest predictor of clinically abnormal prostheses in both bileaflet mechanical and porcine prostheses subgroups. Given the small number of pericardial prostheses studied, no Doppler parameter (Table 4) was shown to be predictive of prosthetic dysfunction.

Receiver operator curve analysis for the differentiation of clinically normal prostheses from those with mitral stenosis or combined mitral stenosis and mitral regurgitation demonstrated that these groups can be differentiated by pressure half-time, with an overall cutoff of 109 ms differentiating both groups across all prostheses. Optimal cutoff values differed by prosthesis type. A pressure half-time ≥100 ms predicted bileaflet mechanical prosthetic stenosis with 81.3% sensitivity, 91.3% specificity, 23.6% positive predictive value, and 99.3% negative predictive value. Analysis of bioprosthetic stenosis yielded a cutoff pressure half-time ≥130 ms, which predicted stenosis with 100% sensitivity, 100% specificity, 100% positive predictive value, and 100% negative predictive value in our cohort of 10 patients.

The sensitivity, specificity, positive predictive value and negative predictive value of MVP ratio, and E velocity are shown in Table 5. Combination of both parameters improved

specificity and positive predictive value compared with either of these parameters alone, with minimal decline in negative predictive value.

Discussion

The principal study findings can be summarized in 4 results. First, TTE-derived Doppler parameters carry high sensitivity and high specificity for the identification of prosthetic valve dysfunction as defined by gold standard TEE. Second, MVP ratio is the best predictor of prosthetic dysfunction and, when used in combination with E velocity, further improved the positive predictive value compared with either parameter alone. Third, cutoff values for Doppler parameters of prosthetic valve function are specific to the prosthesis type assessed. Fourth, pressure half-time was increased in obstructed prostheses but stayed normal in other prostheses, including those with moderate or greater mitral regurgitation.

The potential role of Doppler parameters obtained on TTE examination for identifying prosthetic mitral valve dysfunction has been investigated previously in a smaller cohort of mechanical MVPs, where similar cutoffs for MVP ratio and E velocity were reported (7). The present study not only confirms the value of Doppler-derived parameters in the assessment of mechanical valve prostheses but also demonstrates the potential value of such parameters in bioprosthetic valves. The sensitivity and positive predictive value of E velocity and MVP ratio in the present study are less than those reported previously, likely reflecting the lower prevalence of prosthetic dysfunction in this study (23% vs 46%) (7). Given the relatively low prevalence of abnormal mitral prostheses, our study findings likely reflect real-world performance of these parameters whereby normal parameters are associated with a high negative predictive value, and abnormal parameters carry a more moderate predictive value for the identification of prosthetic dysfunction.

In contrast to flow-dependent Doppler parameters such as mean gradient and E velocity, MVP ratio provides a flow-corrected measure of prosthesis function and should remain normal in a normally functioning MVP independent of cardiac output variation because of the expected proportional changes in both time velocity integral of the MVP and time velocity integral of the left ventricular outflow tract. Conversely, a significant change in MVP ratio should occur only with a change in MVP function. Consistent with this theoretical advantage, MVP ratio was shown to be the strongest predictor of prosthetic dysfunction in both regurgitant and obstructed valves in the present study. For prostheses with clinically significant mitral regurgitation, a high MVP ratio reflects the disproportionate increase in flow across the MVP (due to the regurgitant volume) compared with left ventricular stroke volume. A high MVP ratio in the clinical setting of prosthetic stenosis reflects a significant increase in Doppler flow velocities proportional to a decreased prosthesis effective orifice area (7). The superiority of MVP ratio relative to other Doppler parameters is true not only in the cohort as a whole but also across prosthesis types, particularly bileaflet mechanical and porcine prostheses. Unlike other Doppler parameters studied, MVP ratio appears unaffected by prosthesis size, reflecting the proportionate relationship of MVP size with left ventricular outflow tract diameter.

In previous studies, different valve brands within a particular valve type have exhibited similar hemodynamic characteristics (8-11). However, in our study, significant variability was seen in transthoracic Doppler parameters among different MVP types (eg, mechanical versus porcine) in both normal and abnormal prosthesis groups. Moreover, optimal cutoffs for the prediction of prosthetic valve dysfunction also varied by valve type in our study. This suggests that threshold values used for the identification of prosthetic valve dysfunction should be type specific in decision-making algorithms. Attempts to use a single set of cutoff

values across all valve types may reduce the diagnostic accuracy of such values for the detection of prosthetic valve dysfunction. Proposed diagnostic algorithms for the detection of MVP dysfunction based on our data, including separate algorithms for bileaflet mechanical and porcine prostheses, are presented in Figures 3 through 5. In keeping with the data presented, the algorithms presented combine the parameters of MVP ratio and E velocity to improve specificity and positive predictive value, with minimal decrease in negative predictive value.

Our proposed diagnostic algorithms divide patients into 3 categories: low risk, intermediate risk, and high risk. A normal MVP ratio alone has a strong negative predictive value and can reliably exclude prosthetic dysfunction. This patient group can hence be categorized as low risk and does not require further imaging with TEE. In contrast, patients with both an elevated MVP ratio and increased E velocity carry a high positive predictive value for identification of prosthetic dysfunction, and further evaluation with TEE should be considered. In the small group of patients where MVP ratio and E velocity are discordant, the risk of prosthetic dysfunction is less clear and TEE should be considered on the basis of clinical assessment. High-risk patients can then be further divided by pressure half-time to define the presence of pathologic obstruction or regurgitation. In the presence of increased MVP ratio and E velocity, a short pressure half-time suggests the presence of pathologic regurgitation; by comparison, pressure half-time prolongation is associated with prosthetic obstruction either alone or in combination with pathologic regurgitation. These proposed algorithms provide a simple, effective screening mechanism that reliably classifies patients into those who require further evaluation or closer follow-up, and those who do not.

Further classification of low-risk patients (ie, with a normal MVP ratio) can be attempted for identification of severe prosthesis-patient mismatch using indexed effective orifice

area. Prosthesis-patient mismatch occurs when the implanted prosthesis is too small for the patient's body size and typically results in elevated prosthetic valve gradients secondary to high flow across a normally functioning prosthesis. As shown in Figure 3, in the normal MVP ratio group, 21% could be classified as prosthesis-patient mismatch. Unfortunately, this classification is subject to the technical limitations of effective orifice area calculation and may result in a potentially low rate of accurate classification. Although prosthesis-patient mismatch in MVPs has been associated with an increased incidence of pulmonary hypertension and worse long-term mortality rate, prevention and treatment of this condition poses considerable challenges (12-14). Thus, in the absence of clinically significant symptoms, the inability to detect prosthesis-patient mismatch may be of less clinical importance in patient management. Additional limitations of this study include the relatively small numbers of tilting disk and pericardial valves compared with the other groups. Hence, where overall results are quoted, these results may not be representative of the tilting disk and pericardial groups, and subgroup analysis should be used where available in applying study data to these patient groups. The results and the proposed algorithms need to be validated in prospective studies to confirm the findings of the present retrospective study.

In conclusion, the Doppler parameters MVP ratio, E velocity, mean gradient, and pressure half-time are valuable tools in the TTE assessment of MVP function. MVP ratio demonstrates superior clinical utility in the detection of clinically significant dysfunction in both mechanical and bioprosthetic valves.

Acknowledgments

Funding Source: None. Conflicts of Interest: None. Previously published in poster form: Luis SA, Blauwet L, Mehta R, Samardi H, West C, Luis C, Scalia G, Miller F, Burstow D. Mitral

valve index: a simple and robust parameter for detecting prosthetic mitral valve regurgitation. *J Am Coll Cardiol* 2015;65(Suppl):A1331. Used with permission.

References

1. Zoghbi WA, Chambers JB, Dumesnil JG, Foster E, Gottdiener JS, Grayburn PA, Khandheria BK, Levine RA, Marx GR, Miller FA Jr, Nakatani S, Quinones MA, Rakowski H, Rodriguez LL, Swaminathan M, Waggoner AD, Weissman NJ, Zabalgoitia M; American Society of Echocardiography's Guidelines and Standards Committee; Task Force on Prosthetic Valves; American College of Cardiology Cardiovascular Imaging Committee; Cardiac Imaging Committee of the American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography; Canadian Society of Echocardiography; American College of Cardiology Foundation; American Heart Association. Recommendations for evaluation of prosthetic valves with echocardiography and Doppler ultrasound: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese

Society of Echocardiography, and Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2009;22:975-1014.

2. Muratori M, Montorsi P, Teruzzi G, Celeste F, Doria E, Alamanni F, Pepi M. Feasibility and diagnostic accuracy of quantitative assessment of mechanical prostheses leaflet motion by transthoracic and transesophageal echocardiography in suspected prosthetic valve dysfunction. *Am J Cardiol* 2006;97:94-100.
3. Shanewise JS, Cheung AT, Aronson S, Stewart WJ, Weiss RL, Mark JB, Savage RM, Sears-Rogan P, Mathew JP, Quinones MA, Cahalan MK, Savino JS. ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography. *J Am Soc Echocardiogr* 1999;12:884-900.
4. Lancellotti P, Moura L, Pierard LA, Agricola E, Popescu BA, Tribouilloy C, Hagendorff A, Monin JL, Badano L, Zamorano JL; European Association of Echocardiography. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). *Eur J Echocardiogr* 2010;11:307-332.
5. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of

Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1-39.e14.

6. Quinones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA; Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. *J Am Soc Echocardiogr* 2002;15:167-184.
7. Fernandes V, Olmos L, Nagueh SF, Quinones MA, Zoghbi WA. Peak early diastolic velocity rather than pressure half-time is the best index of mechanical prosthetic mitral valve function. *Am J Cardiol* 2002;89:704-710.
8. Blauwet LA, Malouf JF, Connolly HM, Hodge DO, Herges RM, Suri RM, Miller FA Jr. Comprehensive hemodynamic assessment of 368 normal St. Jude Medical mechanical mitral valve prostheses based on early postimplantation echocardiographic studies. *J Am Soc Echocardiogr* 2013;26:381-389.
9. Blauwet LA, Malouf JF, Connolly HM, Hodge DO, Herges RM, Sundt TM 3rd, Miller FA Jr. Comprehensive hemodynamic assessment of 305 normal CarboMedics mitral valve prostheses based on early postimplantation echocardiographic studies. *J Am Soc Echocardiogr* 2012;25:173-181.
10. Blauwet LA, Malouf JF, Connolly HM, Hodge DO, Evans KN, Herges RM, Sundt TM 3rd, Miller FA Jr. Comprehensive echocardiographic assessment of normal mitral Medtronic Hancock II, Medtronic Mosaic, and Carpentier-Edwards Perimount bioprostheses early after implantation. *J Am Soc Echocardiogr* 2010;23:656-666.

11. Blauwet LA, Malouf JF, Connolly HM, Hodge DO, Evans KN, Herges RM, Sundt TM 3rd, Miller FA Jr. Doppler echocardiography of 240 normal Carpentier-Edwards Duraflex porcine mitral bioprostheses: a comprehensive assessment including time velocity integral ratio and prosthesis performance index. *J Am Soc Echocardiogr* 2009;22:388-393.

12. Magne J, Mathieu P, Dumesnil JG, Tanne D, Dagenais F, Doyle D, Pibarot P. Impact of prosthesis-patient mismatch on survival after mitral valve replacement. *Circulation* 2007;115:1417-1425.

13. Li M, Dumesnil JG, Mathieu P, Pibarot P. Impact of valve prosthesis-patient mismatch on pulmonary arterial pressure after mitral valve replacement. *J Am Coll Cardiol* 2005;45:1034-1040.

14. Pibarot P, Dumesnil JG. Prosthesis-patient mismatch: definition, clinical impact, and prevention. *Heart* 2006;92:10221029.

Figure 1. Selection Criteria and Characteristics of MVP. BPM indicates beats per minute; ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assist device; LVOT, left ventricular outflow tract; MVP, mitral valve prostheses; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

Figure 2. Receiver Operator Characteristic Analysis for the Differentiation of Clinically Normal From Clinically Abnormal MVPs. A, Analysis of E velocity. B, Analysis of mean gradient. C, Analysis of pressure half-time. D, Analysis of MVP ratio. MVP indicates mitral valve prosthesis.

Figure 3. Proposed Clinical Algorithm for the Evaluation of All Mitral Prostheses Using MVP Ratio, E Velocity, and PHT. These proposed algorithms are based on cutoff values determined from receiver operating curve analysis. They suggest that a normal MVP ratio can reliably exclude prosthetic dysfunction, whereas coexistent elevations in both MVP ratio and E velocity carry a high positive predictive value for identification of prosthetic dysfunction, warranting further investigation with TEE. Where MVP ratio and E velocity are discordant, the risk of prosthetic dysfunction is intermediate, and further investigation and management should be based on the clinical assessment. Groups in the lower colored panels (ie, normal, uncertain, regurgitation, and obstruction) were defined by frequency and type of dysfunction present at TEE, as itemized in each panel. This definition allowed for designation of the dysfunction risk (bottom panels) and subsequent TEE recommendation. Asterisk indicates that E velocity could not be measured in 1 patient. Double asterisk indicates that PHT cutoff was rounded from 109 ms defined by receiver operator characteristic analysis to 110 ms. PHT could not be measured in 10 studies: 4 prostheses with severe regurgitation, 3 with obstruction, and 3 with normal leaflet function but severe prosthesis-patient mismatch. Sword symbol indicates inclusion of 125 prostheses in the low-risk group, 51 prostheses in the intermediate-risk group, 34 patients in the

pathologic regurgitation group, and 3 patients in the pathologic obstruction group with severe prosthesis-patient mismatch (as defined by indexed effective orifice area <0.9 cm^2/m^2). MR indicates mitral regurgitation; MS, mitral stenosis; MS/MR, combined mitral stenosis and mitral regurgitation; MVP, mitral valveprosthesis; PHT, pressure half-time; TEE, transesophageal echocardiography.

Figure 4. Proposed Clinical Algorithm for Evaluation of Bileaflet Mechanical Mitral Prostheses. Methodology was used as shown in Figure 3. Asterisk indicates that E velocity could not be measured in 1 patient. Double asterisk indicates that PHT could not be measured in 4 studies: 2 prostheses with obstruction, 1 prosthesis with severe regurgitation, and 1 prosthesis with normal leaflet function but severe prosthesis-patient mismatch. The sword symbol indicates inclusion of 66 prostheses in the low-risk group, 19 prostheses in the intermediate-risk group, 18 patients in the pathologic regurgitation group, and 3 patients in the pathologic obstruction group with severe prosthesis-patient mismatch (as defined by indexed effective orifice area <0.9 cm^2/m^2). MR indicates mitral regurgitation; MS, mitral stenosis; MS/MR, combined mitral stenosis and mitral regurgitation; MVP, mitral valve prosthesis; PHT, pressure half-time; TEE, transesophageal echocardiography.

Figure 5. Proposed Clinical Algorithm for Evaluation of Porcine Mitral Prostheses. Methodology was used as shown in Figure 3. Asterisk indicates that PHT could not be measured in 5 studies, including 3 prostheses with severe regurgitation, 1 with obstruction, and 1 with a normal leaflet function but severe prosthesis-patient mismatch. The sword symbol indicates inclusion of 62 prostheses in the low-risk group, 14 prostheses in the intermediate-risk group, and 16 patients in the pathologic regurgitation group with severe prosthesis-patient mismatch (as defined by indexed effective orifice area <0.9 cm^2/m^2). MR indicates mitral regurgitation; MS,

mitral stenosis; MS/MR, combined mitral stenosis and mitral regurgitation; MVP, mitral valve prosthesis; PHT, pressure half-time; TEE, transesophageal echocardiography.

Table 1. Normal Transthoracic Doppler Parameters by MVP Type

	MVP Type, Mean (SD)						
	Mechanical		Bioprosthetic				
Parameter	Bileaflet (n=367)	Tilting Disk (n=16)	Porcine (n=174)	Pericardial (n=24)	Unclassified (n=8)	All (n=589)	*P* Value
Mean gradient (mm Hg)	5.4 (2.0)	5.9 (2.1)	6.5 (2.3)	5.1 (1.7)	7.0 (1.9)	5.7 (2.2)	<.001
E velocity (m/s)	1.8 (0.4)	2.0 (0.4)	2.0 (0.4)	1.7 (0.3)	1.8 (0.3)	1.9 (0.4)	<.001
PHT (ms)	75 (20)	87 (22)	87 (24)	95 (20)	86 (29)	79 (22)	<.001
TVI_{MVP}	39 (9)	47 (13)	48 (10)	42 (9)	49 (10)	42 (11)	<.001
TVI_{LVOT}	21 (4)	22 (4)	22 (4)	22 (4)	22 (6)	22 (4)	.31
MVP ratio	1.9 (0.4)	2.1 (0.5)	2.2 (0.5)	1.9 (0.4)	2.4 (0.7)	2.0 (0.5)	<.001
EOA	2.1 (0.5)	2.0 (0.5)	1.8 (0.5)	2.0 (0.5)	1.8 (0.6)	2.0 (0.5)	<.001
Indexed EOA	1.1 (0.3)	1.1 (0.2)	1.0 (0.3)	1.1 (0.3)	1.0 (0.3)	1.1 (0.3)	<.001

Abbreviations: EOA, effective orifice area; MVP, mitral valve prosthesis; PHT, pressure half-time; TVI_{LVOT}, time velocity integral of the left ventricular outflow tract; TVI_{MVP}, time velocity integral of the mitral valve prosthesis.

Table 2. Transthoracic Doppler Parameters by TEE Diagnosis

	TEE Diagnosis, Mean (SD)					
	Clinically Normal		Clinically Abnormal			
Parameter	Normal (n=589)	<Moderate MR (n=156)	Moderate or >MR (n=188)	Mitral Stenosis (n=28)	MS/MR (n=10)	*P* Value
Mean gradient (mm Hg)	5.7 (2.2)	5.8 (2.2)	8.1 (3.2)	16.4 (6.6)	17.7 (3.7)	<.001
E velocity (m/s)	1.9 (0.4)	1.9 (0.4)	2.3 (0.4)	2.6 (0.5)	2.9 (0.3)	<.001
PHT (ms)	79 (22)	72 (17)	79 (20)	167 (43)	184 (42)	<.001
TVI_{MVP}	42 (11)	42 (10)	54 (14)	81 (22)	97 (21)	<.001
TVI_{LVOT}	22 (4)	22 (5)	21 (4)	21 (5)	21 (5)	.03
Stroke volume, mL	81 (21)	82 (22)	79 (22)	77 (26)	77 (24)	.49
MVP ratio	2.0 (0.5)	1.9 (0.5)	2.7 (0.7)	4.0 (1.3)	4.8 (1.2)	<.001

Abbreviations: MR, mitral regurgitation; MS/MR, combined mitral stenosis and mitral regurgitation; MVP, mitral valve prosthesis; PHT, pressure half-time; TEE, transesophageal echocardiographic; TVI_{LVOT}, time velocity integral of the left ventricular outflow tract; TVI_{MVP}, time velocity integral of the mitral valve prosthesis.

Table 3. Optimal Cutoff Values by Receiver Operator Curve Analysis for Differentiation of Clinically Normal and Clinically Abnormal Prostheses

	Mitral Valve Prosthesis		Mean Gradient,
Prosthesis Type	**Ratio**	**E Velocity, m/s**	**mm Hg**
All	2.3	2.2	6.0
Bileaflet mechanical	2.2	2.1	6.0
Pericardial	2.3	2.0	6.0
Porcine	2.6	2.2	8.2

Table 4. Predictors of Mitral Valve Dysfunction by Prosthesis Type

Prosthesis Type	Index	Odds Ratio (95% CI)	*P* Value
All	MVP ratio	10.34 (6.43-16.61)	<.001
	E velocity (m/s)	3.23 (1.61-6.47)	<.001
	Mean gradient (mm Hg)	1.13 (1.02-1.25)	.02
	PHT (ms)	0.99 (0.98-0.999)	.04
Bileaflet mechanical	MVP ratio	29.63 (13.58-64.65)	<.001
	E velocity (m/s)	2.68 (1.05-6.96)	.04
	Mean gradient (mm Hg)	1.08 (0.94-1.25)	.29
	PHT (ms)	0.99 (0.97-1.00)	.07
Pericardial	MVP ratio	4.40 (0.54-35.79)	.17
	E velocity (m/s)	138.15 (0.70->999.99)	.07
	Mean gradient (mm Hg)	1.38 (0.66-2.88)	.39
	PHT (ms)	1.00 (0.95-1.04)	.85
Porcine	MVP ratio	8.60 (3.30-22.40)	<.001
	E velocity (m/s)	2.44 (0.52-11.52)	.26
	Mean gradient (mm Hg)	1.36 (1.10-1.68)	.004
	PHT (ms)	0.99 (0.97-1.01)	.21

Abbreviations: MVP, mitral valve prosthesis; PHT, pressure half-time.

Table 5. E Velocity and MVP Ratio for Differentiation of Clinically Normal From Clinically Abnormal Prostheses

Prosthesis Type	Index	Sensitivity, %	Specificity, %	PPV	NPV
All	E velocity ≥2.2 m/s	74.33	75.51	41.99	92.50
	MVP ratio ≥2.3	81.82	79.72	49.04	94.84
	E velocity ≥2.2 m/s **and** MVP ratio ≥2.3	64.71	91.84	65.41	91.60
Bileaflet mechanical	E velocity ≥2.1 m/s	75.96	70.55	34.65	93.46
	MVP ratio ≥2.2	76.92	81.43	45.98	94.50
	E velocity ≥2.1 m/s **and** MVP ratio ≥2.2	63.46	90.91	58.93	92.37
Pericardial	E velocity ≥2.0 m/s	100.00	75.68	59.09	100.00
	MVP ratio ≥2.3	92.31	81.08	63.16	96.77
	E velocity ≥2.0 m/s **and** MVP ratio ≥2.3	92.31	91.89	80.00	97.14
Porcine	E velocity ≥2.2 m/s	82.69	64.88	37.39	93.66
	MVP ratio ≥2.6	86.54	80.49	52.94	95.93
	E velocity ≥2.2 m/s **and** MVP ratio ≥2.6	75.00	89.27	63.93	93.37

Abbreviations: MVP, mitral valve prosthesis; NPV, negative predictive value; PPV, positive predictive value.