

Prognostic value of echocardiography with particular reference to patients with valvular heart disease

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Abstract

Echocardiography is comparatively inexpensive relative to other modern cardiovascular imaging tools. It is widely available, even in poor countries, and provides a comprehensive evaluation of cardiac structure and function. It is an ideal tool for the evaluation of patients with valvular heart disease and provides important prognostic information. This review of recent literature highlights reports on outcomes data and provides a clinically valuable summary in table format.

Introduction and context

The diagnostic criteria for echocardiographic assessment of valvular heart disease are well established [1]. An ever-growing preponderance of literature highlights the usefulness of echocardiography as a prognostic indicator for outcomes in valvular heart disease, particularly aortic valve (AV) and mitral valve (MV) disorders. This review focuses on recent published reports that are intended to provide the physician with the necessary data to transition from an anatomic report to a more prognostic report in an effort to improve patient management choices.

Recent advances

Aortic stenosis

A preoperative left ventricular (LV) end-systolic index of less than 27.5 mm/m² as measured by echocardiography has been shown to be a strong predictor of good intermediate LV recovery following aortic valve replacement (AVR) surgery for severe aortic stenosis (AS) [2].

Furthermore, prior to AVR, an extremely poor (21%) 2-year event-free survival can be expected in asymptomatic patients with mostly calcific AS and a peak gradient of greater than 64 mm Hg (peak Doppler velocity >4.0 m/s) [3]. This point emphasizes the critical role of serial echocardiography and clinical evaluation of these patients.

In patients with a bicuspid AV, a peak gradient of at least 80 mm Hg and an aortic valve area (AVA) of not more than 0.75 cm² have been shown to predict the need for urgent AV surgery [4].

In patients with AS and normal left ventricular ejection fraction (LVEF), mitral annular tissue Doppler imaging (TDI) correlates significantly with AVA and amino-terminal pro-B-type natriuretic peptide (BNP) levels. Mortality and the need for AVR are better predicted by a reduced septal annular diastolic atrial velocity (A') of less than 9.6 cm/s than with AVA or BNP [5]. In patients with AS and reduced LV contractility, a critical understanding of LV contractile reserve (CR) is required if the mean AV gradient is low (<30 mm Hg). In these patients, low-dose dobutamine infusion (up to 20 µg/kg per minute) allows the differentiation between patients with true severe (fixed) AS who will benefit from AVR from those with either nonsevere (relative) AS or a late-stage (nonviable) cardiomyopathy for whom AVR may be harmful. In a multicenter prospective evaluation of patients with AS (AVA of approximately 0.7 cm²) and a low AV gradient (mean of approximately 29 mm Hg), those with a 20% increase in LV stroke volume during dobutamine infusion had an operative mortality significantly lower than those without (5% versus 32%) [6]. Furthermore, a lack of CR or a very low mean gradient (<20 mm Hg) was

a multivariate predictor of operative mortality, with odds ratios of 10.9 and 4.7, respectively.

Proper prosthesis selection is of crucial importance in preventing prosthesis patient mismatch (PPM), an independent predictor of mortality after AVR [7]. Recently, transcatheter AVR has become possible and will certainly be advanced in subsequent years. Outcomes in these patients are variable, and the need for permanent pacemaker insertion is not uncommon. Recently, this has been predicted by two simple two-dimensional echocardiography (2DE) features: severe septal hypertrophy (>17 mm) and baseline thickness of the native non-coronary cusp (>8 mm) as measured by transesophageal echocardiography (TEE) [8].

Aortic regurgitation

In the setting of aortic regurgitation (AR), current guidelines recommend surgery for asymptomatic patients with a maximal left ventricular end-diastolic diameter (LVDd) of greater than 55 mm or an LVEF of less than 50% [9]. This stems from the knowledge that outcomes worsen when these values are exceeded. Use of an indexed LVDd of less than 25 mm/m² in patients with a body surface area (BSA) of not more than the 25th percentile (BSA of 1.43-1.68 m²) is associated with a drop in age-adjusted mortality and is also a better prognostic indicator for unfavorable outcomes 1 year after surgery as measured by an LVEF of less than 50% [10]. Asymptomatic patients with severe quantitative AR [an effective regurgitant orifice (ERO) of >35 mm², a regurgitant volume of >60 mL, or a regurgitant fraction percentage of >50%] and normal LVEF (>50%) have a greater than fivefold increase in mortality. Furthermore, cardiac events at 10 years were 90% with an end-systolic volume index (ESVI) of greater than 45 mL/m² but only 40% with an ESVI of less than 45 mL/m² [11].

Mitral valve disease

Functional mitral regurgitation (MR) due to left ventricular dysfunction is associated with a poor outcome when the MR is quantified as more than mild (ERO >20 mm²) and the left ventricular end-systolic volume is increased at rest (>95 mL/m²) or after exercise (left ventricular end-diastolic volume >120 mL/m²) [11]. In patients with MV prolapse, outcomes can be predicted simply via the serial progression of demonstrated MR, regardless of age, gender, prolapse location, valve thickening, or pre-existing MR [12]. Increases in MR by greater than 1 MR grade are associated with left atrial and ventricular dilatation and an overall poor prognosis.

Flail leaflet plays a major role in the etiology of organic MR. In addition, the presence of flail leaflet is a poor

prognostic indicator, with much of this patient population dying or requiring surgery within 10 years of receiving the diagnosis [13]. Early surgery, particularly MV repair, in both the symptomatic and asymptomatic patient population has been shown to reduce the rates of cardiac events [14]. However, the recurrence of 2/4 grade or worse MR in patients undergoing MV repair for flail leaflet is between 2% and 4% per year [15]. The use of real-time three-dimensional echocardiography (RT3DE) permits direct analysis of mitral annular geometry and precise quantitative analysis of leaflet geometry. This tool holds great promise in improving our understanding of flail leaflet in MR as well as enhancing the surgical precision in techniques used for repair [15].

Patients may develop LV dysfunction (EF <50%) after MV surgery. Large preoperative MR volumes (≥80 mL) are strongly associated with unexpected postoperative LV dysfunction and are useful in the timing of surgical intervention in asymptomatic patients [16]. A mitral E/E' (early mitral filling velocity/early diastolic mitral annular velocity) ratio of greater than 13.5 as determined by the average septal and lateral mitral annular TDI velocities predicts a twofold worse event-free survival, particularly in patients with severe secondary MR due to heart failure [17]. In patients with asymptomatic severe MR, an end-systolic diameter of less than 45 mm, and an ejection fraction (EF) of greater than 60%, peak systolic tissue Doppler velocities at the lateral mitral annulus accurately predicted postoperative reductions in EF and therefore LV dysfunction. Specifically, a myocardial systolic wave velocity of not more than 10 cm/s appears to be predictive of a postoperative EF reduction of at least 10% [18].

Of interest is the growing usefulness of RT3DE, which permits full or partial volume image acquisition in multiple planes [19]. Real-time assessment of mitral annular geometry has enhanced our understanding of the pathophysiology of MR [20]. In our opinion, in the near future, most of the prognostic M-mode echocardiography and 2DE parameters previously reported will be even more accurate at risk-stratifying patients by using results of 3DE (owing to its superior reproducibility and fewer restrictions on heart size and shape). This technique is useful in quantifying mitral regurgitant flows, usually underestimated with the proximal isovelocity surface area method using 2DE [21]. In fact, while 2DE measurement of vena contracta width is a commonly accepted method of assessing MR severity, RT3DE permits more accurate assessment of this dimension. RT3DE measures nonspherical regurgitant orifices by direct planimetry without using calculations based on inaccurate assumptions [22].

Table 1. Echocardiographic prognostic variables listed by valve disease

Criteria	Value	Prognosis	Reference
Aortic stenosis			
Late diastolic annular velocity (septal A')	<9.6 cm/s	Predictor of cardiac mortality or need for aortic valve replacement ~50% at 1 year	[35]
Interventricular septal thickness	>17 mm	Specificity (100%) pacemaker implantation after transcatheter aortic valve implantation	[7]
Noncoronary cusp thickness (apical three-chamber view)	>8 mm	Specificity (100%) pacemaker implantation after transcatheter aortic valve implantation	[7]
LVESD index	<27.5 mm/m ²	Sensitivity and specificity of 73% and 64% for predicting recovery of LV function (LVEF improvement >10%) at 48 months after AVR	[2]
Peak gradient	>64 mm Hg	79% 2-year event rate	[3]
Peak velocity	>4.0 m/s		
Peak gradient AVA	≥80 mm Hg ≤0.75 cm ²	Need for AVR in bicuspid AV, with 84% event-free survival at 1 year after valve replacement	[4]
Prosthesis patient mismatch			
Indexed EOA (aortic position)	>0.85 cm ² /m ²	Mild PPM (not clinically significant)	[29]
Indexed EOA (aortic position)	≤0.65 cm ² /m ²	Severe PPM (persistent high gradients, worse outcomes)	[29]
Indexed EOA (mitral position)	>1.2 cm ² /m ²	Mild PPM (not clinically significant)	[29]
Indexed EOA (mitral position)	≤0.9 cm ² /m ²	Severe PPM (persistent high gradients, worse outcomes)	[29]
Aortic regurgitation			
Indexed LVDD	≥25 mm/m ²	88% chance of EF <50% 1 year after valve replacement, age-adjusted expected EF <50% in 24.27% vs. 37.94% with ESD >50 mm	[8]
QASE severe AR	RV ≥60 mL RF >50% ERO ≥30 mm ²	Cardiac events at 10 years: 63% vs. 34% (moderate AR) and 21% (mild AR)	[10]
ESVI	≥45 mL/m ²	Cardiac events at 10 years: 87% vs. 40%	[10]
Pulmonic regurgitation			
PR	RVESV _i <150 mL/m ²	Increased cardiac event rate and persistent RV dilation in absence or delay of PVR	[33]
Mitral stenosis			
Updated MS score (calcification)	No calcification = 0 Leaflet margins = 2 Leaflet bodies = 4 Commissures = 6		[36]
Updated MS score (subvalvular involvement)	None = 0 <50% chord = 2 ≥50% chord = 4 Entire chord = 6		[36]
Total summed updated MS score	>4	Poor outcome: less success with PBMV	[36]
Mitral regurgitation			
Peak stress end-diastolic volume	120 mL/m ²	50% survival at 25-month follow-up vs. 88.9% (peak stress EDVI <120 mL/m ²)	[11]
Resting end-systolic volume	≥95 mL/m ²	36% survival at 25-month follow-up vs. 92.6% (ESV <95 mL/m ²)	[11]
Effective regurgitant orifice (baseline)	≥20 mm ²	50% survival at 25-month follow-up vs. 92% ERO <20 mm ²	[11]
Mitral regurgitation volume	≥80 mL	Unexpected postoperative LV dysfunction in 20% of patients	[16]
E/E' ratio	>13.5	Event-free survival 64% vs. 31% (E/E' ratio ≤13.5) in patients with MR	[17]
MVP	Increase ≥1 MR grade	60% MVP-related cardiac events at 6.2 ± 2.9 years vs. 26% of nonprogressors	[12]
Sm velocity	≤10 cm/s	Postoperative EF reduction ≥10% with 78% sensitivity, 95% specificity	[18]
Indexed mitral EOA	<1.2 cm ² /m ²	Associated with a postoperative PA systolic pressure >40 mm Hg	[37]
Preoperative PAP	≥50 mm Hg	53% incidence of postoperative LV dysfunction	[22]

A', late (atrial) diastolic mitral annular velocity; AR, aortic regurgitation; AV, aortic valve; AVA, aortic valve area; AVR, aortic valve replacement; E/E', early mitral filling velocity/early diastolic mitral annular velocity; EDVI, end-diastolic volume index; EF, ejection fraction; EOA, effective orifice area; ERO, effective regurgitant orifice; ESD, end-systolic diameter; ESV, end-systolic volume; ESVI, end-systolic volume index; LV, left ventricle; LVDD, left ventricular diastolic dysfunction; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; MR, mitral regurgitation; MS, mitral stenosis; MVP, mitral valve prolapse; PA, pulmonary artery; PAP, pulmonary artery systolic pressure; PBMV, percutaneous balloon mitral valvuloplasty; PPM, prosthesis patient mismatch; PR, pulmonic regurgitation; PVR, pulmonary valve replacement; QASE, quantitative American Society of Echocardiography; RF, regurgitant fraction; RV, right ventricle; RVESV_i, right ventricular end-systolic volume index; Sm, myocardial systolic wave velocity.

An important complication of MV disease [both MR and mitral stenosis (MS)] is pulmonary hypertension (PH) with subsequent right ventricular dysfunction and failure [23]. A preoperative pulmonary artery systolic pressure (PAP) of at least 50 mm Hg is an independent predictor of postoperative LV dysfunction as compared with patients with a PAP of not more than 30 mm Hg and a similar preoperative LVEF. While current guidelines indicate surgical intervention at a PAP of greater than 50 mm Hg, these findings may suggest the need for a more aggressive surgical approach to patients with MR and PH [23]. An important avoidable complication of mitral valve replacement (MVR) is PPM, which is strongly associated with PH after surgery. An indexed mitral effective orifice area (EOA) of less than $1.2 \text{ cm}^2/\text{m}^2$ is associated with a postoperative PAP of greater than 40 mm Hg [24]. With the onset of MS, left atrial pressure increases. As severity of the disease progresses, increases in PAP occur with subsequent RV dysfunction, tricuspid annular dilation (TAD), and tricuspid regurgitation (TR) [24]. Moderate to severe postoperative TR in MVR is a strong predictor of all-cause mortality [25]. TR also indicates poor prognosis in patients undergoing balloon mitral valvotomy [24]. Reduction of PAP as a result of MVR may not prevent persistent TAD post-operatively. Right ventricular dysfunction, once symptomatic, may already be irreversible. Echocardiographic assessment of the tricuspid valve is therefore a necessary diagnostic component in patients with MS. A 2DE finding of a TAD of greater than 3.5 cm (regardless of severity of TR) indicates the consideration for tricuspid annuloplasty to be performed concomitantly with MV surgery [24].

Pulmonic regurgitation

One important right-sided valve lesion to mention, as its incidence is increasing, is pulmonic regurgitation (PR) [26]. There are now more adults living in the US with congenital heart disease than children and most of the former arrive there via successful pediatric surgical interventions. Progressive PR is common in these adolescents and adults. Initially, the RV responds well, but variably, to severe PR. However, at some point, the RV will fail. This 'point of no return' seems to be an RV ESVI of greater than $150 \text{ mL}/\text{m}^2$ [23].

Implications for clinical practice

This review confirms the importance of quantifiable information gathered via M-mode, 2D, 3D, and Doppler echocardiography in predicting patient outcomes. The updated parameters are easily obtained and are more accurate at risk-stratifying patients than previously used qualitative values [27]. These measurements are crucial for determining prognosis and utilization of surgical and

percutaneous interventions in patients with valvular heart disease.

In the setting of AS, prognostic parameters that integrate the valvular, ventricular, and vascular components of the disease may allow more optimal timing of intervention [28]. The fact that the tissue Doppler echocardiography A' is a better predictor of mortality than AVA is consistent with the acknowledged importance of compensatory left atrial function in the natural history of AS [5]. Aortic, and to a lesser extent mitral, PPM may be avoided by calculating the projected indexed EOA of the considered prosthesis prior to intervention. The indexed EOA is calculated by dividing the EOA of the prosthesis by the patient's BSA and may be used to select prostheses as well as to quantify the severity of PPM according to the guidelines in Table 1 [29]. For patients with AR, a number of prognostic echo values that should be considered as criteria for valve surgery are provided [8].

One of the major reasons echocardiography is such a frequently employed diagnostic tool is that it allows serial exams to be performed safely. By knowing the quantitative dimensions that provide pertinent prognostic information, the physician may choose to alter the interval for subsequent evaluation. For example, an asymptomatic patient normally followed annually with moderate to severe AR and a recently determined LV diastolic index of $24 \text{ mm}/\text{m}^2$ would warrant very close follow-up (as well as quantitation of AR severity). This patient, on the edge of LV failure, should probably not wait another year prior to evaluation. On the contrary, if the LVDd is only $18 \text{ mm}/\text{m}^2$, then waiting a year remains reasonable. Furthermore, increases in MR by greater than 1 MR grade on serial echocardiography are associated with left atrial and ventricular dilatation and an overall poor prognosis [14].

Early surgery is associated with improved clinical outcome in patients with severe asymptomatic MR [30]. This fact is valid only when the regurgitation is carefully quantitated and confirmed to be severe. This practice of operating on asymptomatic MR should not be recommended based upon the visual qualitative assessment of MR severity. Color Doppler is notoriously poor at identifying the population of asymptomatic patients who would improve with valve surgery. In asymptomatic patients with organic MR, annualized rate of change of the effective regurgitant orifice area is strongly associated with progression of symptoms and LV dysfunction [31].

Recent advances in the 3D matrix-array TEE technology have improved the assessment of native MV components, and this technology has become a valuable tool in the assessment of prosthetic valves, particularly mitral

prosthetic valves [32]. This new tool not only provides prognostic assessment of both native and prosthetic MVs before surgery but also serves as a superior means of postoperative evaluation.

Three-dimensional echocardiography, either transthoracic or TEE, is useful in planning for MV repair and will certainly play a crucial role in the percutaneous treatment of MV disease [20]. Moreover, given the improved quantitation of LV and RV volumes, the role of 3DE in expanding our knowledge of patient outcomes will continue to improve. Since the major consequence of valvular heart disease is not the valve per se but the myocardium, which remains in jeopardy of failing if the valve disease is left unrepaired too long, careful measurement of serial myocardial volumes will be crucial. This fact has been recently highlighted with pulmonary regurgitation. An aggressive surgical intervention policy that intervenes with pulmonary valve replacement prior to a right ventricular end-systolic volume of greater than 150 mL/m² will result in a normalization of volumes as well as improvement in both biventricular systolic function and exercise capacity [33]. Through adherence to this quantitative prognostic concept, it is hoped that RV dysfunction will be less common and in time patient outcomes for this valve disease will show improvement.

Valvular heart disease is a well-known cause of left ventricular dysfunction and heart failure symptoms. Measurements obtained via TDI can be used in the classification and prognosis of patients with LV dysfunction [34]. The E/E' ratio predicts functional class in patients with heart failure (class IV = 12.9 ± 2.8 versus class III = 8.3 ± 1.7) [34]. This simple measure, routinely performed during all echo exams, holds true for patients with MR, in whom the E/E' ratio predicts all-cause mortality and worsening heart failure [17]. This value should be used clinically as a guide to increase afterload-reducing agents or diuretic therapy or both if the E/E' ratio exceeds 15-20.

Conclusions

Given our greater understanding of the prognostic implications of these readily obtained echocardiographic variables, this diagnostic tool will remain the primary workhorse for the evaluation of patients with valvular heart disease. Use of these variables may indicate the need for early surgery for some patients with valvular heart disease. Echo should be considered at least partly responsible for the significant reductions in morbidity and mortality that have recently been demonstrated in patients with valvular heart disease. Physicians with expertise in this field should expand their evaluation

beyond the basic structural and functional interpretation to a more clinically valuable prognostic report, taking the findings summarized in Table 1 into consideration.

Abbreviations

2D, two-dimensional; 2DE, two-dimensional echocardiography; 3D, three-dimensional; 3DE, three-dimensional echocardiography; A', late (atrial) diastolic mitral annular velocity; AR, aortic regurgitation; AS, aortic stenosis; AV, aortic valve; AVA, aortic valve area; AVR, aortic valve replacement; BNP, B-type natriuretic peptide; BSA, body surface area; CR, contractile reserve; E/E', early mitral filling velocity/early diastolic mitral annular velocity; EF, ejection fraction; EOA, effective orifice area; ERO, effective regurgitant orifice; ESVI, end-systolic volume index; LV, left ventricle; LVdD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; MVR, mitral valve replacement; PAP, pulmonary artery systolic pressure; PH, pulmonary hypertension; PPM, prosthesis patient mismatch; PR, pulmonic regurgitation; RT3DE, real-time three-dimensional echocardiography; RV, right ventricle; TAD, tricuspid annular dilation; TDI, tissue Doppler imaging; TEE, transesophageal echocardiography; TR, tricuspid regurgitation.

Competing interests

The authors declare that they have no competing interests.

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