Right-Sided Valve Disease Deserves a Little More RESPECT
Charles J. Bruce, MB, ChB; Heidi M. Connolly, MD

Historically, right-sided valvular disease has received less attention from clinicians and researchers than left-sided valve disease, in part because of a protracted latent asymptomatic period. Moreover, because tricuspid regurgitation (TR) is often due to left-sided valve disease and pulmonary regurgitation (PR) is often secondary to congenital cardiac disease, the underlying disorder rather than the valve lesion tends to dominate the clinical picture.

It is increasingly recognized that right-sided valve disease is not benign and has a significant and independent impact on morbidity and mortality. Today, diagnostic techniques and appropriate management strategies for patients with right-sided valve disease are established and continually refined. In this era of increasing awareness and improved treatment options for patients with valve disease, it is important that clinicians consider the diagnosis of right-sided valve disease, understand its pathophysiology, choose appropriate confirmatory testing, and refer patients for timely intervention to prevent clinical deterioration with associated adverse consequences.

This review examines the causes of right-sided valve disease and the latest diagnostic advances and treatment options for these often-neglected valve lesions. Patients with native right-sided valve disease are rarely affected by endocarditis, and indications for prophylaxis have recently changed.¹

Tricuspid Valve Disease

Tricuspid Regurgitation
TR that is at least moderate in severity is most frequently “functional” in nature and by definition not related to primary tricuspid valve (TV) leaflet pathology but rather secondary to another disease process causing right ventricular (RV) dilatation, distortion of the subvalvular apparatus, tricuspid annular dilatation, or a combination of these. Furthermore, a moderate or greater degree of TR, regardless of primary origin, usually engenders additional TR as a result of the adverse hemodynamic consequence of RV volume overload. Causes of clinically significant TR are outlined in Table 1; 2 classic examples of primary tricuspid leaflet pathology are demonstrated in Figure 1. Symptoms of TR are often nonspecific, and severe TR may be well tolerated, producing few overt symptoms for a protracted period. With isolated severe TR, patients may complain of fatigue and decreased exercise tolerance as a result of low cardiac output. Elevated right atrial (RA) pressure also leads to peripheral edema and hepatic congestion with decreased appetite and abdominal fullness. Long-standing severe TR results in right-heart failure, ascites, and anasarca.

Jugular venous distention with a visible systolic v wave is present in 35% to 75% of patients with severe TR.²⁻⁴ Hepatomegaly is present in 90%, but systolic pulsation of the liver is noted inconsistently. Classically, the holosystolic murmur of TR is heard along the sternal border, increasing in intensity with inspiration as a result of increased systemic venous return.³ However, the murmur is heard in <20% of patients with documented severe valve dysfunction caused by equalization of pressures between the RA and RV.²⁻⁴

The hemodynamic changes depend on duration and severity of TR and include an elevated RA mean pressure with a systolic v wave and reduced cardiac output.³ Hemodynamic catheterization is rarely required to confirm the diagnosis of severe TR, and right ventriculography is not helpful because the catheter may induce TR.

Echocardiography is the diagnostic cornerstone confirming the presence, severity, and cause of TR, as well as its impact on RV size and function. Although 2-dimensional echocardiography can provide a morphological assessment of RV dimension and function,⁶ it is challenging because of the complex 3-dimensional RV anatomy. Three-dimensional echocardiographic imaging offers future promise.⁶ Doppler-derived surrogate measures of RV function include the right-sided index of myocardial performance,⁷ peak systolic velocity and displacement of the tricuspid annulus with tissue Doppler imaging,⁸–¹⁰ measures of change in pressure over time (dP/dt),¹¹ and myocardial acceleration during isovolumic contraction.¹² TR can be qualitatively and semiquantitatively graded with Doppler imaging. As many as 80% to 90% of patients referred for echocardiography have some degree of TR.¹³ A dense “dagger-shaped” early-peeking systolic continuous-wave Doppler signal is appreciated with severe TR as a result of early equilibration of RA and RV pressures. The vena contracta, determined by color-flow Doppler, indirectly reflects the effective regurgitant orifice area (severe TR is present when >0.7 cm).¹⁴,¹⁵ Quantitative assessment also is feasible using the proximal isovelocity surface area method. Other ancillary findings of severe TR include inferior vena
The independent effect of TR also was evaluated in 60 patients undergoing TV repair with and without ring annuloplasty.21 In this study, the in-hospital mortality for patients undergoing TV repair with an annuloplasty ring was associated with improved midterm, and event-free survival than TV replacement (5- and 10-year survival for repair, 90% and 7%, respectively).21,22

In patients with “primary” or organic TV disease, TV repair, if feasible, is associated with better perioperative, midterm, and event-free survival than TV replacement (5- and 10-year survival for repair, 90±3% and 76±5%, respectively, versus 63±6% and 55±6% for replacement).22 For patients with organic TR, this survival benefit occurs despite increased TR severity during follow-up. Recurrent TR is less common in patients with functional TR and is determined in part by whether an annuloplasty ring is used. In a study in which three quarters of patients had functional TR, the freedom from recurrent TR at 15 years was 39±11% for those without compared with 82±5% for those with ring annuloplasty. In patients undergoing TV repair and replacement for organic TV disease, multivariable predictors of poor survival included TV replacement, age, male gender, poor left ventricular function, active endocarditis, preoperative stroke or renal failure, and concomitant mitral valve surgery. During long-term follow-up, moderate to severe RV dysfunction was significantly higher in the TV replacement group (replacement, 28%; repair, 9%).21,22

### Table 1. Causes of TV Regurgitation

<table>
<thead>
<tr>
<th>Structural abnormality of the TV</th>
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<tbody>
<tr>
<td>Congenital</td>
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<tr>
<td>Ebstein anomaly</td>
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<tr>
<td>TV dysplasia</td>
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<tr>
<td>TV hypoplasia</td>
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<tr>
<td>TV cleft</td>
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<tr>
<td>Double-orifice TV</td>
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<tr>
<td>Unguarded TV orifice</td>
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<tr>
<td>Acquired</td>
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<tr>
<td>Endocarditis</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Carcinoid heart disease</td>
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<tr>
<td>Rheumatic heart disease</td>
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<tr>
<td>TV prolapse</td>
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<tr>
<td>Iatrogenic (radiation, drugs, biopsy, device lead)</td>
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<table>
<thead>
<tr>
<th>Functional (morphologically normal leaflets with annular dilatation)</th>
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<tbody>
<tr>
<td>Idiopathic tricuspid annular dilatation</td>
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<tr>
<td>RV dysplasia</td>
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<tr>
<td>Endomyocardial fibrosis</td>
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<tr>
<td>Primary PHT</td>
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<tr>
<td>Secondary PHT</td>
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<td>Atrial septal defect</td>
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Anomalous pulmonary venous drainage

The natural history of severe TR is often one of a prolonged latent period with eventual progressive RV and RA volume overload. Atrial arrhythmias are common secondary to RA enlargement. Symptoms of right-sided heart failure and volume overload can be palliated with diuretics. As the disease progresses, hepatic congestion and resultant anorexia develop.

Severe TR has an important impact on clinical outcome and survival. Patients with severe TR have a significant reduction in exercise capacity caused by impaired cardiac output response.17 TR also has a negative impact on long-term survival. This was seen in patients with mitral stenosis after percutaneous balloon valvuloplasty18 and in a retrospective study of >5000 patients in whom increasing TR severity was associated with worse survival regardless of left ventricular ejection fraction or pulmonary artery pressure. Moreover, severe TR was associated with a poor prognosis that was independent of age, biventricular systolic function, and RV size (Figure 2).19

The independent effect of TR also was evaluated in 60 patients with flail TV leaflets resulting mainly from trauma, as well as myxomatous change and endocarditis. These patients demonstrated an increased risk of atrial fibrillation, symptoms, heart failure, surgery, or death (Figure 3). Symptomatic improvement was noted in 88% of operated patients; conversely, excess mortality was noted in the unoperated group. In addition, right-sided chamber enlargement affected clinical outcome with an increase in morbidity even in asymptomatic patients. The operative risk is low, and symptomatic improvement can be expected.20

The patient’s clinical status and TR origin usually determine the appropriate therapeutic strategy (Tables 2, 3, and 4).14 If a correctable cause such as pacer lead impingement or pulmonary hypertension (PHT) secondary to underlying sleep apnea is identified, it is treated initially if possible. Symptomatic treatment includes diuretics combined with fluid and sodium restriction. Intravenous diuresis may be needed when concomitant bowel edema renders oral diuretics ineffective. Although diuretics improve edema, the associated decrease in cardiac output may worsen fatigue and dyspnea. No data are available on the efficacy of various medical treatment modalities in patients with severe TR.

TV surgery is the only demonstrated effective treatment for symptomatic TR. At our institution, where operative outcomes for TV disease are excellent, TV repair or replacement is recommended for patients with severe TR and (1) symptoms of reduced cardiac output, declining exercise capacity, or medically refractory right-sided heart failure; (2) mitral valve disease or other cardiac disease requiring surgery; (3) progressive RV enlargement or dysfunction; and (4) select asymptomatic patients such as patients with traumatic TV flail with severe TR. Surgery also is recommended in patients with moderate or worse TR undergoing other cardiac surgery.

Surgical options include TV repair or replacement. Repair can be undertaken with a purse-string annuloplasty or ringed annuloplasty. A purse-string annuloplasty is usually used in combination with left-sided valve replacement in patients with functional TR without PHT. Ringed annuloplasty is most commonly performed when TR is the main operative indication and only mild to moderate PHT is present. TV repair with an annuloplasty ring is associated with improved long-term survival, event-free survival, and freedom from recurrent TR compared with simple purse-string annuloplasty alone.21 In this study, the in-hospital mortality for patients undergoing TV repair with and without ring annuloplasty was 4% and 7%, respectively.21

In patients with “primary” or organic TV disease, TV repair, if feasible, is associated with better perioperative, midterm, and event-free survival than TV replacement (5- and 10-year survival for repair, 90±3% and 76±5%, respectively, versus 63±6% and 55±6% for replacement).22 For patients with organic TR, this survival benefit occurs despite increased TR severity during follow-up. Recurrent TR is less common in patients with functional TR and is determined in part by whether an annuloplasty ring is used. In a study in which three quarters of patients had functional TR, the freedom from recurrent TR at 15 years was 39±11% for those without compared with 82±5% for those with ring annuloplasty. In patients undergoing TV repair and replacement for organic TV disease, multivariable predictors of poor survival included TV replacement, age, male gender, poor left ventricular function, active endocarditis, preoperative stroke or renal failure, and concomitant mitral valve surgery. During long-term follow-up, moderate to severe RV dysfunction was significantly higher in the TV replacement group (replacement, 28%; repair, 9%).21,22
TV replacement is indicated for patients with symptomatic TR and PHT or for patients whose valves are not amenable to repair. Right-sided bioprostheses have superior durability compared with left-sided bioprostheses, likely related to lower transvalvular pressure gradients.23 Pericardial bioprostheses are generally avoided in the tricuspid position because of leaflet stiffness and risk of obstruction. Indications for mechanical TV replacement include an established indication for long-term anticoagulation.

No difference has been found in survival among patients with mechanical versus biological TV prostheses.24 In a large pooled study of mechanical and bioprosthetic TVs implanted between 1970 and 2002, no difference was found in late survival, thrombosis, or structural valve deterioration.25 In this study, the hospital mortality for TV replacement was 19%. In the current era, the operative risk for TV replacement or repair is considerably lower; Guenther et al26 noted a significant decline in 30-day mortality after TV surgery from 33.3% (1974 to 1979) to 11.1% (2000 to 2003). The American Heart Association/American College of Cardiology (AHA/ACC) guidelines for the timing of TV repair and replacement have recently been revised.14 These guidelines and those from the European Society of Cardiology (ESC) are summarized in Tables 2, 3, and 4.14,16

Early surgery should be considered for patients with severe TR resulting from blunt chest trauma because the long-term prognosis of flail TV leaflets is poor20 and the likelihood of repair is high. When severe symptomatic TR is secondary to leaflet perforation or lead impingement from a pacemaker lead, removal or repositioning of the lead may decrease the degree of TR. If this is not feasible, TV repair or replacement should be performed.27

Carcinoid heart disease is best treated surgically with valve replacement because it improves patient survival.28 Indications for surgery include progressive symptoms and right-sided heart failure. Asymptomatic patients with severe carcinoid heart disease may require valve replacement, enabling partial hepatic resection or liver transplantation. Carcinoid heart disease patients represent a high-risk surgical subgroup primarily because of perioperative hemodynamic lability (carcinoid crisis) characterized by profound peripheral vasodilatation and hypotension; this must be treated expeditiously with octreotide.

![Figure 1](http://circ.ahajournals.org/). Top, Ebstein anomaly is characterized by apical displacement from the annulus of both the septal (arrow) and posterior leaflets of the TV as seen in this apical 4-chamber view (middle). The corresponding gross anatomy is shown (left). Severe TR was present (right). Bottom, The pathological image demonstrates a septal tricuspid leaflet (arrowhead) exhibiting marked thickening characteristic of carcinoid heart disease (left). Two-dimensional echocardiographic systolic image (RV inflow view) demonstrates thickened septal and anterior TV leaflets (arrowheads) and enlargement of the right ventricle (RV) and right atrium (RA) in a patient with carcinoid heart disease (middle). Color-flow Doppler image demonstrates severe TR (Right). LV indicates left ventricle; LA, left atrium; and ARV, atrialized RV. Courtesy of Dr William D. Edwards, Department of Pathology, Mayo Clinic, Rochester, Minn.
In patients with PHT and severe TR secondary to pulmonary thromboembolic disease, pulmonary thromboendarterectomy alone has been shown to reduce PHT and usually reduces TR severity without the need for concomitant tricuspid annuloplasty even if the TV annulus is dilated. In contrast, TR secondary to severe primary PHT usually is treated with pulmonary vasodilator and diuretic therapy alone because of the risk of cardiac surgical intervention and overall poor prognosis.

The 2006 ACC/AHA valvular heart disease guidelines advocate TV annuloplasty at the time of left-sided valve surgery even when only mild TR is present if associated annular dilatation is present. Tricuspid annular size can be measured by 2- and 3-dimensional echocardiography. In a recent study of patients with TR, maximal systolic dimensions measured from an apical 4-chamber view were 31 ± 1 mm in normal control subjects compared with 41 ± 3 mm in patients with idiopathic severe TR. Interestingly, a number of observational studies have documented improvement in TR severity when percutaneous balloon mitral valvuloplasty is performed in patients with mitral stenosis, severe PHT, and significant functional TR. Nevertheless, Song et al demonstrated that TV repair combined with mitral valve replacement is better than percutaneous balloon mitral valvuloplasty alone in patients with severe functional TR, especially if atrial fibrillation or RV enlargement is present.

Table 2. Management of Patients With Severe TR (AHA/ACC 2006 Guidelines)

<table>
<thead>
<tr>
<th>Class</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>I</td>
<td>TV repair is beneficial for severe TR in patients with MV disease requiring MV surgery (Level of Evidence: B)</td>
</tr>
<tr>
<td>IIa</td>
<td>TV replacement or annuloplasty is reasonable for severe primary TR when symptomatic (Level of Evidence: C)</td>
</tr>
<tr>
<td></td>
<td>TV replacement is reasonable for severe TR secondary to diseased/abnormal TV leaflets not amenable to annuloplasty or repair (Level of Evidence: C)</td>
</tr>
<tr>
<td>IIb</td>
<td>Tricuspid annuloplasty may be considered for less than severe TR in patients undergoing MV surgery when PHT or tricuspid annular dilatation is present (Level of Evidence: C)</td>
</tr>
<tr>
<td>III</td>
<td>TV replacement of annuloplasty is not indicated in asymptomatic patients with TR whose pulmonary artery systolic pressure is &lt; 60 mm Hg in the presence of a normal MV (Level of Evidence: C)</td>
</tr>
<tr>
<td></td>
<td>TV replacement or annuloplasty is not indicated in patients with mild primary TR (Level of Evidence: C)</td>
</tr>
</tbody>
</table>

Classification of recommendations and level of evidence expressed in the ACC/AHA format

- Class I: conditions for which evidence for and/or general agreement exists that the procedure or treatment is beneficial, useful, and effective
- Class II: conditions for which evidence is conflicting and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment exists
  - Class IIa: weight of evidence/opinion is in favor of usefulness/efficacy
  - Class IIb: usefulness/efficacy is less well established by evidence/opinion
- Class III: conditions for which evidence and/or general agreement exists that the procedure/treatment is not useful/effective and in some cases may be harmful

Level of Evidence:
- Level of Evidence A: data derived from a single randomized trial or nonrandomized studies
- Level of Evidence B: data derived from single randomized trials or nonrandomized studies
- Level of Evidence C: only consensus opinion of experts, case studies, or standard of care

MV indicates mitral valve.

TR. Interestingly, a number of observational studies have documented improvement in TR severity when percutaneous balloon mitral valvuloplasty is performed in patients with mitral stenosis, severe PHT, and significant functional TR. Nevertheless, Song et al demonstrated that TV repair combined with mitral valve replacement is better than percutaneous balloon mitral valvuloplasty alone in patients with severe functional TR, especially if atrial fibrillation or RV enlargement is present. In this study, events were defined as death, repeat surgical or percutaneous intervention, and readmission because of heart failure. The estimated actuarial 7-year event-free survival rate was 77 ± 8% in the percutaneous balloon mitral valvuloplasty group and 95 ± 3% in the TV repair group.

The outlook for patients who have previously undergone left-sided valvular surgery who subsequently present with symptomatic severe TR is less optimistic. Repeat surgery to specifically address TR in these patients can be performed with acceptable early mortality (8.8%) and significant symptomatic...
isolated mitral valve disease, it is difficult to separate symptoms

accomplished with lower-than-predicted mortality, holding

surgery have recently been shown to be both feasible and

minimal-access procedures to correct TR after previous cardiac

tricuspid stenosis (TS) is an excep-

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sequence of this procedure.14

Severe PS may cause fatigue and dyspnea. Systemic or

disease may cause PS but essentially always occur in con-

tricuspid balloon valvotomy has been advocated for some

patients with TS. However, severe TR is a common conse-

quence of this procedure.14

Tricuspid Stenosis

In developed countries, tricuspid stenosis (TS) is an excep-

tionally rare clinical condition in that rheumatic heart disease

accounts for ≈90% of cases. Moreover, in patients with

rheumatic mitral valve disease, only 3% to 5% have concur-

rent TS.36 Causes of TS are outlined in Table 5.

Because patients with rheumatic TS invariably have coex-

isting mitral valve disease, it is difficult to separate symptoms

specific to TV obstruction; they include fatigue, dyspnea, and

peripheral edema.36 The venous pressure is elevated with a

prominent a wave and slow y descent. An opening snap,

followed by a diastolic rumbling murmur at the right sternal

border that varies with respiration, is characteristic. As with

TR, physical examination findings may be subtle and the

murmur often inaudible.

Echocardiography is useful for the diagnosis and assessment

of TS. Rheumatic changes include commissural fusion and diastolic doming with thickened and shortened chordae. The mean tricuspid diastolic gradient can be calculated by Doppler echocardiography. TS is considered severe when the valve area is <1.0 cm²; however, estimating TV area with echocardiography is not well established.14,37,38

Medical therapy for symptomatic TS usually is ineffective, and TS is best treated by valve replacement. If atrial fibril-

lation is present, ventricular rate control is important to

promote diastolic filling14,16 (Tables 3 and 4).

Tricuspid balloon valvotomy has been advocated for some

patients with TS. However, severe TR is a common conse-

quence of this procedure.14

Pulmonary Valve Disease

Pulmonary Valve Stenosis

The majority (>95%) of pulmonary stenosis (PS) cases are

related to congenital or genetic disorders. Noonan syndrome,

an autosomal dominant disorder, is commonly associated

with PS. The abnormal pulmonary valve (PV) may be
classified as acommissural, unicommissural, bicuspid, or dys-
plastic (Figure 4). Carcinoid syndrome and rheumatic valve
disease may cause PS but essentially always occur in con-

junction with other valve disease.

Most patients with mild to moderate PS are asymptomatic.

Severe PS may cause fatigue and dyspnea. Systemic or

suprasystemic RV pressures can cause exertional lighthead-

edness or syncope and eventually right-sided heart failure.

Patients with mild PS manifest a pulmonary ejection sound that
decreases in intensity with inspiration and a pulmonary
ejection murmur that increases with inspiration. In severe PS, a
jugular venous a wave and RV lift are common. A pulmonary
ejection systolic murmur is audible and may be palpable at the
upper left sternal border with radiation to the neck. With
increasing PS severity, the ejection click moves closer to the first
heart sound and eventually disappears; the second heart sound
becomes widely split. Ultimately, PV closure is no longer
audible. A right-sided fourth heart sound may be heard.

Table 3. Indications for Intervention in TV Disease
(ESC 2007 Guidelines)

<table>
<thead>
<tr>
<th>Class</th>
<th>Indication</th>
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<tbody>
<tr>
<td>Class I</td>
<td>Severe TR in a patient undergoing left-side valve surgery (Level of Evidence: C)</td>
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<tr>
<td></td>
<td>Severe primary TR and symptoms despite medical therapy without severe RV dysfunction (Level of Evidence: C)</td>
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<tr>
<td></td>
<td>Severe TS (with or without TR) with symptoms despite medical therapy* (Level of Evidence: C)</td>
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<tr>
<td></td>
<td>Severe TS (with or without TR) in a patient undergoing left-side valve intervention* (Level of Evidence: C)</td>
</tr>
<tr>
<td>Class II</td>
<td>Moderate organic TR in a patient undergoing left-sided valve surgery (Level of Evidence: C)</td>
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<tr>
<td></td>
<td>Moderate secondary TR with dilated annulus (&gt;40 mm) in a patient undergoing left-side valve surgery (Level of Evidence: C)</td>
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<tr>
<td></td>
<td>Severe TR and symptoms; after left-side valve surgery; in the absence of left-sided myocardial, valve, or RV dysfunction; and without severe PHT (systolic pulmonary artery pressure ≤60 mm Hg) (Level of Evidence: C)</td>
</tr>
<tr>
<td>Class IIa</td>
<td>Severe isolated TR with mild or no symptoms and progressive dilation or deterioration of TV function (Level of Evidence: C)</td>
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* Percutaneous technique can be attempted as a first approach if TS is isolated.

Table 4. Recommendation Classes and Levels of Evidence

<table>
<thead>
<tr>
<th>Class</th>
<th>Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, and effective</th>
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<tbody>
<tr>
<td>Class II</td>
<td>Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a given treatment or procedure</td>
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<tr>
<td>Class IIa</td>
<td>Weight of evidence/opinion is in favor of usefulness/efficacy</td>
</tr>
<tr>
<td>Class IIb</td>
<td>Usefulness/efficacy is less well established by evidence/opinion</td>
</tr>
<tr>
<td>Level of evidence A</td>
<td>Data derived from multiple randomized clinical trials or meta-analyses</td>
</tr>
<tr>
<td>Level of evidence B</td>
<td>Data derived from a single randomized clinical trial or large nonrandomized studies</td>
</tr>
<tr>
<td>Level of evidence C</td>
<td>Consensus of opinion of the experts and/or small studies, retrospective studies, registries</td>
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</table>

Table 5. Causes of TS

<table>
<thead>
<tr>
<th>Cause</th>
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<tbody>
<tr>
<td>Rheumatic heart disease</td>
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<tr>
<td>Congenital TS</td>
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<tr>
<td>RA tumors</td>
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<tr>
<td>Carcinoid heart disease</td>
</tr>
<tr>
<td>Endomyocardial fibrosis</td>
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<tr>
<td>Valvular vegetations</td>
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<td>Extracardiac tumors</td>
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ECG in severe PS is characterized by RA enlargement, right-axis deviation, RV hypertrophy, and RV strain pattern. Right-sided heart enlargement, dilatation of the pulmonary artery, and diminished vascular lung markings may be noted on the chest radiograph.

Transthoracic echocardiography is recommended for the diagnosis and follow-up of PS. Two-dimensional echocardiography demonstrates thickened PV cusps with systolic doming and the presence of subvalvular or supravalvular obstruction. The severity of PS is determined by continuous-wave Doppler peak transpulmonic velocity and gradient. Severe PS is defined as a peak gradient $\geq 50$ mm Hg, moderate PS as a peak gradient of 36 to 60 mm Hg, and mild PS as a peak gradient $<36$ mm Hg. Cardiac catheterization should be considered when discordant data are present or to facilitate intervention.

The long-term follow-up of 592 patients with PS in the Second Natural History Study reported an overall survival at 25 years of 96% (Figure 5). Event-free survival was closely related to pressure gradient. On the basis of these surgical data, relief of PS is recommended for all patients with a peak gradient $\geq 50$ mm Hg; percutaneous pulmonary balloon valvuloplasty (PBV) is the treatment of choice for most patients.

In patients with mild PS, symptoms are uncommon, progression is minimal, and outcome is excellent. Periodic follow-up is recommended. Approximately 25% of patients with moderate PS eventually require intervention. Predictors of the need for intervention include higher peak systolic gradient and reduced cardiac output.

Intervention in the Second Natural History Study involved surgical valvotomy. Reoperation was reported in only 4% of patients during a 10-year follow-up. In a subsequent longitudinal study of 90 consecutive patients with PS treated with operation, reoperation was required in 15%, primarily for PR (9%). At last follow-up, moderate to severe PR was present in 37%, emphasizing the importance of follow-up after PS intervention.

Asymptomatic athletes with a peak PS gradient $<40$ mm Hg and normal RV function can participate in all competitive sports with annual reevaluation. Athletes with a peak PS gradient

**Figure 4.** The abnormal PV may be classified as acommissural (A) with prominent systolic doming of the valve cusps and an eccentric orifice, unicommissural (B), bicuspid with fused commissures (C), or dysplastic (D) with severely thickened and deformed valve cusps. Courtesy of Dr William D. Edwards, Department of Pathology Mayo Clinic, Rochester, Minn.

**Figure 5.** Survival curve from Second Natural History Study. Kaplan–Meier curves of percentage free from surgery for 300 PS patients managed medically, grouped by gradient at admission to the First Natural History Study (NHS-1). Numbers in parentheses indicate number of patients remaining under observation 25 years after admission. Reprinted from Hayes et al with permission of the publisher. Copyright © 1993, the American Heart Association.
>40 mm Hg can participate in low-intensity competitive sports or can be referred for intervention. Two to 4 weeks after PBV, asymptomatic athletes with mild residual PS and normal ventricular function can participate in all competitive sports. After operation, an interval of 3 months is suggested before sports participation is resumed.41

Pregnancy is generally well tolerated in PS patients. Severe PS may be associated with an increased risk during labor and delivery and postpartum. PBV can be performed with low risk during pregnancy for symptomatic severe PS. These patients are at increased risk of having an infant with congenital heart disease, particularly those with Noonan’s syndrome.42

PBV is the procedure of choice for children and adults with severe or symptomatic PS and carries a low risk of morbidity, mortality, and restenosis.43–48 However, a high frequency of PR has been reported; after PBV, 57% of children had moderate or severe PR at the last follow-up.49 These data demonstrate unpredictable durability and may degenerate prematurely, particularly those with Noonan’s syndrome.42

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PS often is associated with some degree of subvalvular muscular obstruction resulting from hypertrophy of the RV myocardium. After relief of PS, infundibular obstruction may worsen transiently but then tends to regress over months with eventual resolution.50,51 Acute severe obstruction can cause “suicide” RV, which results in suprasystemic RV pressure with resultant cyanosis and hemodynamic instability. β-Blocker therapy is recommended before PBV to prevent or reduce the severity of this complication; therapy generally is discontinued after 3 to 6 months.

In patients who have a poor result with PBV, unfavorable valve morphology, hypoplastic pulmonary annulus, fixed subvalvar or supravalvar PS, or severe PR, surgical valvotomy or valve replacement may be preferred.

The choice of PV prosthesis type must be individualized. Bioprostheses are preferred for PV replacement. Homografts demonstrate unpredictable durability and may degenerate prematurely, with obstruction, regurgitation, or both, especially in the setting of PHT.52 Mechanical valves are thrombogenic and generally not used in the low-pressure right side of the heart unless the patient requires lifelong warfarin for another reason.53

Percutaneous PV implantation has been reported in 155 patients with stenosis and/or regurgitation and facilitates significant reduction in RV systolic pressure and RV outflow tract gradient; freedom from reoperation was 70% at 70 months. This procedure might reduce the number of operations needed over the total lifetime of patients with RV-to-pulmonary artery conduits.54

**PV Regurgitation**

In adults, pathological PR most often is the consequence of prior interventions for congenital heart disease such as tetralogy of Fallot repair with placement of an outflow tract patch55 or surgical valvotomy for isolated congenital PS.40 Additional causes of PR include rheumatic or carcinoid heart disease, trauma, endocarditis, and pulmonary artery and annular dilation; PR also can occur secondary to PHT.

Patients with long-standing severe PR develop progressive RV dilation and reduced RV function. This can lead to the inability to augment cardiac output with exercise and to congestive heart failure. In addition, the dilated and dysfunctional RV is associated with QRS prolongation, ventricular arrhythmias, and sudden death. This mechanical-electric association has been well documented in patients with transannular patch repair of tetralogy of Fallot.56

PR patients may demonstrate a parasternal lift when the RV is enlarged. The murmur of PR is typically a soft, diastolic, decrescendo murmur best heard in the left upper sternal region in patients with normal pulmonary pressures. It begins after the pulmonic closure sound and may be accompanied by a pulmonic systolic ejection murmur. An increase in intensity of the murmur may be noted during inspiration. The murmur is easily audible and occasionally palpable in patients with PHT.

Nonspecific ECG findings are noted in patients with PR. The total QRS duration and the rate of QRS increase reflect the impact of PR on the RV in patients with tetralogy of Fallot. Chest radiography may demonstrate cardiomegaly, involving the right-sided chambers and pulmonary artery enlargement.

The diagnosis of PR is usually made by echocardiography and graded on a 1 to 4 scale with color Doppler imaging. A trivial or mild degree of PR is detectable in most normal individuals.13 Pathological PR is typically a wide holodiastolic jet. The density of the continuous-wave Doppler signal and deceleration pressure half-time correspond to the degree of regurgitation and the RV pressures. When PR is unrestricted and the pulmonary pressures are low, the Doppler color-flow map may be laminar, leading to underappreciation of the PR severity.15,57

Cardiac magnetic resonance imaging is commonly used to assess right-sided heart size and function in asymptomatic patients with severe PR to determine the optimum time of valve replacement. Cardiac catheterization is rarely performed to assess PR.

Most patients with mild degrees of PR have a benign clinical course. Chronic severe PR often is well tolerated for many years. However, the RV may dilate and develop systolic dysfunction, analogous to the effect of chronic aortic regurgitation on the left ventricle. Severe RV dilation is associated with an increased risk of sudden death related primarily to arrhythmias.56

No medical therapy has been demonstrated to be effective in reducing the degree of PR or affecting the impact of PR on the RV. The most common indications for intervention for PR occur in patients with previous surgery for tetralogy of Fallot or PS. As the intervention options improve and the morbidity related to long-standing PR is increasingly recognized, indications for intervention are being refined. In our practice we recommend PV replacement for severe PR for (1) symptoms related to PR, including arrhythmias; (2) decreased RV
systolic function (ejection fraction <40% by cardiac magnetic resonance imaging); (3) progressive RV dilation (cardiac magnetic resonance imaging RV end-diastolic volume ≥160 mL/m² or 82 mL/m² for RV end-systolic volume)58,59; (4) decline in functional aerobic capacity; (5) moderate or worse TR related to progressive annular dilatation; (6) severe PR in a patient requiring another cardiac operation; and (7) concern about risk of arrhythmia in patients with prolonged or increasing QRS duration (total QRS duration ≥180 milliseconds or QRS duration increase >3.5 ms/s).56

RV size tends to normalize and functional status improves after PV replacement for PR late after tetralogy of Fallot surgery.55 However, RV function may not fully recover once marked enlargement and systolic dysfunction are evident.58,60

The type of PV prosthesis should be individualized (see the section on PS).

Conclusions

As a result of heightened clinical suspicion and advances in imaging technologies and research, there has been substantial progress in the recognition and management of right-sided valve disease. It is imperative that we apply these technologies and research strategies to provide improved clinical outcomes for patients with previously incompletely appreciated valve disease. Superior patient outcomes will be achieved as we continue to advance our understanding of the complex and interdependent interaction between abnormal right-sided valves and global cardiac function.

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Disclosures

None.

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