Tricuspid Valve Intervention
New Direction and New Hope*

Brian P. O’Neill, MD,a William W. O’Neill, MDb

Increasingly, attention has turned toward therapies that correct severe tricuspid regurgitation (TR), stimulated in part by the success of transcatheter therapies for aortic stenosis and mitral regurgitation. In addition, recent evidence suggesting worse survival for patients with untreated isolated severe TR (1) has provided a clinical imperative to develop new therapies. Although surgery remains an effective treatment for the disease (2), <1% of eligible patients are treated annually in the United States (3). This is due in part to the comorbidities of these patients, compounded by the fact that up to 50% of patients with previous mitral valve surgery may go on to develop significant TR (4). For these reasons, the development of percutaneous therapies to address severe TR has experienced tremendous growth.

The etiology of TR involves pathology of the valve or annular dilation. Leaflet pathology due to infective endocarditis, trauma from right ventricular (RV) biopsy, diet drugs, or damage to the septal leaflet from pacemaker and implantable cardioverter-defibrillator leads will require valve replacement. Failure of leaflet coaptation from annular dilation may be more amenable to annular plication and/or leaflet tethering technologies.

Because of the varying etiology of tricuspid failure, devices undergoing evaluation have sought to address the problem in different ways. Ongoing trials of new devices being tested in patients with severe TR are summarized in Table 1. The Mitralign device (Mitralign, Inc., Tewksbury, Massachusetts), uses pledgeted sutures placed on either side of the posterior tricuspid valve leaflet to create a bicuspidization of the valve (5). Improved coaptation through annular reduction, such as with the TriCinch device (4Tech Cardio, Galway, Ireland), has been shown to be effective in a patient with prohibitive surgical risk (6). Annular reduction through external compression also has demonstrated efficacy in reducing TR in an animal model (7). The FORMA device (Edwards Lifesciences, Irvine, California) acts to improve native leaflet coaptation through the placement of a spacer across the annulus (8). In addition to therapies that act directly on the tricuspid valve, caval valve implant offers another option for patients who are at high surgical risk (9). Although edge-to-edge repair using the MitraClip device (Abbott Vascular, Santa Clara, California) in the tricuspid position has shown varying levels of effectiveness in several patients with refractory right heart failure (10,11), the number of clips needed or which leaflets to clip is unknown.

In this issue of the Journal, Vismara et al. (12) help us to better understand this question. Using a porcine model of functional TR, the authors performed edge-to-edge repair of the various combinations of tricuspid valve leaflets as well as the varying positions within the leaflets. Although degrees of TR improvement were not reported, hemodynamics were provided in a physiological state, a pathological state with severe TR, and then after intervention. Improvement in cardiac output was seen when a single clip was placed involving the medial portion of the leaflets. Cardiac output was not significantly changed when a clip was placed in a commissural position in any of the 3 leaflets. There was no significant gradient observed across the tricuspid valve.
with either the medial or commissural treatments. When a 2-clip strategy was used, the largest increases in cardiac output were observed with a septal-anterior commissural and a septal-posterior medial position. Of note, clips placed in the anterior-posterior commissural and septal-posterior commissural induced a decrease in cardiac output, although it was not statistically significant.

The authors should be commended on the rigorous nature of this study and for the important information it has provided. Although the concepts are quite clear, attempts to mimic these observations in humans will be quite challenging. The currently available mitral device was not optimally designed for tricuspid valve access, and the clips are too short for the large leafllet gaps that occur in end-stage TR patients. Additionally, the authors had direct visualization of the valve leaflets to precisely position the clips. It is unlikely that current transesophageal imaging will ever be sufficiently precise to allow positioning in medial versus commissural positions.

Moving forward in humans, several other challenges remain for this technique. In patients with long-standing untreated TR, the degree of annular dilation—many times in excess of 40 mm—may be too large to allow the leaflets to be clipped in the medial position. The authors demonstrated the best improvement in hemodynamics with the clipping of the septal leaflet. This also may present challenges in patients with pacemakers, as previous studies have demonstrated the leads might impinge on the septal leaflet in 23% of cases (13). Finally, a redesign of the delivery system might be required to allow for reliable delivery of the clips from either the internal jugular or the femoral vein.

Despite these obstacles, Abbott is exploring a redesign of their mitral device to more reliably deploy clips on tricuspid leaflets. Vismara et al. (12) provided a great service to the field in allowing a conceptual framework to the systematic repair of the tricuspid leaflets. Advances in imaging and catheter design are likely to make tricuspid clip procedures more reproducible and more successful.

Future trials in man are needed to confirm the authors’ hemodynamic findings with the various clip positions and to assess for the degree of reduction of TR itself. Given the variable size of the tricuspid annulus, it is unlikely that any of the current transcatheter techniques alone will be sufficient to treat all patients. Rather, a combination technique, such as annular reduction with edge-to-edge repair, may prove superior. The effect of pacemaker/implantable cardioverter-defibrillator leads on TR will require further study. Advanced imaging will continue to

### Table 1: Ongoing TR Device Trials

<table>
<thead>
<tr>
<th>Trial Acronym</th>
<th>Trial Name and Device</th>
<th>Inclusion</th>
<th>Exclusion</th>
<th>Principal Investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREVENT</td>
<td>Percutaneous Treatment of TR with the TriCinch System</td>
<td>Functional symptomatic TR ≥ 3+ on a scale of 4+ with annular dilation ≥40 mm</td>
<td>At the heart team's judgment, patient IVC dimension not adequate for device implantation</td>
<td>Antonio Colombo, MD</td>
</tr>
<tr>
<td>HOVER</td>
<td>Heterotopic Implantation of the Edwards-Sapien XT Transcatheter Valve in the Inferior Vena Cava for the Treatment of Severe TR Regurgitation</td>
<td>TR should be functional in nature, without anatomical abnormalities of the tricuspid valve leaflets themselves</td>
<td>Mean pulmonary artery pressures ≤40 mm Hg and PVR &gt;4 Wood units as assessed by right heart catheterization</td>
<td>Brian P. O’Neill, MD</td>
</tr>
<tr>
<td>TRICAVAL</td>
<td>Treatment of Severe Secondary TR in Patients With Advance Heart Failure With Cavtal Vein Implantation of the Edwards Sapien XT Valve</td>
<td>Severe symptomatic TR with a significant regurgitation jet into the caval and hepatic veins</td>
<td>IVC diameter &gt;32 mm, severe left ventricular dysfunction with LVEF &lt;30%</td>
<td>Karl Stangl, MD</td>
</tr>
<tr>
<td>SPACER</td>
<td>Repair of TR Using the Edwards Tricuspid Transcatheter Repair System</td>
<td>Clinically significant, symptomatic (NYHA functional class II or greater); TR (per applicable guidelines) requiring tricuspid valve repair or replacement as assessed by the heart team; functional TR as the primary etiology</td>
<td>Tricuspid valve/right heart anatomy not suitable for the study device</td>
<td>Not announced</td>
</tr>
<tr>
<td>SCOUT</td>
<td>Early Feasibility of the Mitralign Percutaneous TriCusp Valve Annuloplasty System (PTVAS)</td>
<td>Chronic functional TR with a minimum of moderate TR</td>
<td>Tricuspid valve annular diameter ≥40 mm (or 21 mm/m²) and ≤55 mm (or 29 mm/m²)</td>
<td>Rebecca Hahn, MD</td>
</tr>
</tbody>
</table>

IVC = inferior vena cava; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PVR = pulmonary vascular resistance; TR = tricuspid regurgitation.
play an important role, as will accurate determination of RV size and function. Standardized performance measures of success will need to be created to better assess the effect of this therapy on patients. A critical question to address early will be when to intervene with TR during the natural history of this disease.

Transcatheter tricuspid therapy will be very difficult when investigators wait until patients are high-risk or inoperable. Massive RV dilation, annular dilation, ascites, and severe coagulopathy will exist if we wait too long to intervene; consequently, whatever approach we take will be unlikely to provide much clinical benefit. Massive RV dilation will also make leaflet repair nearly impossible. The natural history of TR related to annular dilation starts with right atrial and left atrial dilation. Later, as TR progresses, severe atrial dilation followed by annular dilation and finally RV dilation occurs. Rather than waiting for end-stage disease, randomized trials of prophylactic therapy in patients with atrial dilation and moderate TR may make technical success more likely and may produce important clinical benefit. Given the great morbidity and mortality of this condition, the field waits with great hope and excitement for advances in devices that are specifically tailored to this pathology.

REFERENCES


KEY WORDS—coaptation, leaflet, regurgitation, transcatheter.