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Multiple and Mixed

Valvular Heart Disease Many acquired and congenital cardiac lesions may result in stenosis and/or regurgitation of one or more heart valves. For example, rheu matic heart disease can involve the mitral (mitral stenosis [MS], mitral regurgitation [MR], or MS and MR), aortic (aortic stenosis [AS], aortic regurgitation [AR], or AS and AR), and tricuspid (tricuspid stenosis [TS], tricuspid regurgitation [TR], or TS and TR) valve, alone or in combination. The common association of functional TR with sig nificant mitral valve disease is discussed in Chap. 277. Severe mitral annular calcification can result in regurgitation (due to decreased annular shortening during systole) and mild or moderate stenosis (caused by extension of the calcification onto the leaflets resulting in restricted valve opening). Patients with severe AS and left ventricular (LV) remodeling may develop functional MR that may not improve after isolated aortic valve replacement (AVR). Primary MR due to mitral valve prolapse or chordal rupture has been noted in patients with severe AS. Aortic valve infective endocarditis (IE) may second arily involve the mitral apparatus either by abscess formation and contiguous spread via the intervalvular fibrosa or by “drop metastases” from the aortic leaflets onto the anterior leaflet of the mitral valve. Mediastinal radiation may result in aortic, mitral, and even tricus pid valve disease, most often with mixed stenosis and regurgitation. Carcinoid heart disease may cause mixed lesions of either or both the tricuspid and pulmonic valves. Ergotamines, and the previously used combination of fenfluramine and phentermine, can rarely result in mixed lesions of the aortic and/or mitral valve. Patients with Marfan syndrome may have both AR from aortic root dilation and MR due to mitral valve prolapse (MVP). Myxomatous degeneration causing pro lapse of multiple valves (mitral, aortic, tricuspid) can also occur in the absence of an identifiable connective tissue disorder. Bicuspid aortic or pulmonic valve disease can result in mixed stenosis and regurgita tion. The former is also associated with aortic aneurysm disease and a predisposition to aortic dissection. ■ ■PATHOPHYSIOLOGY In patients with multivalvular heart disease, the pathophysiologic derangements associated with the more proximal valve disease can mask the full expression of the attributes of the more distal valve lesion. For example, in patients with rheumatic mitral and aortic valve disease, the reduction in cardiac output

(CO) imposed by the mitral valve dis ease will decrease the magnitude of the hemodynamic derangements related to the severity of the aortic valve lesion (stenotic, regurgitant, or both). Alternatively, the development of atrial fibrillation (AF) dur ing the course of MS can lead to sudden worsening in a patient whose aortic valve disease was not previously felt to be significant. The devel opment of reactive pulmonary vascular disease, sometimes referred to as a “secondary obstructive lesion in series,” can impose an additional challenge in these settings. As CO falls with progressive tricuspid valve disease, the severity of any associated mitral or aortic disease can be underestimated. One of the most common examples of multivalve disease is that of functional TR in the setting of significant mitral valve disease. Func tional TR occurs as a consequence of right ventricular and annular dilation; pulmonary artery (PA) hypertension may be present. The tricuspid leaflets are morphologically normal. Progressive degrees of TR lead to right ventricular volume overload and continued chamber and annular dilation. The TR is usually central in origin; reflux into the right atrium (RA) is expressed as large, systolic c-v waves in the RA pressure pulse. The height of the c-v wave is dependent on RA compliance and the volume of regurgitant flow. The RA waveform may become “ventricularized” in advanced stages of chronic, severe TR. CO falls and the severity of the associated mitral valve disease may become

more difficult to appreciate. Findings related to advanced right heart failure (e.g., ascites, edema) predominate. Primary rheumatic tricus pid valve disease may occur with rheumatic mitral disease and cause hemodynamic changes reflective of TR, TS, or their combination. With TS, the y descent in the RA pressure pulse is prolonged. Typically, however, findings related to the mitral valve disease predominate over those related to the tricuspid valve disease.

CHAPTER 279 Another example of rheumatic, multivalve disease involves the com bination of mitral and aortic valve pathology, frequently characterized by MS and AR. In isolated MS, LV preload and diastolic pressure are reduced as a function of the severity of inflow obstruction. With con comitant AR, however, LV filling is enhanced and diastolic pressure may rise depending on the compliance characteristics of the chamber. Because the CO falls with progressive degrees of MS, transaortic valve flows will decline, masking the potential severity of the aortic valve lesion (AR, AS, or its combination). As noted above, onset of AF in such patients can be especially deleterious. The loss of atrial systole with AF may result in a critical reduction in CO, a rise in left atrial (LA) and LV diastolic pressures, and a further deleterious increase in heart rate. Multiple and Mixed Valvular Heart Disease Secondary (functional) MR may complicate the course of some patients with severe AS. The mitral valve leaflets and chordae tendineae are usually normal. Incompetence is related to changes in LV geometry (remodeling) and abnormal systolic tethering of the leaflets in the context of markedly elevated LV systolic pressures. Relief of the excess afterload with surgical or transcatheter AVR may result in reduction of the secondary MR. Persistence of significant, secondary MR following AVR is associated with impaired functional outcomes and reduced sur vival. Identification of patients who would benefit from concomitant treatment of their secondary MR at time of AVR is quite challenging. Most surgeons perform mitral valve repair of moderate-to-severe or severe secondary MR at time of surgical AVR. Significant primary MR may also coexist with AS and is routinely managed with repair (or replacement) at the time of AVR. There is increasing experience with the combination of transcatheter aortic valve implantation (TAVI) and transcatheter edge-to-edge mitral valve repair (TEER) in high surgical risk patients with severe AS and moderate-severe primary or secondary MR. Decision-making regarding the need for mitral valve intervention can be challenging. In patients with mixed AS and AR, assessment of valve

stenosis can be influenced by the magnitude of the regurgitant valve flow. Because transvalvular systolic flow velocities are augmented in patients with AR and preserved LV systolic function, the LV-aortic Dopplerderived pressure gradient and the intensity of the systolic murmur will be elevated to values higher than expected for the true systolic valve orifice size as measured by planimetry. Uncorrected, the Gorlin formula, which relies on forward CO (systolic transvalvular flow) and the mean pressure gradient for calculation of valve area, is not accurate in the setting of mixed aortic valve disease. Similar considerations apply to patients with mixed mitral valve disease. The peak mitral valve Doppler E wave velocity (v0) is increased in the setting of severe MR because of enhanced early diastolic flow and may not accurately reflect the contribution to LA hypertension from any associated MS. When either AR or MR is the dominant lesion in patients with mixed aortic or mitral valve disease, respectively, the LV is dilated. When AS or MS predominates, LV chamber size will be normal or small. It can sometimes be difficult to ascertain whether stenosis or regurgitation is the dominant lesion in patients with mixed valve disease, although an integrated clinical and noninvasive assessment can usually provide clarification for purposes of patient management. For patients with moderate, mixed AS and AR in whom stenosis is the dominant lesion, the natural history tends to parallel what might be expected for isolated severe AS, and the treatment approach should be accordingly aligned. Patients with significant AS, a nondilated LV chamber, and concen tric hypertrophy will poorly tolerate the abrupt development of aortic regurgitation, as may occur, for example, with IE or after surgical AVR or TAVI complicated by paravalvular leakage. The noncompliant LV is not prepared to accommodate the sudden volume load, and as a result, LV diastolic pressure rises rapidly and severe heart failure develops.

Indeed, significant paravalvular regurgitation is a significant risk fac tor for short- to intermediate-term death following transcatheter AVR. Conditions in which the LV may not be able to dilate in response to chronic AR (or MR) include radiation heart disease, cardiac amyloid, and, in some patients, the cardiomyopathy associated with obesity and diabetes. Noncompliant ventricles of small chamber size predispose to earlier onset diastolic dysfunction and heart failure in response to any further perturbation in valve function.

PART 6 Disorders of the Cardiovascular System ■ ■SYMPTOMS Compared with patients with isolated, single-lesion valve disease, patients with multiple or mixed valve disease may develop symptoms at a relatively earlier stage in the natural history of their disease. Symptoms such as exertional dyspnea and fatigue are usually related to elevated filling pressures, reduced CO, or their combination. Palpitations may signify AF and identify mitral valve disease as an important component of the clinical presentation, even when not previously suspected. Chest pain compatible with angina could reflect left or right ventricular oxy gen supply/demand mismatch on a substrate of hypertrophy and pres sure/volume overload with or without superimposed coronary artery disease. Symptoms related to right heart failure (abdominal fullness/ bloating, edema) are late manifestations of advanced disease. ■ ■PHYSICAL FINDINGS Mixed disease of a single valve is most often manifested by systolic and diastolic murmurs, each with the attributes expected for the valve in question. Thus, patients with AS and AR will have characteristic midsystolic, crescendo-decrescendo and blowing, decrescendo diastolic murmurs at the base of the heart in the second right interspace and along the left sternal edge, respectively. Many patients with significant AR have mid-systolic outflow murmurs even in the absence of valve sclerosis/stenosis, and other findings of AS must be sought. The sepa rate murmurs of AS and AR can occasionally be difficult to distinguish from the continuous murmurs associated with either a patent ductus arteriosus (PDA) or

ruptured sinus of Valsalva aneurysm. With mixed aortic valve disease, the systolic murmur should end before, and not envelope or extend through, the second heart sound (S2). The murmur associated with a PDA is heard best to the left of the upper sternum. The continuous murmur heard with a ruptured sinus of Valsalva aneu rysm is often first appreciated after an episode of acute chest pain. An early ejection click, which usually defines bicuspid aortic valve disease in young adults, is often not present in patients with congenital mixed AS and AR. As noted above, both the intensity and duration of these separate murmurs can be influenced by a reduction in CO and trans valvular flow due to coexistent mitral valve disease or AF. In patients with isolated MS and MR, expected findings would include a blowing, holosystolic murmur and a mid-diastolic rumble (with or without an opening snap) best heard at the cardiac apex. An irregularly irregular heart rhythm in such patients would likely signify AF. Findings with TS and TR would mimic those of left-sided MS and MR, save for the expected changes in the murmurs with respiration. The murmurs of pulmonic stenosis and regurgitation behave in a fashion directionally similar to AS and AR; dynamic changes during respiration should be noted. Specific attributes of these cardiac murmurs are reviewed in Chaps. 44 and 277. ■ ■LABORATORY EXAMINATION The electrocardiogram (ECG) may show evidence of ventricular hypertrophy and/or atrial enlargement. ECG signs indicative of rightsided cardiac abnormalities in patients with left-sided valve lesions should prompt additional assessment for PA hypertension and/or right-sided valve disease. The presence of AF in patients with aortic valve disease may be a clue to the presence of previously unsuspected mitral valve disease in the appropriate context. The chest x-ray can be reviewed for evidence of cardiac chamber enlargement, valve and/ or annular calcification, and any abnormalities in the appearance of the pulmonary vasculature. The latter could include enlargement of the main and proximal pulmonary arteries with PA hypertension and

pulmonary venous redistribution/engorgement or Kerley B lines with increasing degrees of LA and pulmonary venous hypertension. An enlarged azygos vein in the frontal projection indicates RA hyperten sion. Roentgenographic findings not expected based on a single or mixed valve lesion may reflect other valve disease. Transthoracic echocardiography (TTE) is the most commonly used imaging modality for the diagnosis and characterization of multiple and/or mixed valvular heart disease and may often demonstrate find ings not clinically suspected. Transesophageal echocardiography (TEE) may sometimes be required for more accurate assessment of valve anatomy (specifically, the mitral valve) and when IE is considered responsible for the clinical presentation. TTE findings of particular interest include those related to valve morphology and function, cal cification, chamber size, ventricular wall thickness, biventricular func tion, estimated PA systolic pressure, and the dimensions of the great vessels, including the root and ascending aorta, PA, and inferior vena cava. Exercise testing (with or without echocardiography) can be use ful when the degree of functional limitation reported by the patient is not adequately explained by the findings on TTE performed at rest. An integrated assessment of the clinical and TTE findings is needed to help determine the dominant valve lesion(s) and establish an appropriate plan for treatment and follow-up. Natural history is usually influenced to a relatively greater degree by the dominant lesion. Cardiac magnetic resonance (CMR) imaging can be used to provide additional anatomic and physiologic information when echocardiog raphy proves suboptimal but is less well suited to the evaluation of valve morphology. Cardiac computed tomography (CT) has been used to assess intracardiac structures in patients with complicated IE. It is invaluable in planning for transcatheter valve implantation. Coronary CT angiography provides a noninvasive alternative for the assess ment of coronary artery anatomy prior to surgery or transcatheter intervention. Invasive hemodynamic evaluation with right and left heart cath eterization may be required to characterize

more completely the individual contributions of each lesion in patients with either multiple or mixed valvular heart disease. It is strongly recommended when there is a discrepancy between the clinical and noninvasive find ings in a symptomatic patient. Measurement of PA pressures and calculation of pulmonary vascular resistance (PVR) can help inform clinical decision-making in certain patient subsets, such as those with advanced mitral and tricuspid valve disease. It is important to identify any potential contribution to the clinical picture from pulmonary vas cular disease. Attention to the accurate assessment of CO is essential. Coronary angiography (if indicated) can be performed as part of the procedure. Contrast ventriculography and great vessel angiography are performed infrequently. TREATMENT Multiple and Mixed Valve Disease Management of patients with multiple or mixed valve disease can be challenging. As noted above, it is helpful to determine the dominant valve lesion and proceed according to the treatment and follow-up recommendations for it (Chaps. 272–278), being mind ful of deviations from the expected course due to the contributions of more than one valve lesion. For example, AF that emerges in the course of moderate mitral valve disease may precipitate heart failure in patients with concomitant, severe aortic valve disease that was previously asymptomatic. Medical therapies are limited and include diuretics when indicated for relief of congestion and anticoagulation to prevent stroke and thromboembolism in patients with AF. Blood pressure– lowering medications may be needed to treat systemic hyperten sion, which may aggravate left-sided regurgitant valve lesions, but should be initiated and titrated carefully. Pulmonary vasodilators to lower PVR are not generally effective in this context.

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