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Review article

Assessment of the patient with valvular heart disease: An integrative approach

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INTRODUCTION

In managing the patient with valvular heart disease (VHD), three major issues must be addressed: (1) assessment of the severity of disease, (2) the effect the disease is having or is likely to have on the patient and his/her cardiovascular system, and (3) the timing and type of intervention to be used to correct the lesion. Existing guidelines are helpful in addressing these tenets in many cases, often using quantifiable parameters to aid the clinician in making key clinical decisions. Many times these guidelines allow the physician and patient to arrive easily at a management strategy. However, in other cases it may take every piece of available data to develop a management plan that is still only a best guess at the proper course to take.

Overall, the indications for intervention in VHD are straightforward: valvotomy (in mitral stenosis), or valve repair or valve replacement is indicated when severe VHD causes symptoms or cardiac dysfunction. In some cases, low-risk intervention such as mitral valve repair may be undertaken in the absence of symptoms or dysfunction when it seems inevitable that deterioration will occur because of markedly severe disease. These assessments are rarely made using one test and usually require the integration of all the clinical acumen that can be summoned to address the issues above.

The following will summarize the general approach to the assessment of VHD severity, impact, and timing of intervention, with attention paid to the specifics of each individual disease.

SEVERITY OF DISEASE

The AHA/ACC guidelines for assessing severity of disease are displayed in Table 1 [1]. The distinction between mild, moderate and severe disease is thought crucial since it is believed that, in most cases, mild and moderate disease are tolerated indefinitely (unless severity worsens) and only severe disease (as defined) causes symptoms and cardiac dysfunction. It is critical to understand that these definitions have been developed from consensus of opinion and are not from the result of any large, randomized trials. Rather they are built upon the general experience of experts, and expert opinion is not monolithic. For instance, the mean transvalvular gradient consistent with severe aortic stenosis (AS) was deemed to be 50 mm Hg in the guidelines published in 1998 [2] but was revised to be 40 mm Hg in the 2006 guidelines [1]. This change was not derived from new data acquired between the writing of the two sets of guidelines; rather, it reflected differences of opinion due to changes to the committee make-up from one writing committee to the next. In addition, the 2006 writing committee removed the adjective "critical" as a descriptor of AS to indicate that while a manmade definition of "severe" was a matter of consensus, the definition of "critical" (a valve area certain to cause morbidity or death) was unknown.

OBJECTIVE ASSESSMENT OF DISEASE SEVERITY

The physical examination

In this age of high-tech diagnostic modalities, the physical examination, and the skill applied when performing it, seem to be diminishing. However, the importance of the physical exam cannot be

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Table 1. Taken from Ref. [1] with permission.

A. Left-sided valve disease

	Aortic Stenosis		
Indicator	Mild	Moderate	Severe
Jet velicity (m per second)	Less than 3.0	3.0–4.0	Greater than 4.0
Mean gradient (mm HG) [1]	Less than 25	25–40	Greater than 40
Valve area (cm^2)	Greater than 1.5	1.0–1.5	Less than 1.0
Valve area index (cm^2 per m^2)			Less than 0.6
	Mitral Stenosis		
	Mild	Moderate	Severe
Mean gradient (mm Hg) [1]	Less than 5	5–10	Greater than 10
Pulmonary artery systolic pressure (mm Hg)	Less than 30	30–50	Greater than 50
Valve area (cm^2)	Greater than 1.5	1.0–1.5	Less than 1.0
	Aortic Regurgitation		
	Mild	Moderate	Severe
Qualitative			
Angiographic grade	1+	2+	3–4+
Color Doppler jet width	Central jet, width less that 25% of LVOT	Greater than mild but no signs of severe AR	Central jet, width greater than 65% LVOT
Doppler vena contracta width (cm)	Less than 0.3	0.3–0.6	Greater than 0.6
Quantitative (cath or echo)			
Regurgitant volume (ml per beat)	Less than 30	30–59	Greater than or equal to 60
Regurgitant fraction (%)	Less than 30	30–49	Greater than or equal to 50
Regurgitant orifice area (cm^2)	Less than 0.10	0.10–0.29	Greater than or equal to 0.30
Additional essentail criteria			
Left ventricular size			Increased
	Mitral Regurgitation		
	Mild	Moderate	Severe
Qualitative			
Angiographic grade	1+	2+	3–4+
Color Doppler jet area	Small, central jet (less than 4 cm^2 or less than 20% LA area)	Signs of MR greater than mild present but no criteria for severe MR	Vena contracta width greater than 0.7 cm with large central MR jet (area greater than 40% of LA area) or with a wall-impinging jet of any size swirling in LA
Doppler vena contracta width (cm)	Less than 0.3	0.3–0.6	Greater than or equal to 0.70
Quantitative (cath or echo)			
Regurgitant volume (ml per beat)	Less than 30	30–59	Greater than or equal to 60
Regurgitant fraction (%)	Less than 30	30–49	Greater than or equal to 50
Regurgitant orifice area (cm^2)	Less than 0.20	0.2–0.39	Greater than or equal to 0.40
Additional essentail criteria			
Left atrial size			Enlarged
Left ventricular size			Enlarged

(*continued on next page*)

overemphasized because it lays the Bayesian foundation for all tests that follow. Bayes' theory states that the accuracy of any test is determined by the pretest probability that the condition being tested for is present. Since no test in VHD is 100 percent accurate, the physical exam lays the basis for subsequent tests, directing them toward the condition hypothesized from the exam data.

IMAGING

Echocardiography

Echocardiography forms the mainstay of laboratory diagnosis in VHD. Echo's low-cost, accuracy, portability and reproducibility make it ideal for both the initial assessment of the patient with VHD as

Table 1 (*continued*)

B. Right-sided valve disease	Characteristic
Severe tricuspid stenosis:	Valve less than 1.0 cm^2
Severe tricuspid regurgitation:	Vena contracta width greater than 0.7 cm and systolic flow reversal in hepatic veins
Severe pulmonic stenosis:	Jet velocity greater than 4 m per second or maximum gradient greater than 60 mm Hg
Severe pulmonic regurgitation:	Color jet fills outflow tract; dense continuous wave Doppler signal with a steep deceleration slope

[1] Valve gradients are flow dependent and when used as estimates of severity of valve stenosis should be assessed with knowledge of cardiac output or forward flow across the valve. Modified with permission from Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802 (27).
AR indicates aortic regurgitation; cath, catheterization, echo, echocardiography; LA, left atrial/atruim, LVOT, left ventricular outflow tract; and MR, mitral regurgitation.

well as for the repeated studies necessary to follow the progression of the disease. Provided that the patient's sonographic window is adequate, the echocardiogram gives information about valve pathoanatomy, transvalvular pressure gradients, severity of valvular regurgitation and the impact of the pathophysiology of a patient's VHD on cardiac chamber geometry and function. Quantitative measures of valvular stenosis are quite accurate when compared with other methods of assessment. Although quantitative methods of the assessment of valvular regurgitation have been introduced, they are generally less precise and less applied than those for assessing valvular stenosis and thus are more subjective.

With regards to pathoanatomy, transesophogeal echocardiography produces excellent images of the mitral valve, and 3-D echocardiography produces a view akin to what the surgeon sees at the operating table.

Magnetic resonance imaging (MRI)

The strength of MRI lies in its ability to very precisely measure left ventricle (LV) volumes allowing for accurate evaluation of the effect of valvular regurgitation on LV remodeling, LV ejection fraction and quantification of regurgitant flow and regurgitant fraction [3].

Invasive hemodynamics

If after a careful history, physical examination and non-invasive imaging, the diagnosis and/or degree of disease severity is still unclear, invasive hemodynamic investigation is performed to arrive at a final diagnosis. Invasive investigation affords direct measurement of intracardiac pressures, and cardiac output, which are in fact the essentials of cardiac function. It must be noted that invasive evaluation has its own pitfalls and these have been magnified more recently by lack of specific training in this discipline in many training programs. Invasive evaluation relies upon careful pressure measurement using meticulously calibrated manometers connected to properly-placed and flushed catheters, as well as careful measurement of cardiac output [4].

IMPACT OF VHD ON THE PATIENT

Symptoms

For every type of severe VHD lesion, the presence of symptoms referable to that lesion are indications for mechanical therapy because prognosis worsens with their presence [5–8]. While symptoms are obviously subjective and not as elegant a measurement as transvalvular gradient, for instance, symptoms do offer a measurement of cardiovascular integrity that other techniques of assessment cannot avail. Symptoms develop from integrated abnormalities in left and right ventricular systolic function, diastolic function, atrial compliance, filling pressures, coronary blood flow and cardiac output. No objective measure of cardiovascular function has this capability. Thus it is not surprising that the presence or absence of symptoms has prognostic implication for the management of every valvular lesion. Unfortunately history-taking skills may be waning as medicine concentrates on more high-tech methods of evaluation. In obtaining a good history of a patient's symptomatic state, it is important to get the information not only from the patient but also from the spouse or close associate because the patient may fail to recognize his/her symptoms or may simply deny that they are present.

Exercise tolerance

Because of the subjective nature of the symptomatic state and because of its importance in decision making, it is almost always advisable to observe a formal (or even informal) episode of exercise. Carefully monitored exercise testing of the asymptomatic patient with VHD is safe and also quite logical since the patient who feels he is asymptomatic might exercise with impunity. If indeed such a patient is at risk because he/she fails to recognize symptoms, it is better to detect them under the watchful eye of the physician (such studies should not be left to the care of technical personnel). If the patient has a perfectly normal test, achieving age-predicted exercise tolerance and normal hemodynamics, it is reassuring to both the physician and patient that continued "watchful waiting" is safe and appropriate [9–12]. However if the patient has unexpectedly poor exercise tolerance, develops hemodynamic instability, or has frank symptoms during exercise, these are usually indications to move to therapeutic intervention.

Ventricular dysfunction

As noted above, severe VHD imposes a volume or pressure overload (or both) on the left and/or right ventricles (LV or RV). If prolonged, this hemodynamic burden damages the myocardium, and leads to heart failure and death. Obviously, early detection of myocardial damage as it leads to LV dysfunction presages the need for intervention before damage becomes irreversible. Unfortunately ejection fraction (EF) remains the primary benchmark for assessing systolic function. Ejection fraction is determined by contractility (the property describing myocardial function), preload and afterload. Because both preload and afterload may be extraordinarily abnormal in VHD, EF becomes a potentially very confounded measure of LV function. Thus high afterload in aortic stenosis may cause depressed EF despite relatively well-preserved contractility that could mislead the clinician into believing his patient has a falsely poor prognosis (Fig. 1) [13]. Conversely increased preload in mitral regurgitation enhances EF and causes it to overestimate myocardial contractility [14]. While literally dozens of other measures of ventricular function have been developed, those more accurate than EF have proved cumbersome and have never received widespread clinical usage. Instead, a number of caveats have been developed to tailor EF according to the effect that a given lesion has upon it.

One index that is clinically useful is end systolic dimension or (volume). Because end systolic dimension is dependent upon contractility, afterload and LV remodeling **but independent of preload** [15], this measure has been favored as an indicator of systolic function in volume overload VHD where increased preload most affects EF [16,17].

More advanced measures of LV function including strain rate imaging have been investigated as potentially more sensitive to early changes in both systolic and diastolic function [18]. While showing promise, none have become routine in clinical decision making in VHD.

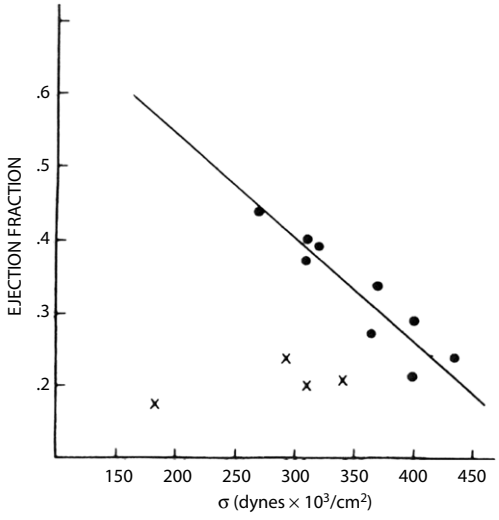


Figure. 1 Ejection fraction (EF) is plotted against systolic wall stress (σ) (afterload) for patients with AS and heart failure. For some patients (circles) EF is reduced almost entirely due to excess afterload. In others, (x) EF is reduced primarily due to myocardial damage and contractile dysfunction. Taken with permission from Ref. [13].

Biomarkers

The imprecision of symptoms and the measures of ventricular function noted above have led to a search for better indicators to help time intervention for VHD. B-type natriuretic peptide (BNP) and its precursor NT proBNP are thought to be secreted by the ventricles as a result of sarcomere stretch. Thus as the hemodynamic overloads of VHD cause the ventricles to rely more on preload reserve for compensation, these biomarkers are released in greater quantities. Indeed BNP is increased in severe VHD, while many cutoff values have been suggested as indicating decompensation in VHD [19–21], none has been widely employed as a surrogate marker indicating the need for intervention. On the other hand, low BNP offers some reassurance of ventricular compensation and the presence of normal filling pressures.

SPECIFIC DISEASES

Aortic stenosis

The asymptomatic patient with severe disease. Management of the patient with **symptomatic** severe aortic stenosis constitutes one of the most straightforward decisions in Cardiology because of the remarkable lethality of the disease. Either the patient undergoes aortic valve replacement (AVR) or suffers a 75 percent chance of death in 3 years [5,22,23]. The advent of transcatheter aortic valve implantation (TAVI) offers an alternative to surgical AVR for patients with risk factors that make surgery untenable [24].

Conversely the **asymptomatic** patient with severe disease presents much more of a challenge. The risk of sudden death is small but palpable (about 0.5 percent/year) [25,26], but the risk of AVR is also minimal, making it hard to weigh the clinical options in such patients. A high jet velocity (exceeding 4.0 m/sec), heavy valve calcification, poor exercise tolerance (or a fall in blood pressure during exercise), severe LVH and/or a rising BNP are indicators of higher than average risk and that AVR will be required soon because of the onset of symptoms or LV dysfunction [9,19,26–28]. In such cases elective AVR may be advisable, especially for patients with few comorbidities and for those wishing to pursue an active life style or whose occupations might increase the risk of exercise-induced sudden death.

In most cases, echocardiographic imaging with Doppler interrogation of the aortic valve is adequate to establish AS severity. However, in some cases obtaining invasive hemodynamics is necessary to fully evaluate the disease. In such instances exact transducer balancing and calibration, and exact catheter placement together with a carefully obtained cardiac output are needed to insure that an aortic valve area can be calculated accurately [29]. Because there is often a pressure gradient between the body of the LV and the LV outflow tract, it is important to place the LV catheter well within the body of the LV. Because there is substantial pressure recovery distal to where flow exits the valve, the distal catheter should be placed in the ascending aorta never in the femoral artery where the pressure gradient can be severely underestimated (Fig. 2) [30].

The patient with far advanced LV dysfunction, low gradient and low EF. Left ventricular hypertrophy is thought to occur in AS in response to the pressure overload that AS engenders. Afterload can be quantified as wall stress (σ) where $\sigma = Pxr/2th$ and $P = LV$ pressure, $r =$ ventricular radius and $th =$ wall thickness. Grossman et al. postulated that as pressure increases in the stress equation numerator it causes concentric LVH to develop whereby increased pressure is offset by increased wall thickness in the equation's denominator [31]. In this manner, wall stress (afterload) is normalized, a compensatory function since LV ejection is inversely related to afterload. However, in some patients, LVH is inadequate to normalize stress, afterload increases and EF falls [13]. Such patients have a high transvalvular gradient and an excellent prognosis following surgery [32].

In other patients EF and LV stroke volume are reduced not by exceptionally high afterload but by severely compromised myocardial contractility. Such patients typically have a low gradient (LV pressure and afterload are only modestly increased) and a poor prognosis [33–35]. Valve area may be very misleading in this group of patients because valve area can be flow dependent, increasing as flow increases until cardiac output reaches about 5 l/min [36]. In low flow, low gradient, low EF patients, a dobutamine challenge either in the echocardiographic or catheterization laboratories may be very useful [35]. Three different responses to dobutamine may be seen (Table 2). First there may be an substantial (>20 percent) increase in stroke volume with a concomitant increase in gradient and only a small increase in AVA. Such patients have severe AS, inotropic reserve and a relatively

good prognosis at surgery (Fig. 3) [35]. A second response is an increase in stroke volume, little increase in gradient and a large increase in AVA. It is thought that in these patients there is only moderate AS and that increasing flow increases valve area by physically opening the valve to a greater orifice area. Since the AS was in fact not truly severe despite an initially calculated AVA that suggested severe AS (pseudo-AS) [37], it is believed that AVR will not lead to much improvement in the patient's condition. A third response is that stroke volume fails to increase with dobutamine (lack of inotropic reserve). Such patients have a poor prognosis at AVR although EF may improve substantially if they survive the surgery [38]. Prognosis is especially poor for patients with severe coronary disease, with a mean gradient of <20 mm Hg, who also lack inotropic reserve [39].

The patient with low flow, low gradient and normal EF. In still other patients there is concentric LV remodeling without LVH (LV weight is not increased) leading to a small thick chamber with reduced end diastolic volume. Even though EF is normal, stroke volume is reduced and thus so is transvalvular gradient although is usually exceeds 25 mm Hg. Symptomatic patients with this condition have severe symptomatic AS, a good prognosis with AVR but a poor prognosis if untreated [40,41].

Thus management decisions in the AS patient may be very straightforward in the symptomatic patient with a large transvalvular gradient, or conversely they may require the integration of data from every modality available in the case of the patient with low flow and low gradient. In these difficult cases the clinician cannot rely upon a single number, whether AVA, jet velocity or gradient to make the ultimate decision regarding mechanical intervention. He/she must integrate all the data available and combine it with clinical judgment and experience to arrive at the best course of action.

Chronic aortic regurgitation

Assessment of lesion severity and its impact on the heart. Severe aortic regurgitation (AR) is generally well tolerated for many years, progressing to symptom onset or asymptomatic LV dysfunction at a rate

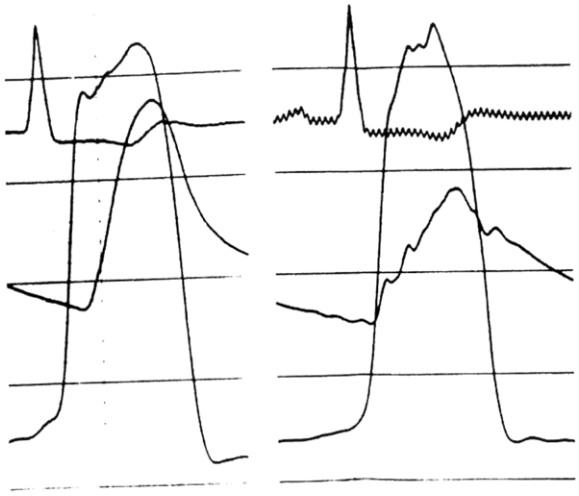


Figure. 2 Left ventricular (LV) and femoral artery (FA) tracings (left panel) are compared with pressure recordings from LV and aorta (right panel) in the same patient with AS. Time delay and pressure recovery cause the LV-FA recording to severely underestimate the true transvalvular gradient.

Table 2. Potential responses to dobutamine in aortic stenosis patients with low gradient, low ejection fraction.

	CO		GRAD		AVA	
TRUE	R	D	R	D	R	D
AS	3.5	5.0	25	42	0.7	0.75
PSUEDO AS	3.5	5.0	25	27	0.7	1.0
Negative Response	3.5	3.6	25	26	0.7	0.7

AS = Aortic Stenosis, AVA = Aortic Valve Area cm², CO = Cardiac Output l/min, D = Dobutamine, GRAD = transvalvular gradient mm Hg, R = Rest

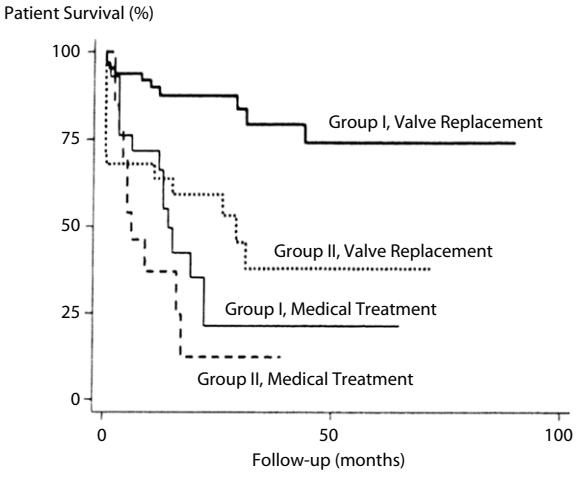
of about four percent per year [42,43]. Severe disease can be defined as that amount of AR that leads to the sequlae noted above. More precisely a regurgitant fraction exceeding 50 percent is generally thought to be the threshold for the amount of AR that leads to adverse outcomes. Echocardiographic jet area, effective regurgitant orifice area (ERO) pressure half time and regurgitant flow also aid in establishing AR severity [44]. Regurgitant flow can also be estimated using cardiac magnetic resonance imaging [45]. If the severity of AR is still uncertain after non-invasive imaging, cardiac catheterization is useful to assess both severity of the lesion and its impact on the LV. Contrast aortography provides direct imaging of the regurgitant flow and a good estimation of AR severity provided that enough contrast is injected to opacify both the dilated LV and aorta. Assessment of LV filling pressure at rest and during static or active exercise can help determine whether a patient's symptoms have a hemodynamic basis or whether hemodynamics are significantly deranged despite the absence of symptoms (Fig. 4).

Sudden death in AR is rare but does occur sporadically in patients with very dilated left ventricles, those exceeding an end diastolic dimension of 75 mm [42]. As with aortic stenosis, the onset of symptoms marks a worsening prognosis although without the immediate dire consequences seen in AS [6]. Because the patient may deny symptoms or fail to recognize them, formal exercise testing is helpful in defining both the presence of symptoms and also is of prognostic import [46]. Prognosis is also reduced even in the absence of symptoms if asymptomatic LV dysfunction intervenes as documented by an EF falling toward 50% or an end systolic dimension approaching 50–55 mm [16,47].

Aortopathy and bicuspid aortic valve. Although controversial [48] many experts believe that some patients with a congenitally bicuspid aortic valve also have disease of the aorta making it more prone to dilate and eventually dissect and rupture. Thus assessment of the patient with AR (and AS) should always include delineation of valve morphology and an assessment of the aortic root, its dimensions and whether it should be addressed at the time of surgery. Following careful assessment, outcome can be excellent even in the face of aortic dilatation [49].

Organic mitral regurgitation (MR)

Assessing severity of MR. The ability to easily visualize the MR jet as it enters the left atrium has led to many approaches for assessing MR severity as defiend in Table 1. A common cause of misinterpretation is failure to look at LV and left atrial (LA) volume in the context of estimated MR severity. If MR is both chronic and severe it must lead to LV and LA dilatation in so that the LV generates adequate forward stroke volume to compensate for that lost to MR, and for the LA to



Kaplan–Meier survival estimates by group and treatment.

Figure. 3 Survival for low gradient low EF AS patients is plotted according the inotropic reserve. Group I patients with inotropic reserve fared better than patients without inotropic reserve and also had a better outcome with aortic valve replacement than with medical therapy. Taken from Ref. [35] with permission.

accommodate the MR at a tolerable filling pressure. Thus, if the diagnosis of chronic severe MR is made, the left-sided chambers should be dilated. These and all other clues, including ERO, systolic pulmonary vein flow reversal and estimated pulmonary pressure, should be assessed to establish whether or not the patient's MR is severe [50–54]. For the patient complaining of exercise-induced symptoms, exercise echocardiography may be very revealing [12]. In some cases, exercise induces a substantial increase in the amount of MR present, and in other cases, there may be a large increase in pulmonary artery pressure. Both conditions help to explain why symptoms develop during exercise despite a more benign resting echocardiogram.

If after non-invasive evaluation, MR severity is still unclear, cardiac catheterization may clarify the issue. Direct measurement of LV filling pressure at rest or with exercise can help establish whether there is a hemodynamic basis for the patient's symptoms. Although fallen into disuse, a carefully performed left ventriculogram that avoids LV ectopy and uses enough contrast to opacify the enlarged LA and LV can directly visualize regurgitant flow and help evaluate MR severity.

The impact of mitral valve repair. For patients with AS, the aortic valve must virtually always be replaced, and it must usually be replaced for patients with AR. However, in most cases of non-rheumatic MR the mitral valve is repairable, a fact which has far-reaching implications for patient management. A durable repair carries none of the risks inherent to the implantation of a prosthetic valve. Operative risk for repair is approximately one-fourth that of valve replacement, and following repair there is no need for prolonged anticoagulation and obviously no risk of prosthetic valve

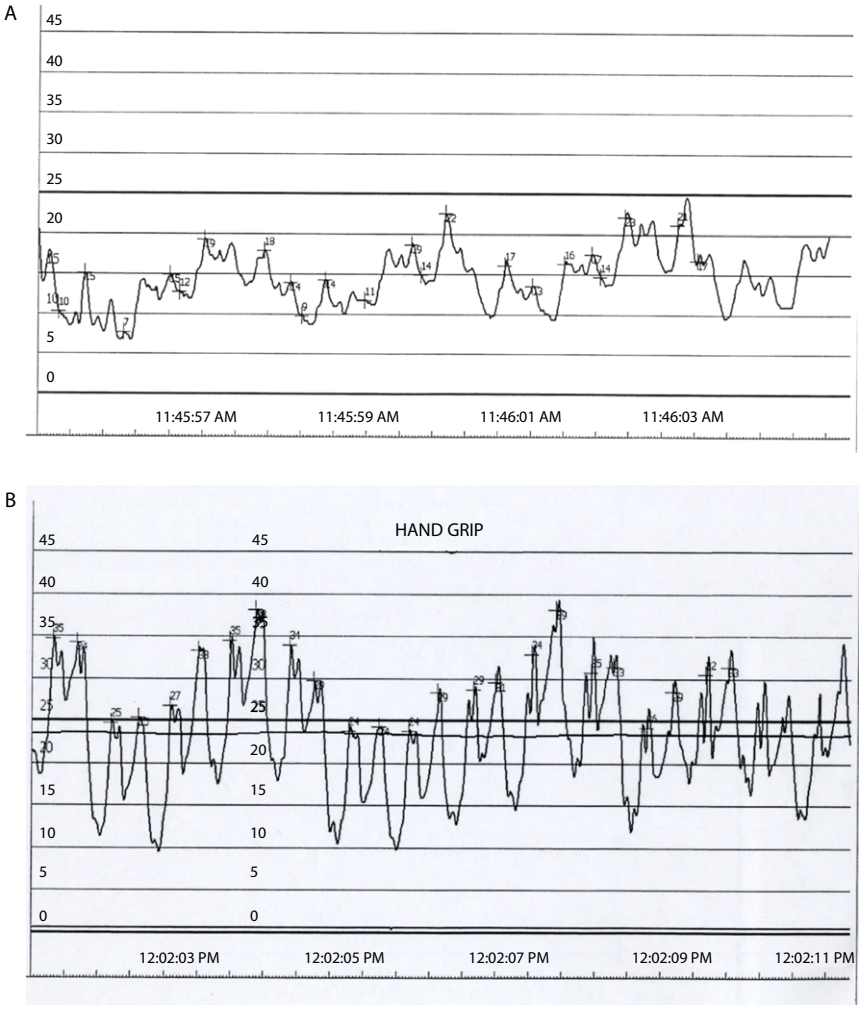


Figure. 4 **Pulmonary capillary wedge pressure (PCW) at rest (left panel, 4A) and during handgrip exercise (right panel, 4B) is shown for a patient with AR. Afterload increased by handgrip causes a substantial increase in PCW.**

structural deterioration [55–57]. These factors allow consideration of mitral repair for severe MR even before symptoms develop and before there is evidence of LV deterioration [1]. However, the patient, and his/her referring physician and cardiac surgeon must have a very high level of confidence that the valve can be repaired to engage in this management strategy. Replacement (and its attendant risks) instead of a repair in an asymptomatic patient with normal LV function constitutes a serious disservice to the patient. In making this decision, excellent preoperative imaging is key. High-grade 2D or 3D echo images may permit the surgeon to predict whether or not the valve pathoanatomy is consistent with his/her ability to repair the valve and thus whether or not to embark upon early surgery.

Timing of surgery if valve reparability is in question. If it is uncertain that the mitral valve can be repaired and might need to be replaced as in rheumatic MR or in highly complex myxomatous valves, surgery should be performed at the onset of symptoms or when there is evidence of LV dysfunction [7,17,58]. Many consider the advent of pulmonary hypertension at rest or with exercise and/or the onset of atrial fibrillation also to be indications for proceeding to mitral valve surgery. Because the increased preload in MR together with normal afterload facilitate ejection, an EF of 0.60 has been established as a threshold for surgical intervention, bolstered by evidence that preoperative deterioration to a lower EF results in poor postoperative outcomes [58]. Mitral valve surgery should also occur before the LV is unable to contract to an end systolic dimension of 40 mm [17]. As demonstrated in Fig. 5, it is safe to observe the patient until these thresholds are reached but the time until they are reached may be quite short [59]. Thus, very close follow-up is indicated to avoid missing the optimum time for surgical intervention.

Functional MR

In dilated and ischemic cardiomyopathies, severe LV dysfunction, associated wall motion abnormalities, and mitral annular dilatation may act in concert to cause MR. Unlike in organic MR, where valvular abnormalities pose a hemodynamic burden on the heart leading to LV dysfunction, in functional MR the reverse is true: the LV dysfunction causes MR. While the presence of MR in cardiomyopathy worsens prognosis [60], it is not clear whether the MR itself is the culprit or whether the presence of MR simply implies worse LV function, which is the actual cause of poorer outcome. In support of this latter concept is the difficulty in demonstrating that repair of functional MR prolongs life or that it leads to long-term improvement in the quality of life [61–65] as would be expected if the MR itself were a key determinant of outcome. For this reason, mechanical correction of functional MR is reserved for those patients who are very symptomatic after institution of a maximum medical regimen for heart failure [1].

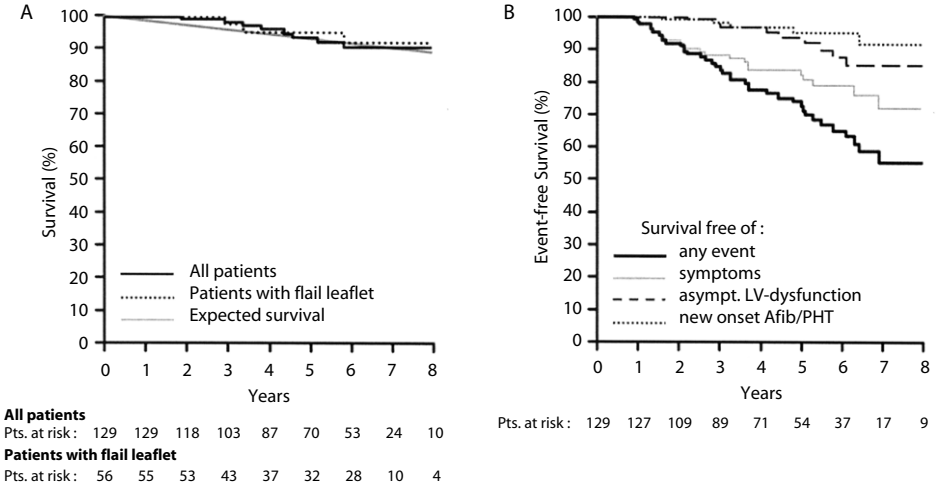


Figure. 5 Survival for patients with severe MR initially observed but then treated with surgery when symptoms or LV dysfunction occurred is shown in the left panel (5A) and is not different from a normal population. However the time until adverse events developed was short (right panel, 5B). Taken from Ref. [59] with permission.

Mitral stenosis (MS)

Assessing lesion severity. Facile imaging of the mitral valve makes assessment of MS relatively straightforward. Valve area can be directly planimetered or established by Doppler interrogation of the valve [66–68]. Pulmonary pressure is easily estimated if any tricuspid regurgitation is present.

If severity is still in question, catheterization can establish the transvalvular gradient. Because an error of only a few mm Hg can make a significant difference in the calculated mitral valve area, careful attention to transducer zeroing, balancing and calibration is mandatory. If pulmonary capillary wedge pressure is substituted for LA pressure, confirmation that the pulmonary catheter is truly wedged by demonstrating that highly oxygenated LA blood can be withdrawn from it is essential [4]. Valve area is then established using a carefully measured transvalvular pressure gradient and cardiac output in concert with the Gorlin formula. Hemodynamic assessment during exercise can be especially revealing in MS. The patient with nearly normal LA and pulmonary pressures at rest may develop striking increases in both during exercise, helping to establish a cause for the patient's symptoms and support that mechanical intervention will be beneficial.

Timing and selection of mechanical therapy. Mitral stenosis should be corrected when more than mild symptoms develop or when asymptomatic pulmonary hypertension develops [1,69,70]. In many cases balloon mitral valvotomy (BMV) offers a durable correction by performing a satisfactory commissurotomy in patients with severe MS and less than moderate MR [71–73]. A scoring system that allots 1–4 points each for the severity of valve calcification, leaflet mobility, leaflet thickening and disease of the subvalvular apparatus (4–16 points) helps establish the feasibility of BMV [74]. A valve score of <9 is favorable for a successful BMV. However many patients with higher scores still may undergo a successful BMV while not everyone with a low score enjoys success.

If BMV is thought inadvisable because of significant MR (that often worsens post BMV) or because of a high valve score, mitral valve replacement is then undertaken.

Tricuspid regurgitation

Tricuspid regurgitation (TR) frequently accompanies mitral valve disease. TR is often thought to be secondary to mitral disease's attendant pulmonary hypertension. Accordingly, TR may be expected to improve following successful mitral valve intervention [75]. While such improvement often occurs, it is unfortunately unpredictable [76]. Therefore it is advisable to address TR during mitral surgery by simply installing a ring annuloplasty that helps prevent TR from persisting or worsening following mitral surgery.

SUMMARY

Unlike most other fields in Cardiology where data from clinical trials help prescribe therapy, the lack of large, randomized trials in VHD means that decision-making is often based upon guidelines developed from consensus of opinion. Given the uncertainty to which this leads in many cases, integration of the very best bedside skills, imaging, and hemodynamic data must be brought to bear to arrive at the best management strategy. Assessments of lesion severity, the effect of the lesion on the patient and his heart and the method of lesion correction require a careful analysis of all the data available and rarely if ever can be left to a single diagnostic modality.

References

[1] Bonow RO, Carabello BA, Kanu C, De Leon AC Jr, Faxon DP, Freed MD, Gaasch WH, Lytle BW, Nishimura RA, O'Gara PT, O'Rourke RA, Otto CM, Shah PM, Shanewise JS, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Page RL and Riegel B. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease); developed in collaboration with the Society of Cardiovascular Anesthesiologists; endorsed by the Society of Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. Circulation. 2006 Aug 1;114:5, e84.231.

[2] Bonow RO, Carabello BA, deLeon AC, Edmunds LH, Fedderly BJ, Freed MD, Gaasch WH, McKay CR, Nishimura RA, O'Gara PT, O'Rourke RA, Rahimtoola SH, Ritchie JL, Cheitlin MD, Eagle KA, Gardner TJ, Garson A, Gibbons RJ, Russell RO, Ryan TJ and Smith SC. Guidelines for the management of patients with valvular heart disease; executive summary report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients with Valvular Heart Disease). Circulation. 1998;98:18, 1949–1984.

[3] Ozdogan O, Yuksel A, Gurgun C, Kayikcioglu M, Yavuzgil O and Cinar CS. Assessment of cardiac remodeling in asymptomatic mitral regurgitation for surgery timing: a comparative study of echocardiography and magnetic resonance imaging. Cardiovasc Ultrasound. 2010 Aug 13;8:32.
[4] Carabello BA and Grossman W. Calculation of stenotic valve orifice area. Grossman W (ed.) Cardiac Catheterization and Angiography. 7th edition, Lea and Febiger., Philadelphia. 2006. 173–183.
[5] Ross Jr and Braunwald E. Aortic stenosis. Circulation. 1968;38:61–67.
[6] Klodas E, Enriquez-Sarano M, Tajik AJ, Mullany CJ, Bailey KR and Seward JB. Optimizing timing of surgical correction in patients with severe aortic regurgitation: role of symptoms. J Am Coll Cardiol. 1997;30:746–752.
[7] Tribouilloy CM, Enriquez-Sarano M and Schaff HB et al. Impact of preoperative symptoms on survival after surgical correction of organic mitral regurgitation: rationale for optimizing surgical indications. Circulation. 1999;99:400–405.
[8] Rowe JC, Bland EF and Sprague HB et al. The course of mitral stenosis without surgery: ten- and twenty- year perspectives. Ann Intern Med. 1960;52:741.
[9] Das P, Rimington H and Chambers J. Exercise testing to stratify risk in aortic stenosis. Eur Heart J. 2005 Jul;26:13, 1309–1313.
[10] Amato MC, Moffa PJ, Werner KE and Ramires JA. Treatment decision in asymptomatic aortic valve stenosis: role of exercise testing. Heart. 2001 Oct;86:4, 381–386.
[11] Picano E, Pibarot P, Lancellotti P, Monin JL and Bonow RO. The emerging role of exercise testing and stress echocardiography in valvular heart disease. J Am Coll Cardiol. 2009 Dec 8;54:24, 2251–2260.
[12] Messika-Zeitoun D, Johnson BD, Nkomo V, Avierinos JF, Allison TG, Scott C, Tajik AJ and Enriquez-Sarano M. Cardiopulmonary exercise testing determination of functional capacity in mitral regurgitation: physiologic and outcome implications. J Am Coll Cardiol. 2006 Jun 20;47:12, 2521–2527.
[13] Carabello BA, Green LH, Grossman W, Cohn LH, Koster JK and Collins JJ Jr. Hemodynamic determinants of prognosis of aortic valve replacement in critical aortic stenosis and advanced congestive heart failure. Circulation. 1980;62:1, 42–48.
[14] Carabello BA. The relationship of left ventricular geometry and hypertrophy to left ventricular function in valvular heart disease. J Heart Valve Dis. 1995;4:Suppl II, S-132–S-139.
[15] Carabello BA and Spann JF. The uses and limitations of the end-systolic indexes of left ventricular function. Circulation. 1984;69:5, 1058–1064.
[16] Henry WL, Bonow RO, Rosing DR and Epstein SE. Observations on the optimum time for operative intervention for aortic regurgitation. II. serial echocardiographic evaluation of asymptomatic patients. Circulation. 1980 Mar;61:3, 484–492.
[17] Matsumura T, Ohtaki E, Tanaka K, Misu K, Tobaru T, Asano R, Nagayama M, Kitahara K, Umemura J, Sumiyoshi T, Kasegawa H and Hosoda S. Echocardiographic prediction of left ventricular dysfunction after mitral valve repair for mitral regurgitation as an indicator to decide the optimal timing of repair. J Am Coll Cardiol. 2003;42:458–463.
[18] Carabello BA. Evolution of the study of left ventricular function: everything old is new again. Circulation. 2002;105:23, 2701–2703.
[19] Bergler-Klein J, Klaar U and Heger M et al. Natriuretic peptides predict symptom-free survival and postoperative outcome in severe aortic stenosis. Circulation. 2004;109:2303–2308.
[20] Iwahashi N, Nakatani S, Umemura S, Kimura K and Kitakaze M. Usefulness of plasma b-type natriuretic peptide in the assessment of disease severity and prediction of outcome after aortic valve replacement in patients with severe aortic stenosis. J Am Soc Echocardiogr. 2011 May 11.
[21] Klaar U, Gabriel H, Bergler-Klein J, Pernicka E, Heger M, Mascherbauer J, Rosenhek R, Binder T, Maurer G and Baumgartner H. Prognostic value of serial b-type natriuretic peptide measurement in asymptomatic organic mitral regurgitation. Eur J Heart Fail. 2011 Feb;13:2, 163–169.
[22] Selzer A. Changing aspects of the natural history of valvular aortic stenosis. N Engl J Med. 1987;317:91–98.
[23] Schwarz F, Baumann P and Manthey J et al. The effect of aortic valve replacement on survival. Circulation. 1982;66:1105–1110.
[24] Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Hermann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D and Pocock S. PARTNER Trail Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010 Oct 21;363:17, 1597–1607.
[25] Pellikka PA, Sarano ME and Nishimura RA et al. Outcome of 622 adults with asymptomatic, hemodynamically significant aortic stenosis during prolonged follow-up. Circulation. 2005;111:3290–3295.
[26] Rosenhek R, Zilberszac R, Schemper M, Czerny M, Mundigler G, Graf S, Bergler-Klein J, Grimm M, Gabriel H and Maurer G. Natural history of very severe aortic stenosis. Circulation. 2010 Jan 5;121:1, 151–156.
[27] Otto CM, Burwash JG and Legget ME et al. Prospective study of asymptomatic valvular aortic stenosis: clinical, echocardiographic, and exercise predictors of outcome. Circulation. 1997;95:2262–2270.
[28] Duncan AL, Lowe BS, Garcia MJ, Xu M, Gillinov AM, Mihaljevic T and Koch CG. Influence of concentric left ventricular remodeling on early mortality after aortic valve replacement. Ann Thorac Surg. 2008 Jun;85:6, 2030–2039.
[29] Assey Me, Zile MR, Usher BW, Karavan MP and Carabello BA. Effect of catheter positioning on the variability of measure gradient in aortic stenosis. Cathet Cardiovasc Diagn. 1993;30:287–292.
[30] Folland ED, Parisi AF and Carbone C. Is peripheral arterial pressure a satisfactory substitute for ascending aortic pressure when measuring aortic valve gradients? . J Am Coll Cardiol. 1984;4:1207–1212.
[31] Grossman W, Jones D and McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. J Clin Invest. 1975;53:332–341.
[32] Smith N, McAnulty JH and Rahimtoola SH. Severe aortic stenosis with impaired left ventricular function and clinical heart failure: results of valve replacement. Circulation. 1978 Aug;58:2, 255–264.

[33] Connolly HM, Oh JK and Schaff HV et al. Severe aortic stenosis with low transvalvular gradient and severe left ventricular dysfunction: result of aortic valve replacement in 52 patients. Circulation. 2000;101:1940–1946.
[34] Brogan WC III, Grayburn PA, Lange RA and Hillis LD. Prognosis after valve replacement in patients with severe aortic stenosis and a low transvalvular pressure gradient. J Am Coll Cardiol. 1993;21:1657–1660.
[35] Monin JL, Quere JP and Monchi M et al. Low-gradient aortic stenosis: operative risk stratification and predictors for long-term outcome — a multicenter study using dobutamine stress hemodynamics. Circulation. 2003;108:319–324.
[36] Blais C, Burwash IG, Mundigler G, Dumesnil JG, Loho N, Rader F, Baumgartner H, Beanlands RS, Chayer B, Kadem L, Garcia D, Durand LG and Pibarot P. Projected valve area at normal flow rate improves the assessment of stenosis severity in patients with low-flow, low-gradient aortic stenosis: the multicenter TOPAS (Truly or Pseudo-Severe Aortic Stenosis) study. Circulation. 2006 Feb 7;113:5, 711–721.
[37] Carabello BA, Ballard WL and Gazes PC. Cardiology Pearls. Sahn SA, Heffner JE, Series eds. Hanley & Belfus, Inc., Philadelphia, 1994.
[38] Quere JP, Monin JL and Levy F et al. Influence of preoperative left ventricular contractile reserve on postoperative ejection fraction in low-gradient aortic stenosis. Circulation. 2006;113:1738–1744.
[39] Tribouilly C, Levy F, Rusinaru D, Gueret P, Petit-Eisenmann H, Baleynaud S, Jobic Y, Adams C, Lelong B, Pasquet A, Chauvel C, Metz D, Quere JP and Monin JL. Outcome after aortic valve replacement for low-flow/low-gradient aortic stenosis without contractile reserve on dobutamine stress echocardiography. J Am Coll Cardiol. 2009 May 19;53:20, 1865–1873.
[40] Hachicha Z, Dumesnil JG, Bogaty P and Pibarot P. Paradoxical low-flow, low-gradient severe aortic stenosis despite preserved ejection fraction is associated with higher afterload and reduced survival. Circulation. 2007 Jun 5;115:22, 2856–2864.
[41] Dumesnil JG, Pibarot P and Carabello BA. Paradoxical low flow and/or low gradient severe aortic stenosis despite preserved left ventricular ejection fraction: implications for diagnosis and treatment. Eur Heart J. 2010 Feb;31:3, 281–289.
[42] Bonow RO, Lakatos E, Maron BJ and Epstein SE. Serial long-term assessment of the natural history of asymptomatic patients with chronic aortic regurgitation and normal left ventricular systolic function. Circulation. 1991;84:1625–1635.
[43] Borer JS and Bonow RO. Contemporary approach to aortic and mitral regurgitation. Circulation. 2003;108:2432–2438.
[44] Detaint D, Messika-Zeitoun D, Maalouf J, Tribouilloy C, Mahoney DW, Tajik AJ and Enriquez-Sarano M. Quantitative echocardiographic determinants of clinical outcome in asymptomatic patients with aortic regurgitation: a prospective study. JACC Cardiovasc Imaging. 2008 Jan;1:1, 1–11.
[45] Roes SD, Hammer S and van der Geest RJ et al. Flow assessment through four heart valves simultaneously using 3-dimensional 3-directional velocity-encoded magnetic resonance imaging with retrospective valve tracking in health volunteers and patients with valvular regurgitation. Invest Radiol. 2009 Oct;44:10, 669–675.
[46] Bonow RO, Borer JS, Rosing DR, Henry WL, Pearlman AS, McIntosh CL, Morrow AG and Epstein SE. Preoperative exercise capacity in symptomatic patients with aortic regurgitation as a predictor of postoperative left ventricular function and long-term prognosis. Circulation. 1980 Dec;62:6, 1280–1290.
[47] Bonow RO, Rosing DR, Maraon BJ, McIntosh CL, Jones M, Bacharach SL, Green MV, Clark RE and Epstein SE. Reversal of left ventricular dysfunction after aortic valve replacement for chronic aortic regurgitation: influence of duration of preoperative left ventricular dysfunction. Circulation. 1984 Oct;70:4, 570–579.
[48] El-Hamamsy I and Yacoub MH. A measured approach to managing the aortic root in patients with bicuspid aortic valve disease. Curr Cardiol Rep. 2009 Mar;11:2, 94–100.
[49] El-Hamamsy I, Eryligit Z, Stevens LM, Sarang Z, George R, Clark L, Melina G, Takkenberg JJ and Yacoub MH. Long-term outcomes after autograft versus homograft aortic root replacement in adults with aortic valve disease: a randomized controlled trial. Lancet. 2010 Aug 14;376:9740, 524–531. Epub 2010 Aug 3.
[50] Spain MG, Smith MD and Grayburn PA et al. Quantitative assessment of mitral regurgitation by Doppler color flow imaging: angiographic and hemodynamic correlations. J Am Coll Cardiol. 1989;13:585–590.
[51] Bargiggia GS, Tronconi L and Sahn D et al. A new method for quantification of mitral regurgitation based on color flow Doppler imaging of flow convergence proximal to regurgitant orifice. Circulation. 1991;86:1481–1489.
[52] Vanderboort PM, Rivera JM and Mele D et al. Application of color Doppler flow mapping to calculate effective regurgitant orifice area: An in vivo study and initial clinical observations. Circulation. 1993;88:1150–1156.
[53] Hall S, Brickner M and Willett D et al. Assessment of mitral regurgitation by Doppler color flow mapping of the vena contracta. Circulation. 1997;95:636–642.
[54] Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, Detaint D, Capps M, Nkomo V, Scott C, Schaff HV and Tajik AJ. Quantitative determinants of the outcomes of asymptomatic mitral regurgitation. N Engl J Med. 2005 May 26;352:21, 2245–2246.
[55] Enriquez-Sarano M, Schaff HV and Orszulak TA et al. Valve repair improves the outcome of surgery for mitral regurgitation analysis. Circulation. 1995;91:1022–1028.
[56] Horskotte D, Schulte HD, Bircks W and Strauer BE. The effect of chordal preservation on late outcome after mitral valve replacement: a randomized study. J Heart Valve Dis. 1993;2:150–158.
[57] Jokinen JJ, Hippelainen MJ, Pitkanen OA and Hartikainen JE. Mitral valve replacement versus repair: propensity-adjusted survival and quality-of-life analysis. Ann Thorac Surg. 2007 Aug;84:2, 451–458.
[58] Enriquez-Sarano M, Tajik AJ, Schaff HV, Orszulak TA, Bailey KR and Frye RL. Echocardiographic prediction of survival after surgical correction of organic mitral regurgitation. Circulation. 1994;90:830–837.
[59] Rosenhek R, Rader F, Klaar U, Gabriel H, Krejc M, Kalbeck D, Schemper M, Maurer G and Baumgartner H. Outcome of watchful waiting in asymptomatic severe mitral regurgitation. Circulation. 2006 May 9;113:18, 2238–2244. Epub 2006 May 1.

[60] Trichon BH, Felker GM and Shaw LK et al. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. Am J Cardiol. 2003;91:538–543.
[61] Glower DD, Tuttle RH, Shaw LK, Orozco RE and Rankin JS. Patient survival characteristics after routine mitral valve repair for ischemic mitral regurgitation. J Thorac Cardiovasc Surg. 2005 Apr;129:4, 860–868.
[62] Talwalkar NG, Earle NR, Earle EA and Lawrie GM. Mitral valve repair in patients with low left ventricular ejection fractions: early and late results. Chest. 2004 Sep;126:3, 709–715.
[63] Wu AH, Aaronson KD and Billing SF et al. Impact of mitral valve annuloplasty on mortality risk in patients with mitral regurgitation and left ventricular systolic dysfunction. J Am Coll Cardiol. 2005;45:381–387.
[64] Diodato MD, Moon MR, Pasque MK, Barner HB, Moazami N, Lawton JS, Bailey MS, Guthrie TJ, Meyers BF and Damiano RJ Jr. Repair of ischemic mitral regurgitation does not increase mortality or improve long-term survival in patients undergoing coronary artery revascularization: a propensity analysis. Ann Thorac Surg. 2004 Sep;78:3, 794–799. Discussion 794–9.
[65] Mihaljevic T, Lam BK, Rajeswaran J, Takagaki M, Lauer MS, Gillinov AM, Blackstone EH and Lytle BW. Impact of mitral valve annuloplasty combined with revascularization in patients with functional ischemic mitral regurgitation. J Am Coll Cardiol. 2007 Jun 5;49:22, 2191–2203.
[66] Martin RP, Rakowski H and Kleinman JH. Reliability and reproducibility of two-dimensional echocardiographic measurement of the stenotic mitral valve orifice area. Am J Cardiol. 1979 Mar;43:3, 560–568.
[67] Hatle L, Angelsen B, Tromsdal A and Angelsen B. Noninvasive assessment of pressure drop in mitral stenosis by Doppler ultrasound. Br Heart J. 1978 Feb;40:2, 131–140.
[68] Messika-Zeitoun D, Lung B, Brochet E, Himbert D, Serfaty JM, Laissy JP and Vehanian A. Evaluation of mitral stenosis in 2008. Arch Cardiovasc Dis. 2008 Oct;101:10, 653–663. Epub 2008 Oct 26.
[69] Roy SB and Gopinath N. Mitral Stenosis. Circulation. 1968;38:1 Suppl, 68–76.
[70] Vincens JJ, Temizer D, Post JR, Edmunds LH Jr and Hermann HC. Long-term outcome of cardiac surgery in patients with mitral stenosis and severe pulmonary hypertension. Circulation. 1995 Nov 1;92:9 Suppl, 137–142. II.
[71] Reyes VP, Raju BS, Wynne J, Stephenson LW, Raju R, Fromm BS, Rajagopal P, Mehta P, Singh S and Rao DP. Percutaneous balloon valvuloplasty compared with open surgical commissurotomy for mitral stenosis. N Engl J Med. 1994 Oct 13;331:15, 961–967.
[72] Ben Farhat M, Ayari M, Maatouk F, Betbout F, Gamra H, Jarra M, Tiss M, Hammami S, Thaalbi R and Addad F. Percutaneous balloon versus surgical closed and open mitral commissurotomy: seven-year follow-up results of a randomized trial. Circulation. 1998 Jan 27;97:3, 245–250.
[73] Nobuyoshi M, Arita T, Shirai S, Hamasaki N, Yokoi H, Iwabuchi M, Yasumoto H and Nosaka H. Percutaneous balloon mitral valvuloplasty: a review. Circulation. 2009 Mar 3;119:8, e211–e219. Epub 2008 Dec 23.
[74] Wilkins GT, Weyman AE, Abascal VM, Block PC and Palacios IF. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilation. Br Heart J. 1998 Oct;60:4, 299–308.
[75] Skudicky D, Essop MR and Sareli P. Efficacy of mitral balloon valvotomy in reducing the severity of associated tricuspid valve regurgitation. Am J Cardiol. 1994 Jan 15;73:2, 209–211.
[76] Shiran A and Sagie A. Tricuspid regurgitation in mitral valve disease incidence, prognostic implications, mechanism, and management. J Am Coll Cardiol. 2009 Feb 3;53:5, 401–408.