JAMA Insights

Management of Tricuspid Regurgitation

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Valvular heart disease from tricuspid regurgitation (TR) has 5 grades of severity (mild, moderate, severe, massive, and torrential) based on regurgitant volume and estimated regurgitant orifice area determined by echocardiography. Mild TR, defined as a regurgitant frac-



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tion (ie, blood leaking back into the right ventricle through the tricuspid valve) of 15% or less, is

present in approximately 80% of healthy, asymptomatic adults. Moderate TR (regurgitant fraction of 16%-48%) or severe TR (regurgitant fraction of >49%) affect 5.6% of women and 1.5% of men older than 70 years, similar to the prevalence of aortic stenosis.¹

TR is classified as primary, secondary, or cardiovascular implantable electronic device (CIED) related. Primary TR involves disease of the tricuspid leaflets, including fibroelastic degeneration, endocarditis, or rheumatic disease. Secondary TR is the most common cause of TR worldwide, with left-sided valvular heart disease (49.5%), pulmonary hypertension (23%), and atrial fibrillation (AF) being the most frequent etiologies. AF is associated with right atrial remodeling, which causes dilatation of the atrium and tricuspid annulus, resulting in TR in up to one-third of patients with chronic AF. Moderate or severe TR is present in 10% to 45% of patients with a CIED, with 10% to 15% of all cases directly related to device leads. ³

Clinical Presentation

Patients with symptomatic severe TR typically initially present with nonspecific symptoms, such as fatigue, abdominal fullness, and peripheral edema, before developing overt signs of right-sided heart failure (HF), such as hepatomegaly, ascites, and anasarca.

Diagnosis of TR

Transthoracic echocardiography is the initial recommended diagnostic modality to diagnose TR and evaluate its severity. Transthoracic echocardiography can also identify concomitant left-sided valve disease (eg, aortic stenosis, aortic regurgitation, mitral stenosis, mitral regurgitation), evaluate left and right ventricular function, and estimate pulmonary artery pressure. Transesophageal echocardiography should be performed for patients with severe TR being considered for therapeutic interventions to visualize tricuspid leaflet anatomy and determine suitability for transcatheter treatment options. ² Cardiac catheterization for hemodynamic evaluation of significant TR should be performed for most patients prior to therapeutic intervention, and computed tomography or cardiac magnetic resonance imaging may be obtained (Figure).

Medications for TR

First-line medical therapy for patients with TR and right-sided HF is loop diuretics and/or mineralocorticoid antagonists to treat dyspnea and edema. As TR severity increases, gastrointestinal edema due to right-sided HF may cause poor absorption of oral diuretics, so intravenous diuretics may be added to oral therapy. Patients with TR and left ventricular dysfunction should receive guideline-directed

Figure. Management Algorithm for Suspected Tricuspid Regurgitation

Patient presents with suspected symptomatic and severe tricuspid regurgitation (TR)

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Perform diagnostic modalities for TR diagnosis

Transthoracic echocardiography

Initial diagnostic tool that evaluates TR severity, identifies left-sided valve disease, evaluates left and right ventricular function, and estimates pulmonary artery pressure

Transesophageal echocardiography

Visualizes tricuspid leaflet anatomy for transcatheter treatment options in patients with severe TR eligible for intervention

Hemodynamic evaluation (right-heart catheterization)

Evaluates right-sided filling pressures and pulmonary hypertension

Computed tomography (CT) or cardiac magnetic resonance imaging (MRI)
Additional visualization as required

● Optimize medical therapy

- Loop diuretics and/or mineralocorticoid antagonists (oral or intravenous)
- Treat TR, right-sided heart failure, and resulting dyspnea and edema
- Guideline-directed therapies (β-blockers, angiotensin and neprilysin antagonists)
 Treat TR and left ventricular dysfunction
- Pulmonary vasodilators

Treat TR and group 1 pulmonary hypertension to improve right ventricular function



Evaluate for valvular intervention

- Clinical evaluation for right-sided heart failure
- ► Surgical risk assessment using TRI-SCORE
- Evaluation by heart team, including electrophysiologists (for patients with cardiac implantable electronic device)



Consider surgery or transcatheter intervention

- Transcatheter tricuspid edge-to-edge repair (T-TEER)
- Repairs valve coaptation by placing a clip on the tricuspid valve leaflets
- Transcatheter tricuspid valve replacement (TTVR)
- Replaces native valve with bioprosthetic valve
- Surgical annuloplasty

Remodels tricuspid annulus and restores leaflet coaptation

Medical therapies may be used after or in conjunction with surgery

medical therapy with β -blockers, angiotensin and neprilysin antagonists, mineralocorticoid antagonists, and sodium-glucose cotransporter-2 inhibitors. Pulmonary vasodilators, such as treprostinil and sildenafil, should be considered for patients with TR and group 1 pulmonary hypertension (caused by increased resistance to blood flow within the pulmonary arteries) to reduce pulmonary pressures, improve right ventricular function, and decrease TR, although these medications do not affect mortality rates. 4

Surgical Risk Stratification of Patients With Severe TR

Risk stratification tools, such as TRI-SCORE, can be used for patients to predict the likelihood of in-hospital death after isolated tricuspid valve surgery, with patients categorized into low, intermediate, or high risk groups. ⁵ TRI-SCORE incorporates clinical data

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(age ≥70 years, sex, New York Heart Association [NYHA] functional class III or IV, prior left-sided heart valve intervention, permanent pacemaker/defibrillator, AF/flutter, right-sided HF signs, daily dose of furosemide ≥125 mg), biological (kidney and liver dysfunction), mechanism of TR (primary, secondary, or mixed), and echocardiographic parameters (left and right ventricular dysfunction).

Surgical Procedures for TR

Surgical tricuspid valve repair or replacement is associated with high operative risk, particularly in patients with advanced right ventricular dysfunction, end-organ impairment (eg, chronic kidney disease and liver dysfunction), or when performed as an isolated procedure (without another valve repair or replacement). In-hospital mortality rates are 8% to 10%, with higher rates observed with reoperations. ⁶ Surgical repair, typically annuloplasty to remodel the tricuspid annulus and restore leaflet coaptation, is preferred over replacement due to lower perioperative mortality, better preservation of right ventricular function, and fewer prosthesis-related complications. Comparative data suggest that surgical intervention does not provide a mortality benefit over medical therapy for patients undergoing isolated tricuspid valve procedures. However, these data may be affected by late referral of patients with advanced-stage TR.⁷ Given these outcomes, there is increasing interest in less invasive transcatheter tricuspid therapies.

Transcatheter Tricuspid Edge-to-Edge Repair

Transcatheter tricuspid edge-to-edge repair (T-TEER) with the TriClip device is a US Food and Drug Administration (FDA)-approved minimally invasive procedure in which a clip is placed on the tricuspid valve leaflets to reduce tricuspid regurgitation. A randomized clinical trial of 350 patients with symptomatic severe TR reported superiority of T-TEER compared with medical therapy for the primary composite end point of mortality, HF hospitalizations, and improvement in quality of life based on the Kansas City Cardiomyopathy Questionnaire. TR reduction to less than moderate was demonstrated in 87% of patients in the T-TEER group compared with 4.8% in the medical group at 1 year, with a quality of life improvement of

15 points (minimum clinically important difference, 5 points); 98.3% of patients who underwent T-TEER were free from major adverse events at 30 days. 8 Two-year follow-up demonstrated fewer HF hospitalizations among those treated with the T-TEER device vs medical treatment (0.19 events per patient-year vs 0.26 events per patient-year [P = .02]; joint frailty model hazard ratio, 0.72; 1-sided upper CI, 0.93; [P = .02]). Another study of 300 patients with severe symptomatic TR reported higher rates of improvement in the composite primary outcome (change in NYHA class, patient global assessment, and major cardiovascular events at 1 year) in patients randomized to undergo T-TEER and optimal medical therapy (OMT) (74.1%) vs OMT alone (40.6%), primarily due to improvement in NYHA class and patient global assessment. At 30-day follow-up, fewer patients in the T-TEER and OMT group had massive or torrential TR compared with the OMT alone group (6.8% vs 53.5%; P < .001) and the rate of major adverse events was 0.67% in the T-TEER group at 30 days.¹⁰

Transcatheter Tricuspid Valve Replacement

Transcatheter tricuspid valve replacement (TTVR) is an FDA-approved minimally invasive procedure involving transcatheter placement of a bioprosthetic valve in the native tricuspid position, using echocardiographic and fluoroscopic guidance. In a randomized clinical trial of patients with severe symptomatic TR (267 randomized to undergo TTVR and 133 to receive medical therapy), at 1-year follow-up, the win ratio for a hierarchical composite outcome was 2.02, favoring TTVR (95% CI, 1.56-2.62; P < .001). After TTVR, 99.1% of patients had moderate or less TR and 95.3% had mild or less TR. However, with TTVR vs control, severe bleeding (15.4% vs 5.3%; P = .003) and new permanent pacemaker implantation (17.4% vs 2.3%; P < .001) occurred more frequently in the TTVR group.

Conclusions

Patients with severe symptomatic TR despite medical treatment should be considered for transcatheter repair and replacement or surgical tricuspid valve replacement to improve quality of life, reduce HF hospitalizations, and decrease mortality.

ARTICLE INFORMATION

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