Risk stratification for surgery in tricuspid regurgitation

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ABSTRACT

Tricuspid valve (TV) surgery carries high mortality and morbidity, and risk-adjusted mortality has not changed. Patients who can withstand the perioperative period benefit from symptomatic improvement as the right ventricle remodels. Risk stratification for patients undergoing surgical intervention is critically important. The Model for End-Stage Liver Disease (MELD) score is a reliable and accurate mortality risk predictor given the liver and kidney dysfunction that accompany tricuspid regurgitation. Novel clinical risk calculators for isolated TV surgery have also been developed to further guide patients with projected surgical outcomes and reinforce timeliness to intervention.

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Tricuspid regurgitation: background, mechanisms, and impact

Tricuspid valve (TV) regurgitation (TR) has historically been less commonly addressed than left sided valve disease given limited indications for intervention and poor clinical outcomes. Although mortality is high with surgical correction of the TV, patients who withstand the early perioperative risk have dramatically improved symptoms and outcomes as their right ventricle (RV) positively remodels. Thus, selection of patients with TR who have lower surgical risk is of great interest. Herein, we will briefly 1) discuss the anatomy and mechanisms of TR, 2) review guidelines and outcomes for surgical intervention, and 3) present current available risk stratification tools to help identify patients who should undergo surgical correction.
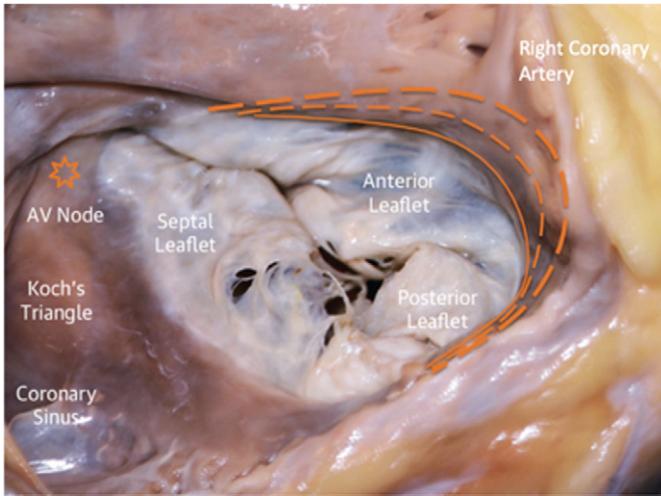
From a surgical standpoint, the tricuspid valve is the easiest valve for the surgeon to access and operate upon due to its anatomic location in the right atrium. Access can reliably be obtained via midline sternotomy or right thoracotomy with excellent valve visibility. The trileaflet TV is surrounded by important structures susceptible to injury during surgical or transcatheter repair including: Atrioventricular node and Bundle of His, coronary sinus, right coronary artery and aortic valve (Fig. 1).[1]

Similar to mitral valve (MV) regurgitation (MR), TR is stratified by primary and secondary causes (Table 1).[1–3] Primary TR, where pathophysiology directly relates to TV leaflets, chords, and/or papillary muscles has numerous etiologies including: rheumatic disease,

Fig. 1. Surgical anatomy of the tricuspid valve. Atrial side, showing the asymmetrical dilation of the tricuspid annulus in its anteroposterior segments. The orange star marks the atrioventricular (AV) node. Reprinted with permission from Taramasso et al.[1]

Table 1
Etiology of tricuspid regurgitation.

Primary tricuspid regurgitation
  Congenital
  - Ebstein's anomaly
  - Tricuspid valve dysplasia, hypoplasia or cleft
  - Double-orifice tricuspid valve
  - Aberrant chordae tendinae with tricuspid leaflet tethering
  - Tricuspid annular remodeling secondary to congenital RA enlargement
  Acquired
  - Rheumatic disease (with left-side disease)
  - Endocarditis
  - Cardiac device (permanent pacemakers/implatable cardioverter-defibrillator leads)
  - Radiation
  - Carcinoid, serotonin-active drugs
  - Trauma (blunt chest wall, RV endomyocardial biopsy)
  - Degenerative bioprosthesis
  - Tricuspid leaflet prolapse, flail

Secondary (functional) tricuspid regurgitation
  Left heart disease
  - Left-side valvulopathy
  - Left-side myocardial disease
    - Systolic dysfunction
    - Diastolic dysfunction
  Right ventricular remodeling
  - RV Infarct
  - Primary RV disease
  - Pulmonary Hypertension
  - Chronic right ventricular pacing (dyssynchrony)
Isolated tricuspid regurgitation
  Atrial fibrillation
  Aging

myxomatous valve degeneration, Ebstein's anomaly, infective endocarditis, infiltrative valvulopathy, or iatrogenic due to pacemaker/implantable defibrillator leads. Despite several primary causes, secondary or functional TR (FTR), compromises 80% or more of TR seen in clinical practice.[3]

FTR results when the RV or tricuspid annulus dilates resulting in tethering of the leaflets and poor coaptation.[4] Compared to the MV the TV is at greater risk for functional regurgitation. Specifically, a 40% change in the tricuspid annular dimension is enough to precipitate severe FTR whereas a 75% enlargement of the mitral annulus is required to cause functional MR.[5] FTR most often occurs due to left-sided heart disease with associated increased left atrial pressure, pulmonary hypertension and increased RV afterload.[2] TA dilation and papillary muscle displacement are both associated with FTR independently, but produce worse FTR in combination. The normal RV was designed to be highly compliant and can increase in size without affecting performance as a response to acute volume overload. One final cause of isolated TR occurs in the setting of right atrial enlargement from long-standing atrial fibrillation resulting in annular dilation and malcoaptation of the TV leaflets.[2] The asymmetrical distortion of the tricuspid annulus that can occur with pathologic RV enlargement is also depicted (Fig. 1).[1]

TV surgery: indications and outcomes

The 2014 American Heart Association/American College of Cardiology guidelines for TV repair is recommended for severe TR (stage C or D) when undergoing left-sided valve surgery (Class I recommendations, Level of Evidence: C).[6] Although still debated, TV repair is less strongly recommended at the time of left-sided valve surgery when mild or worse functional TR is associated with annular dilation >40 mm or right heart failure (HF;Class IIa recommendation, Level of Evidence: B). Concomitant TV repair with less than moderate TR at the time of degenerative mitral surgery remains hotly contested and is the focus of a Cardiothoracic Surgical Trials Network Trial.[7]

Results from the STS Database of >50,000 patients undergoing TV surgery (TVS) indicated cohort operative mortality of 9.6%.[8] Although raw mortality has improved over a 10-year span (2000−2010) decreasing from 10.6% to 8.2% ($p < 0.001$), risk-adjusted yearly operative mortality has not changed. Since the majority of TR is secondary to left-sided disease, over 80% of TV operations are performed at the time of left-sided surgery.[8,9] MV surgery (47.6%; $n = 22,192$), MV surgery plus coronary artery bypass grafting (19.6%; $n = 9133$), and triple-valve surgery involving aortic, MV and TV (12.2%; $n = 5676$) are the most common concomitant procedures, respectively. For patients undergoing MV surgery, concomitant tricuspid annuloplasty is shown to be safe and effective for those with significant annular dilation (>40 mm) or moderate TR on pre-bypass TEE in reducing late moderate TR and RV functional recovery.[10]

Surgical intervention of the TV is most often valve repair as demonstrated by both Society of Thoracic Surgeons (STS;88.9% [$n = 48,322$]) and Nationwide In-patient Sample Database (72.9% [20,951/28,726]) studies.[8,9] The STS data demonstrate that 75.5% of repairs were annuloplasty alone. In a meta-analysis comparing surgical tricuspid annuloplasty techniques, ring annuloplasty was protective for early mortality and freedom from recurrent moderate or worse TR over suture annuloplasty alone.[11] Adjunctive techniques beyond simple tricuspid annuloplasty are occasionally employed including leaflet augmentation with a pericardial patch for insufficient leaflet tissue, chordal replacement for leaflet prolapse, and edge-to-edge repair for insufficient coaptation (Fig. 2). In advanced cases, TV replacement is needed.[3]

Isolated TVS continues to carry high in-hospital mortality at 8.8% with significant variation depending on type of intervention: TV repair (5.9%), bioprosthetic replacement (9.1%), and mechanical replacement (13.6%).[12] This study demonstrated TV replacement was associated with greater mortality versus repair (Odds ratio/OR 1.91 [95% CI 1.18 to 3.08]; $p < 0.009$).

Reoperative TVS carries significant morbidity and mortality, with in-hospital mortality of 13.2%.[13] TV repair via minimally invasive right anterior thoracotomy is a viable option and a recent study demonstrated approach through right anterolateral thoracotomy had improved mortality versus repeat median sternotomy (46.2% in median resternotomy vs 5.9% in thoracotomy group, $p = 0.025$).[14,15]

When compared to medical therapy, transcatheter TV interventions decrease rehospitalization for HF and increase survival (Hazard Ratio [HR] 0.60; 95% CI: 0.46–0.79; $p = 0.003$ unadjusted).[16] The international, multicenter TriValve Registry discovered that although patients who undergo transcatheter TV intervention are high-risk with severe TR, they typically are without RV dysfunction.[17]
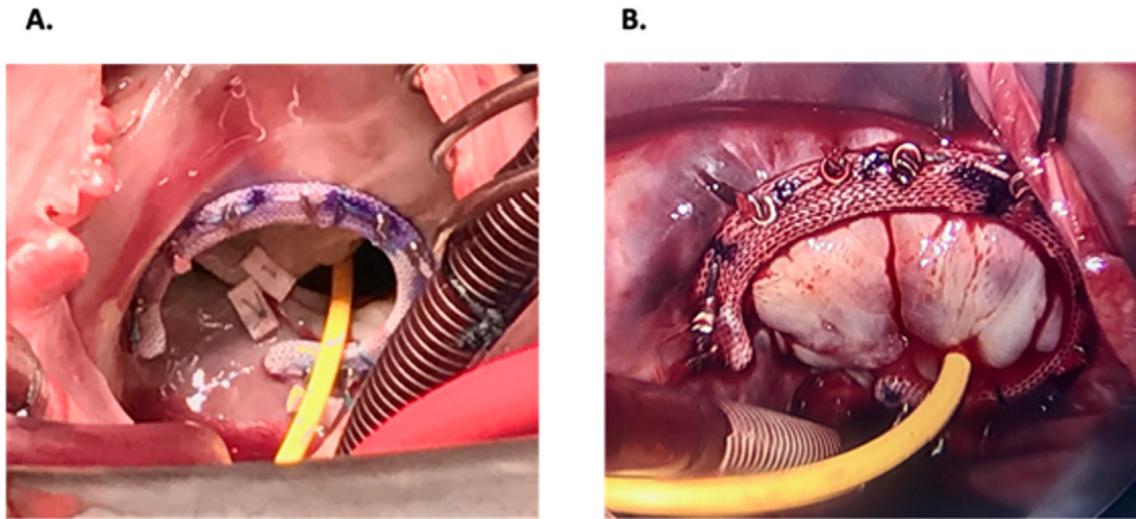
Fig. 2. Intraoperative view of tricuspid valve repair. **A.** TV ring annuloplasty with Alfieri stitch. **B.** TV ring annuloplasty alone.

TVS: risk prediction, models, and clinical risk score (CRS)

TVS continues to be a significant cause of morbidity and mortality.[18] Use of clinical risk assessment tools can help predict morbidity and mortality for patients, guide clinical decision making, and assess performance metrics. Identifying risk factors is paramount to developing these tools. In the analysis from the STS Database, several factors increasing mortality risk were identified including: advanced age (>75 yo), cardiogenic shock, serum creatinine, urgent or emergent surgical status, and congestive HF.[8] There have been a few studies that have attempted to stratify patient risk for TVS.

MELD to predict tricuspid outcomes

The Model for End-Stage Liver Disease (MELD) score is a well-established mortality predictor for liver transplant outcomes. Since advanced TV disease causes liver dysfunction, and liver disease is not captured in the STS database, we hypothesized that MELD may be predictive of outcomes following tricuspid operations.[19] Our group analyzed 168 patients over 14 years who underwent TVS. Preoperative MELD was available for 72.6% (122/168) of the patients. Patients were then stratified into four groups based on MELD score: <10, 10–14.9, 15–19.9, and >20 (Fig. 3).[19] Analyses were performed identifying mortality risk factors in addition to outcome measures related to perioperative variables and operative mortality. To validate utilizing MELD as a risk stratification tool, we compared it to the European System for Cardiac Operative Risk Evaluation logistic risk calculator.

Operative mortality was 8.9% (15/168), consistent with STS data. TV repair (156/168) was more commonly performed than replacement (92.9% vs. 7.1%, $p < 0.0001$). For all patients undergoing TVS, 37 (22%) had known significant liver disease defined by a history of cirrhosis, MELD of 15 or greater, or both. These patients were more often younger, male, and diagnosed with endocarditis. They were also more inclined to have preoperative renal failure (51.4% vs. 13%, $p < 0.0001$) but showed no other difference in preoperative risk factors including age, ejection fraction or HF. Ultimately, patients with liver disease experienced worse outcomes including postoperative sepsis, multisystem organ failure and dialysis-dependent renal failure. Most importantly, their mortality rate was significantly worse (18.9% versus 6.1%, $p = 0.024$). Mortality increased incrementally with worsening MELD (Fig. 3).[19] Specifically, operative mortality for patients with a low MELD (<10) was only 1.9%, however increased to 6.8% for MELD 10–15. A significant increase risk was identified in patients with MELD ≥15. Patients with a preoperative MELD score of 15 to 19.9 and ≥20 had an operative

mortality of 27.3% and 30.8%, respectively ($p = 0.0015$). When utilizing a MELD cutoff of 15 which is the same required for liver transplant listing, operative mortality increases from 4.1% to 29.2% ($p < 0.0001$). Perioperative outcomes of multisystem organ failure ($p = 0.026$), prolonged ventilation ($p < 0.0001$) and hemodialysis-dependent renal failure ($p < 0.0001$) were all significant for MELD scores of 15 or greater.

Univariate analysis of risk factors related to operative mortality only established significance for preoperative renal failure ($p < 0.0001$) and a MELD of 15 or greater ($p = 0.0017$). Through multivariate regression, significant or near-significant risk factors were evaluated, however renal failure was excluded because of its incorporation in MELD score calculation. The model demonstrated that the only independent predictor of operative mortality was a MELD score of 15 or greater (OR = 9.38, 95% CI: 2.25 to 39, $p = 0.0021$). When comparing MELD to EuroSCORE, we determined MELD predicted mortality (Area under the curve/AUC = 0.78) as well as EuroSCORE (AUC = 0.78, $p = 0.96$). This is significant because of the ease of which a MELD can be calculated preoperatively.

Novel clinical risk calculator for TVS

In addition to utilizing MELD as a risk marker for TVS, our group sought to develop a CRS for isolated TVS.[20] Utilizing the STS database, data from patients undergoing isolated TV repair and replacement at >50 cardiac surgery centers that participate in the Virginia and Michigan
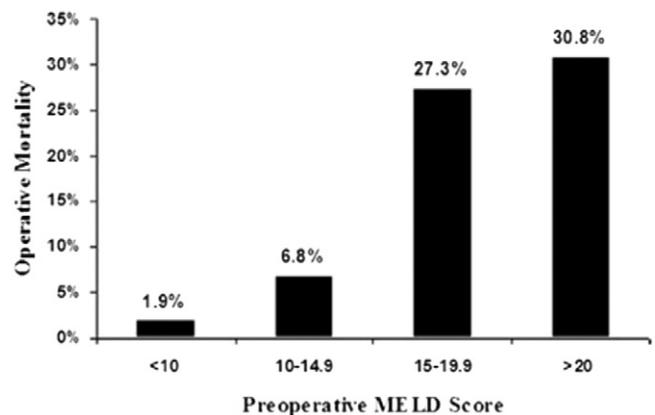

Fig. 3. Operative mortality as a function of preoperative Model for End-Stage Liver Disease (MELD) score Reprinted with permission from Ailawadi et al.[19]

Table 2

Multivariable logistic regression analysis for outcome of operative mortality.

Factor	OR (adj)	95% CI		p Value	CRS value
		LL	UL		
Age, years, versus <40					
60–69	2.26	1.15	4.45	0.02	2
70+	3.27	1.70	6.29	0.001	3
Female	1.41	1.02	1.96	0.04	1
Stroke	2.03	1.29	3.20	0.002	2
Hemodialysis	3.34	2.09	5.33	<0.001	4
Chronic lung disease, versus none					
Moderate	1.56	0.93	2.63	0.09	1
Severe	3.04	1.86	5.00	<0.001	3
NYHA class, versus class I/II					
III	2.05	1.12	3.76	0.02	2
IV	3.33	1.80	6.16	0.001	3
Reoperation	1.59	1.15	2.19	0.005	2
Status, emergent	4.37	2.04	8.99	<0.001	4
Intercept	0.009	0.004	0.02	<0.001	…

CI = confidence interval; CRS = clinical risk score; LL = lower limit; NYHA = New York Heart Association; OR (adj) = adjusted odds ratio; UL = upper limit.
Reprinted with permission from LaPar et al.[20]

statewide STS data collaboratives were obtained. All patients undergoing isolated TVS, including annuloplasty alone, valve replacement, or valve repair with or without annuloplasty were included. The primary outcomes of interest were operative mortality, major morbidity, and risk-adjusted associations of preoperative patient risk factors. The CRS was based upon their estimated relationships. Standardized STS clinical definitions were utilized to ensure repeatability. This data was entered in a multiple-level mixed effects regression to create a parsimonious preoperative risk model.

The study included 2050 patients from hospitals across Virginia and Michigan. TV repair (86%) was more common than replacement (14%). The overall operative mortality rate was 9% and major morbidity was 42%. Significant risk factors associated with mortality and major morbidity were consistent with those found throughout the literature including: age, preoperative hemodialysis, lung disease, New York Heart Association (NYHA) class, reoperation, and urgent or emergency status

Table 3

Multivariable logistic regression analysis for outcome of composite major morbidity.

Factor	OR (adj)	95% CI		p Value	CRS value
		LL	UL		
Age, years, versus <40					
50–59	1.38	0.95	1.99	0.09	1
60–69	1.56	1.08	2.24	0.02	2
70+	1.82	1.27	2.59	<0.001	2
Female	0.82	0.67	1.09	0.06	1
Stroke	2.00	1.40	2.85	<0.001	2
Hemodialysis	1.73	1.19	2.52	0.004	2
Ejection fraction <55%	1.47	1.20	1.81	<0.001	2
Chronic lung disease, versus none					
Mild	1.34	1.03	1.76	0.03	1
Moderate	1.44	1.02	2.02	0.04	1
Severe	1.30	0.88	1.94	0.2	1
NYHA class, versus class I/II					
III	1.72	1.26	2.34	0.001	2
IV	2.95	2.11	4.13	<0.001	3
Reoperation	1.60	1.30	1.96	<0.001	2
Status, emergent					
Urgent	2.04	1.63	2.55	<0.001	2
Emergent	9.40	4.16	21.30	<0.001	9
Intercept	0.14	0.09	0.23	<0.001	…

CI = confidence interval; CRS = clinical risk score; LL = lower limit; NYHA = New York Heart Association; OR (adj) = adjusted odds ratio; UL = upper limit.
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Table 4

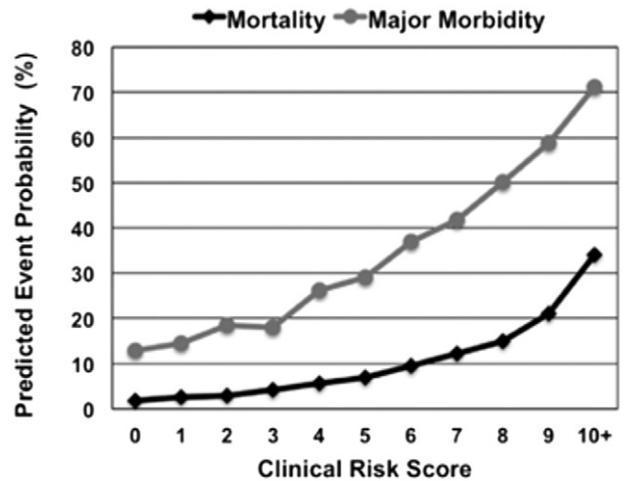Predicted mortality and morbidity risk by clinical risk score.

CRS	Predicted Mortality Risk	Predicted Morbidity Risk
0	2%	13%
1	3%	14%
2	3%	19%
3	4%	18%
4	6%	26%
5	7%	29%
6	9%	37%
7	12%	42%
8	15%	50%
9	21%	59%
10+	34%	71%

CRS = clinical risk score.
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of the operation (all $p < 0.05$). Of all identified risk factors, preoperative hemodialysis (adjusted odds ratio [AOR] 3.3, $p < 0.001$), lung disease (AOR 3.0, $p < 0.001$), NYHA class (AOR 3.3, $p < 0.001$) and emergent operation (AOR 4.4, $p < 0.001$) were most strongly associated with mortality. The significant factors were given corresponding CRS values (Tables 2, 3).[20] When utilizing the risk calculator, morbidity and mortality scores are measured independently. Summation of all risk factor scores generates the cumulative CRS thus determining their morbidity or mortality stratification (Table 4, Fig. 4).[20] While there are certain limitations to our CRS, we are working to further develop and validate our efforts with independent, external datasets and incorporate more clinical data points.

Conclusion

TR is associated with increased mortality and continues to be a challenging disease process to treat. Risk factor stratification and outcome prediction is important when treating patients with TV disease. Clinical risk prediction models and preoperative MELD scores are useful tools when presenting patients with outcome projections and may help guide treatment. Low risk patients could be considered those: without evidence of left-sided HF or low NYHA class, absence of severe pulmonary disease, no preoperative hemodialysis needs, elective surgery and preoperative MELD score <15. Armed with this knowledge, we recommend early referral for surgical intervention in an effort to avoid precipitation of negative risk factors.

Fig. 4. Predicted mortality and morbidity risk by clinical risk score. Clinical risk score (CRS) value assignment to determine predicted probability of mortality (black line) and major morbidity (gray line) after isolated tricuspid valve surgery. Reprinted with permission from LaPar et al.[20]

Declaration of competing interest

Evan Rotar – none

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