

Article

Evaluation Results and Recommendations of a Novel Tricuspid Regurgitation Classification for Isolated Tricuspid Valve Replacement Surgery

Jie Yu^{1,†}, Rui Ma^{2,†}, Lei Dong^{2,†}, Lu Liu^{1,*}, He Wang^{1,*}

¹Department of Cardiovascular Surgery, Changhai Hospital, The Naval Military Medical University, 200433 Shanghai, China

²Department of General Surgery, Changhai Hospital, The Naval Military Medical University, 200433 Shanghai, China

*Correspondence: 932534704@qq.com (Lu Liu); wangheyys@163.com (He Wang)

†These authors contributed equally.

Submitted: 8 March 2024 Revised: 24 May 2024 Accepted: 30 May 2024 Published: 11 July 2024

Abstract

Background: There are still no accepted classification and recommendations for isolated tricuspid valve replacement (ITVR) surgery. So we aim to evaluate the applicability of the tricuspid valve regurgitation classification proposed by Latib in 2018 for ITVR surgery. **Methods:** We enrolled all patients who underwent ITVR from 2000 to 2021 in our center. Based on a novel classification, the patients were divided into five stages, and in-hospital mortality was used as the primary endpoint to analyze whether this classification scheme was a good way to evaluate the prognosis of patients at different stages and with different surgical options. **Results:** A total of 254 patients who underwent ITVR were divided into five stages. None of the patients was classified into stage 1, and stages 4/5 accounted for 159 (62.6%). There was no difference in age, gender, or body mass index (BMI). 178 (70.1%) patients underwent traditional open surgery and 76 (29.9%) opted for the transcatheter option. The main etiology was functional tricuspid regurgitation (FTR), with 64.9% of these patients in stage 4 or above. The overall in-hospital mortality rate was 14.2%, with 14.0% in stage 4 vs. 37.8% in stage 5 ($p < 0.001$). The patients in the intervention group were generally older, and coronary heart disease and atrial fibrillation were also more common ($p < 0.05$). Interventional mortality for stages 4 and 5 was 35.8% vs. 13.2% in the open group, but there was no significant difference between them after propensity score matching. **Conclusions:** The tricuspid regurgitation's (TR's) five-stage classifications can predict prognosis for different patients. After this classification, no difference was found between the two procedures, and open surgery is recommended for patients with acceptable general conditions.

Keywords

tricuspid valve regurgitation; tricuspid valve replacement surgery; classification

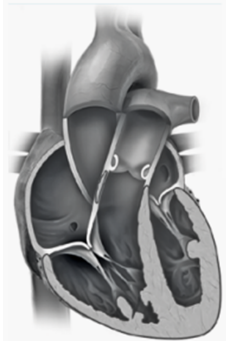
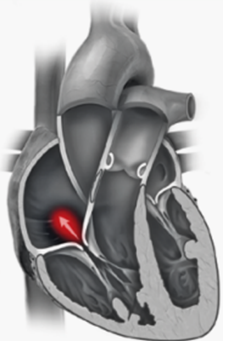
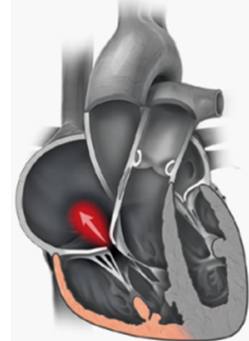
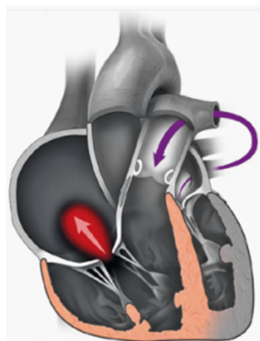
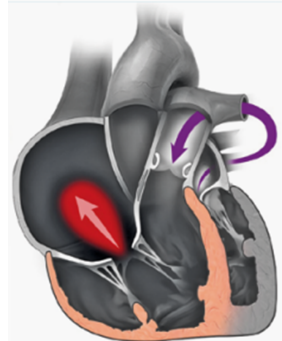
Introduction

Tricuspid regurgitation (TR) is one of the most common valvular diseases, with an overall incidence of nearly 70% of the population. Minimal or mild reflux may be a variant in structurally normal valves, but moderate-to-severe TR is usually pathological, occurring in 5.6% of females over 70 years of age [1,2]. Etiology includes primary and secondary, the latter also known as functional tricuspid regurgitation (FTR). FTR accounts for more than 90%, mostly due to left heart surgery [3]. Regrettably, it has always been a problematic issue as patients are often diagnosed at an advanced stage with multiple complications. Although transcatheter tricuspid valve replacement (TTVR) has introduced new solutions, it is still in its infancy and associated with a high mortality rate.

Patients requiring isolated tricuspid valve replacement (ITVR) surgery represent a complex population with multiple comorbidities at different stages of TR disease. Therefore, surgical interventions are often associated with significant perioperative morbidity and mortality, while safer percutaneous interventions may have limited efficacy. Currently, there is no unified treatment plan for ITVR. In 2018, Latib *et al.* [4] proposed a novel classification that expanded the previous three-stage classification by Dreyfus *et al.* [5] to five stages in a more detailed manner, aiming to understand the distribution of TR patients at different stages and propose suggestions on surgical management.

Latib's [4] classification is based on TR grade, right ventricular (RV) function, symptoms, and medications (Table 1). The patient presented with definite symptoms of right heart failure at stage 3/4, accompanied by an increase in inverse flow and a gradual exacerbation of annular remodeling, with drug treatment escalating to a higher level. This classification scheme essentially captures the characteristics of TR patients, and includes transcatheter intervention surgery in surgical opinions, which currently makes it a relatively comprehensive TR classification method. It may be sufficient for evaluating patients with surgical interventions. Additionally, stage 3 in this category makes ITVR

Table 1. A simplified classification of TR.

					
Symptoms	None	None	None/vague	An episode of RHF	Overt RHF and/or end-organ damage
Regurgitation grade	<Moderate	>Moderate	Severe	Severe	Torrential
Annular remodeling	Normal	Normal or mildly remodeled	Present	Moderate-severe	Severe
RV function and remodeling	Normal	Normal function Absent or mild remodeling	Mild RV dysfunction and/or remodeling	>Moderate dysfunction and remodeling	Severe RV dysfunction and remodeling
Medical	No treatment	None or low-dose diuretics	Diuretics	Moderate to high dose diuretics and/or requirement for IV diuretics	Multiple admissions for RHF. Frequent need for IV diuretics and/or high dose combination diuretics

Although this staging scheme implies linear progression of the disease, in fact there may be patients with little tethering and RV remodelling but with severe TR secondary to severe right atrial dilatation, such as patients with idiopathic FTR. Annular remodeling, leaflet coaptation, and tethering are also included in the criteria, but we have omitted these three to simplify the classification because of the lack of standards or infrequent application. IV, intravenous; RHF, right heart failure; RV, right ventricular; TR, tricuspid regurgitation; FTR, functional tricuspid regurgitation. Reproduced with permission from EuroIntervention; published by EuroIntervention, 2018 10.4244/EIJ-D-18-00533.

a viable option, which is not available in other classifications.

Latib's classification has not previously been validated specifically for patients undergoing ITVR, as existing guidelines recommend treating TR concurrently with left-side heart valve surgery [6]. However, from the data on tricuspid valve surgery patients in the United States, we can see that isolated tricuspid valve surgery has been increasing annually (from 290 in 2004 to 780 in 2013), accounting for 15% of tricuspid valve surgeries, with replacement surgery surpassing repair surgery at 59.2% [7]. Patients undergoing ITVR surgery are typically older, at greater risk, and exhibit a high incidence of postoperative complications, extended hospital stays, and a high in-hospital mortality rate of about 10%. Identifying a more appropriate classification method for ITVR patients, analyzing the characteristics of patients at different stages, and the differences in treatment options will aid physicians in making better clinical decisions. This study aims to evaluate its applicability and simply compare the operation of ITVR, with the goal of finding a more appropriate timing and options.

Methods

This was a single-center retrospective review of all ITVR procedures performed between 2000 and 2021. The study was conducted in accordance with the Declaration of Helsinki [8] (as revised in 2013) and patients sign written informed consent upon admission to the hospital to use some of the data that does not expose patient privacy for scientific purposes. Excluding repair surgeries, there were a total of 254 patients, including 76 cases with TTVR. They were categorized into different stages according to Latib's classification. Subjective data, such as symptoms and medication, were derived from medical histories, while objective data were obtained from echocardiography.

After admission, relevant examinations were completed, diuresis was intensified to improve heart function, and valve replacement surgery was conducted at an optimal time. The traditional thoracotomy uses a median sternal incision. It proceeds via the right atrium with the assistance of extracorporeal cardiopulmonary bypass (CPB) and employs biological and mechanical valves for replacement. Conversely, interventional patients received a prosthesis through a small incision in the right chest. The detailed surgical procedure involved the patient being under general anesthesia with endotracheal intubation, the right shoulder elevated to tilt the body slightly to the left, followed by insertion of the esophageal ultrasound probe. The 5th intercostal incision on the right side was marked, disinfected after full exposure, and the chest was accessed layer by layer. A 6F pigtail catheter was placed in the right atrium for right ventricular angiography, and a valve conveyor was introduced. The tricuspid valve ring was located using contrast and esophageal ultrasound, the artificial valve was de-

ployed and secured, and finally, the chest was closed after the conveyor was withdrawn.

The transcatheter tricuspid valve used in our center is the Lu-Valve, an *in situ* valve replacement device independently developed in China, and is the only valve replacement device that does not rely on radial force for support. The device comprises a Nitinol stent, a biological trilobal valve, an anterior valve holding key, and an interventricular septal anchor. Its safety and efficacy have been validated by several international centers.

Patients required a postoperative intensive care unit (ICU) stay of more than 24 hours. To reduce the statistical bias caused by fewer deaths, in-hospital mortality was taken as the primary endpoint, with the duration of endotracheal intubation and length of ICU stay as the secondary aims to more comprehensively describe the characteristics of the five stages.

In this study, propensity score matching (PSM) was utilized to eliminate confounding factors between the two groups, thereby reducing selection bias and improving the accuracy and validity of the comparison. By matching factors with similar propensity scores in the two groups, the similarity of the two groups in matching variables was ensured. Matching variables, which are independent variables used to establish propensity scores, included age, gender, and disease severity in this study. We employed the regression method to calculate the propensity score for each individual, and conducted one-to-one matching between two groups of individuals with similar propensity scores to assess whether there was a better balance in matching variables between the groups after matching, thus ensuring a more accurate and reliable comparison. Clinicopathological variables without collinearity were used in matching. Patients were matched in a ratio of 1:3, and patients could not be repeatedly matched. The caliper used for matching was set at 0.05.

Statistical Analysis

Categorical variables were presented as absolute numbers and percentages. Normal distribution of continuous variables was assessed with the Shapiro-Wilk test. Continuous variables were expressed as mean \pm standard deviation or median and interquartile range according the distribution of variables. Differences between categorical variables were tested with the χ^2 test or the Fisher's exact test, as appropriate. Differences between continuous variables were examined using either the Kruskal-Wallis test or the Wilcoxon test, depending on the number of groups being compared. Propensity score matching (PSM) was performed to reduce the possibility of selection bias. All statistical analyses were performed using R statistical software (R, version 3.5.0, Boston, MA, USA; R project). The difference was considered statistically significant for both sides ($p < 0.05$).

Results

A total of 254 patients who underwent ITVR surgery were enrolled in the present study and divided into five stages (Table 2). None were classified into stage 1; all suffered at least from moderate-to-severe TR. There were 178 (70.1%) who underwent traditional thoracotomy surgery, and 76 (29.9%) who selected the transcatheter option. There was no significant difference in the proportion of open surgery and interventional surgery across different stages, nor in intraoperative blood loss or CPB duration in open surgery, but the use of biologic flaps exceeded 50% in all patients. The median age of the patients was 59.9 years (interquartile range (IQR): 50.0 to 67.0 years) with 146 (57.5%) being female. The body mass index (BMI) was 22.3 kg/m² (IQR: 20.2 to 23.9 kg/m²). The main etiology was FTR in 185 patients (72.8%), with 64.9% of these in stage 4 or above ($p = 0.044$). An increased proportion of patients presented in New York Heart Association (NYHA) III and IV in advanced stages ($p < 0.001$). Among all patients, 28 (11.0%) had a history of pacemaker implantation, and 175 (68.9%) had atrial fibrillation (AF), the most common comorbidity and more prevalent in higher stages of TR classification ($p < 0.001$). The symptoms of dyspnea also showed significant differences through this classification method ($p = 0.011$). Additionally, high blood pressure accounted for 13.8%, diabetes for 9.1%, coronary heart disease (CHD) for 3.9%, and chronic renal disease (CRD) for 9.1%; these comorbidities did not differ significantly among the four stages.

The median left ventricular ejection fraction (LVEF) was 52% (IQR: 56% to 69%) with no difference among the four stages ($p = 0.316$). However, reflux volume was 63.5 mL (IQR: 49.0 to 88.0 mL) in stage 4 and 75.9 mL (IQR: 56.0 to 123.0 mL) in stage 5 ($p < 0.001$). Similarly, patients with higher stages experienced more severe right heart dilation ($p < 0.001$). The median right atrial (RA) volume was 201.0 mL (IQR: 161.8 to 275.0 mL) in stage 4 versus 300.0 mL (156.0 to 447.0 mL) in stage 5.

Postoperative outcomes were significantly different among stages. In-hospital mortality in the overall population was 14.2%, 3.2% in stages 2/3, 14.0% in stage 4, and 37.8% in stage 5 (Fig. 1). Advancement from one stage to the next correlated with longer ICU stays (46.2 hrs, 46.0 hrs in stages 2/3, 48.0 hrs in stage 4, and 144.0 hrs in stage 5, $p < 0.001$) and increased ventilator duration (11.0 hrs, 14.0 hrs in stages 2/3, 15.2 hrs in stage 4, and 24.0 hrs in stage 5, $p < 0.001$).

The TR classification scheme of Latib was utilized to further determine the differences between traditional open ITVR surgery and TTVR surgery. Univariate and multivariate logistic regression analysis was performed on the characteristics of the two surgical methods, with results listed in Tables 3,4. TTVR patients were older than those

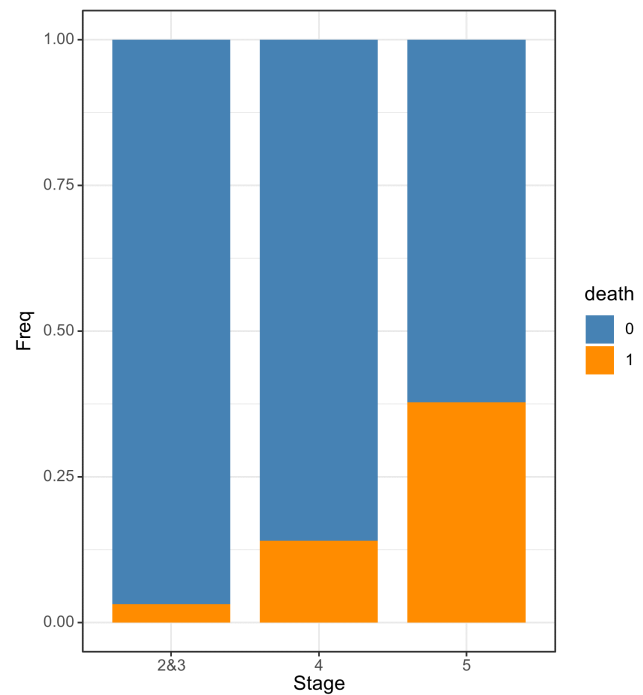


Fig. 1. In-hospital mortality by stage. Stage 2 and stage 3 in the early of the disease were combined.

undergoing open surgery at all stages of the disease ($p < 0.001$), but there was no difference in gender or body size distribution between the two surgical modalities ($p > 0.05$). TTVR patients had worse cardiac function, and a higher prevalence of pacemaker implantation and atrial fibrillation ($p < 0.05$). Additionally, patients eligible for TTVR generally had poorer health, as they also exhibited higher incidences of diabetes, CRD, CHD, and larger right heart volumes.

The median ICU time was 48.0 (45.5, 240.0) hours after TTVR surgery and 72.0 (44.1, 138.4) hours after open surgery, showing no statistical significance. However, the duration of endotracheal intubation was 6.0 (5.0, 22.0) hours for TTVR patients and 19.0 (13.1, 41.1) hours for open surgery patients, with a significantly longer duration in open surgery patients across different stages. Through the analysis of in-hospital mortality, univariate logistic regression analysis revealed that in stages 4/5 of the disease, the mortality rates for patients undergoing open surgery were 35.8% and 13.2%, respectively. Due to significant differences in baseline data between patients undergoing the two different surgical methods, the PSM statistical method was used to reduce errors caused by selection bias. However, after analysis, except for the difference in endotracheal intubation duration, this study did not find any significant differences in ICU stay length or in-hospital mortality outcomes between the two surgical methods. Therefore, we cannot predict the risk factors of the two different surgical procedures of ITVR using this new TR classification method.

Table 2. Distribution of patients by stage.

	Stage 2, n = 18 (7.1%)	Stage 3, n = 77 (30.3%)	Stage 4, n = 114 (44.9%)	Stage 5, n = 45 (17.7%)	Statistical value	p value
Surgery						
Open	15 (83.3)	57 (74.0)	78 (68.4)	28 (62.2)	$\chi^2 = 3.554$	0.314
Intervention	3 (16.7)	20 (26.0)	36 (31.6)	17 (37.8)		
Blood loss, mL	154.0 (122.0, 186.0)	200.0 (140.0, 280.0)	214.5 (162.0, 240.0)	220.0 (182.0, 260.0)	H = 1.247	0.642
CPB duration, min	65.0 (49.0, 90.0)	74.0 (52.0, 102.0)	80.0 (60.0, 114.0)	86.0 (61.0, 120.0)	H = 2.241	0.324
Valve type (open surgery)						
Biovalve	8 (53.3)	30 (52.6)	47 (60.3)	18 (64.3)	$\chi^2 = 1.423$	0.700
Mechanical valve	7 (46.7)	27 (47.4)	31 (39.7)	10 (35.7)		
Diagnosis						
FTR	8 (44.4)	57 (74.0)	85 (74.6)	35 (77.8)	$\chi^2 = 8.115$	0.004
PTR	10 (55.6)	20 (26.0)	29 (25.4)	10 (22.2)		
Baseline characteristic						
Age, yrs.	57.5 (43.5, 64.5)	57.0 (47.0, 66.0)	59.5 (51.2, 68.0)	63.0 (54.0, 69.0)	H = 7.773	0.051
Female	7 (38.9)	43 (55.8)	69 (60.5)	27 (60.0)	$\chi^2 = 3.180$	0.365
BMI, kg/(m ²)	21.3 (20.1, 23.1)	23.1 (20.8, 25.0)	22.2 (20.0, 23.5)	21.9 (20.1, 24.2)	H = 7.673	0.053
NYHA (III–IV)	5 (27.8)	43 (55.8)	104 (91.2)	45 (100.0)	Fisher's Exact Test	<0.001
Pacemaker	0 (0.0)	8 (10.4)	15 (13.2)	5 (11.1)	Fisher's Exact Test	0.503
AF	5 (27.8)	50 (64.9)	87 (76.3)	33 (73.3)	$\chi^2 = 18.108$	<0.001
HP	2 (11.1)	12 (15.6)	17 (14.9)	4 (8.9)	Fisher's Exact Test	0.783
COPD	0 (0.0)	2 (2.6)	15 (13.2)	8 (17.8)	Fisher's Exact Test	0.008
Diabetes	0 (0.0)	9 (11.7)	9 (7.9)	5 (11.1)	Fisher's Exact Test	0.449
CHD	2 (11.1)	3 (3.9)	1 (0.9)	4 (8.9)	Fisher's Exact Test	0.020
CRD	1 (5.6)	8 (10.4)	8 (7.0)	6 (13.3)	Fisher's Exact Test	0.587
Echocardiography						
LVEF, %	63.0 (54.0, 68.8)	63.0 (57.0, 69.0)	61.0 (56.0, 67.0)	65.0 (58.0, 70.0)	H = 3.538	0.316
Reflux volume, mL	24.5 (18.2, 31.5)	34.0 (22.0, 45.0)	63.5 (49.0, 88.0)	75.9 (56.0, 123.0)	H = 100.280	<0.001
RA volume, mL	86.5 (66.2, 116.5)	128.0 (87.0, 171.0)	201.0 (161.8, 275.0)	300.0 (156.0, 447.0)	H = 73.002	<0.001
Outcomes						
ICU stay, hrs.	46.2 (24.8, 72.0)	46.0 (27.0, 68.0)	48.0 (41.5, 116.8)	144.0 (72.0, 384.0)	H = 50.272	<0.001
Endotracheal intubation duration, hrs.	11.0 (5.1, 14.0)	14.0 (6.0, 19.0)	15.2 (7.0, 22.0)	24.0 (7.0, 120.0)	H = 19.335	<0.001
Death in hospital	1 (5.6)	2 (2.6)	16 (14.0)	17 (37.8)	Fisher's Exact Test	<0.001

Values are mean (SD) or median (interquartile range) or n (%). FTR, Functional Tricuspid Regurgitation; PTR, Primary Tricuspid Regurgitation; BMI, Body Mass Index; NYHA, New York Heart Association; AF, Atrial Fibrillation; HP, Hypertension; CHD, Coronary Heart Disease; CRD, Chronic Renal Disease; LVEF, Left Ventricular Ejection Fraction; RA, Right Atrial; ICU, Intensive Care Unit.

Discussion

Functional tricuspid regurgitation (FTR) occurs in up to 40% of patients with severe TR, following left heart surgery, with a median survival of five years [9]. Annulus dilatation leads to an increase in the volume of the RA, which in turn causes the RV to dilate to maintain cardiac output [10]. This is more likely in patients with AF or in the early stages of the disease. A history of left heart surgery or pulmonary hypertension exacerbates reflux by increasing the burden on the right heart, leading to symptoms of heart failure that progress to an advanced stage of the disease [11]. Given that the pathology involves complex anatomical and functional issues, a scoring system for

assessing specific stages of TR is expected to better define the timing and outcomes of interventions [12].

Our study applied Latib's classification scheme to the assessment of ITVR patients, and it has demonstrated clear advantages. However, this approach does not provide detailed explanations or rationales for treatment recommendations, which is a notable drawback. Moreover, it lacks an explanation of the poor conditions that may exist in different stages of TR patients, such as the weight of each criterion and how to accurately determine the stage of disease, which are critical aspects. Indeed, this classification method can also be extended to the evaluation of left heart valves and the selection of treatment options. Initially, begin with the symptoms, subjectively judge the disease stage of the patient, and then provide specific treatment sugges-

Table 3. Characteristics of patients in stage 2 and 3.

Variables	Intervention	Open	Statistical value	p value
	(n = 23)	(n = 72)		
Age, yrs.	66.0 (58.5, 72.5)	52.0 (44.0, 60.0)	W = 1386.0	<0.001
Female	15 (65.2)	35 (48.6)	$\chi^2 = 1.928$	0.165
BMI, kg/(m ²)	22.7 (20.3, 24.8)	22.8 (20.2, 25.0)	W = 846.0	0.891
NYHA (III–IV)	19 (82.6)	29 (40.3)	$\chi^2 = 12.496$	<0.001
Pacemaker	4 (17.4)	4 (5.6)	Fisher's Exact Test	0.094
AF	20 (87.0)	35 (48.6)	$\chi^2 = 10.514$	0.001
HP	5 (21.7)	9 (12.5)	Fisher's Exact Test	0.453
COPD	0 (0.0)	2 (2.8)	Fisher's Exact Test	1.000
Diabetes	2 (8.7)	7 (9.7)	Fisher's Exact Test	1.000
CHD	4 (17.4)	1 (1.4)	Fisher's Exact Test	0.012
CRD	5 (21.7)	4 (5.6)	Fisher's Exact Test	0.035
LVEF, %	59.0 (53.5, 68.0)	63.5 (58.5, 69.2)	W = 671.5	0.175
Reflux volume, mL	31.0 (23.5, 39.5)	32.0 (20.4, 41.2)	W = 824.0	0.976
RA volume, mL	81.0 (72.5, 122.0)	129.5 (97.0, 176.0)	W = 409.0	<0.001
ICU duration, hrs	46.0 (30.5, 48.0)	46.0 (25.8, 72.0)	W = 783.5	0.702
Endotracheal intubation duration, hrs.	6.0 (3.2, 14.5)	14.0 (8.0, 19.2)	W = 479.5	0.002
Death in hospital	1 (4.3)	2 (2.8)	Fisher's Exact Test	1.000

Values are mean (SD) or median (interquartile range) or n (%). BMI, Body Mass Index; NYHA, New York Heart Association; AF, Atrial Fibrillation; HP, Hypertension; CHD, Coronary Heart Disease; CRD, Chronic Renal Disease; LVEF, Left Ventricular Ejection Fraction; RA, Right Atrial; ICU, Intensive Care Unit.

tions with the help of objective indicators such as echocardiography, cardiac magnetic resonance, and catheter examinations. This approach will be more effective in addressing the weight allocation problem mentioned above. Each classification method needs continuous validation; this is the only way to make ongoing progress in treatment strategies.

How Applicable is this Classification?

Currently, there is no universally recognized scheme for classifying TR. An attempt that utilizes symptoms, medications, and echocardiography to divide TR into five stages [4], may be relatively complete and effective for current evaluation indicators. Although symptoms and medications are included, they lack clear criteria and may be difficult to standardize. Echocardiography is ideal for measuring objective indicators such as RV volume. The European Association of Cardiovascular Imaging and the American Society of Echocardiography (EACVI/ASE) provide accurate definitions for the severity of TR and are currently the widely accepted guidelines [13]. However, it should be noted that echocardiography may have limitations and could underestimate the degree of reflux due to increased resistance in patients with pulmonary hypertension. It is recommended that echocardiography be used in conjunction with other methods, particularly since cardiac magnetic resonance (CMR) is considered the gold standard for measuring right heart size and function [14].

In 2021, Sala performed the first retrospective analysis of early outcomes in patients who underwent TV surgery

based on the same classification [15]. The difference in our study is that all patients underwent replacement surgery, without any undergoing repair. Considering surgery specifically for the tricuspid valve, repair alone was deemed not worth the risk. Beyond increasing life expectancy, replacement may offer better long-term outcomes [16,17]. After applying the classification, we can clearly see the differences in prognosis. This may have significant guiding implications for our work.

From the results of this study, it is apparent that TR patients at different stages of the disease show no significant differences in age, sex, BMI, and etiological distribution, which supports the feasibility of this classification standard. As the stage of the disease increases, the evaluation of cardiac function, clinical symptoms, and echocardiographic examination results become more pronounced, validating the relevance and accuracy of the indicators used in this classification. Echocardiographic findings, such as reflux flow and right heart volume, worsen with the progression of the disease. Dyspnea is the most common symptom in TR patients; AF is an independent risk factor for exacerbating TR, and these differences are captured in this classification. Although studies have attempted to assess the natural history and prognostic impact of TR, their findings have been sometimes contradictory, and there is ongoing debate about whether severity of TR, right ventricular function, underlying etiology, or a combination thereof are predictors of poor prognosis. Through prognostic analysis, this classification has proven useful in predicting outcomes, both in terms of in-hospital mortality and the duration of hospital treatment.

Table 4. Characteristics of patients in stage 4 and 5 before and after PSM.

Variables	Before PSM		Statistical value	p value	After PSM		Statistical value	p value
	Intervention (n = 53)	Open (n = 106)			Intervention (n = 23)	Open (n = 40)		
Age, yrs.	69.0 (62.0, 72.0)	54.0 (49.0, 64.0)	W = 4578.5	<0.001	63.8 (8.5)	60.5 (9.4)	t = 1.307	0.198
Female	33 (62.3)	63 (59.4)	$\chi^2 = 0.118$	0.731	18 (78.3)	27 (67.5)	$\chi^2 = 0.829$	0.363
BMI, kg/(m ²)	22.3 (21.3, 23.1)	22.0 (20.0, 23.6)	W = 2989.5	0.511	22.2 (20.4, 22.5)	20.8 (19.5, 23.3)		0.209
NYHA (III–IV)	52 (98.1)	97 (91.5)	Fisher's Exact Test	0.167	23 (100.0)	38 (95.0)	Fisher's Exact Test	0.529
Pacemaker	15 (28.3)	5 (4.7)	$\chi^2 = 17.873$	<0.001	5 (21.7)	2 (5.0)	Fisher's Exact Test	0.089
AF	46 (86.8)	74 (69.8)	$\chi^2 = 5.504$	0.019	18 (78.3)	35 (87.5)	Fisher's Exact Test	0.476
HP	9 (17.0)	12 (11.3)	$\chi^2 = 0.988$	0.320	1 (4.3)	3 (7.5)	Fisher's Exact Test	1.000
COPD	6 (11.3)	17 (16.0)	$\chi^2 = 0.635$	0.426	3 (13.0)	8 (20.0)	Fisher's Exact Test	0.732
Diabetes	9 (17.0)	5 (4.7)	Fisher's Exact Test	0.016	0 (0.0)	3 (7.5)	Fisher's Exact Test	0.293
CHD	5 (9.4)	0 (0.0)	Fisher's Exact Test	0.004	0 (0.0)	0 (0.0)	Fisher's Exact Test	1.000
CRD	13 (24.5)	1 (0.9)	Fisher's Exact Test	<0.001	1 (4.3)	1 (2.5)	Fisher's Exact Test	1.000
LVEF, %	63.8 (9.3)	61.3 (8.9)	t = 1.584	0.117	64.2 (10.4)	61.7 (8.8)	t = 0.863	0.394
Reflux volume, mL	62.0 (48.0, 89.0)	68.0 (52.0, 97.8)	W = 2504.5	0.267	64.0 (53.5, 79.5)	64.5 (54.9, 108.0)	W = 417.0	0.547
RA volume, mL	200.0 (150.0, 275.0)	213.0 (165.0, 352.0)	W = 2478.5	0.228	174.0 (138.5, 242.0)	213.0 (173.0, 292.2)	W = 334.0	0.073
ICU duration, hrs.	48.0 (45.5, 240.0)	72.0 (44.1, 138.4)	W = 2719.5	0.745	48.0 (41.5, 104.0)	72.0 (41.4, 124.1)	W = 380.0	0.259
Endotracheal intubation duration, hrs.	6.0 (5.0, 22.0)	19.0 (13.1, 41.1)	W = 1660.0	<0.001	6.0 (3.0, 18.0)	17.0 (13.0, 57.0)	W = 79.0	<0.001
Death in hospital	19 (35.8)	14 (13.2)	$\chi^2 = 11.013$	0.001	5 (21.7)	5 (12.5)	Fisher's Exact Test	0.476

Values are mean (SD) or median (interquartile range) or n (%). As the Age and LVEF data adhere to a normal distribution, we have chosen to represent it using mean (standard deviation). PSM, Propensity Score Matching; BMI, Body Mass Index; NYHA, New York Heart Association; AF, Atrial Fibrillation; HP, Hypertension; CHD, Coronary Heart Disease; CRD, Chronic Renal Disease; LVEF, Left Ventricular Ejection Fraction; RA, Right Atrial; ICU, Intensive Care Unit.

Comparing the two groups of patients who underwent transcatheter intervention and open surgery, those who underwent transcatheter intervention were generally in poorer condition, being older, having worse heart function, and more comorbidities. These differences were also evident across different stages. It is understandable that these patients, who opted for TTVR, were not suitable candidates for traditional open surgery. Interestingly, however, analysis after PSM did not reveal differences in prognosis among the different surgical procedures. This aligns with initial observations when the classification was first proposed, suggesting it may not be adequate for assessing the complexity and heterogeneity of patients undergoing transcatheter therapy.

Over the years, the in-hospital mortality rate for ITVR has remained stable at about 10% [7,18]. The procedure itself is not technically demanding, and outcomes depend almost entirely on the patient's baseline condition. The absence of a valid risk score for this procedure further complicates the determination of the best management strategies and the correct timing for intervention [19].

When is ITVR Surgery Appropriate?

Simultaneous treatment of tricuspid valve (TV) issues with left heart surgery may indeed be the most optimal solution. Adding TV surgery does not significantly increase surgical risk but can improve right heart remodeling and cardiac function [20]. Conversely, having a history of left heart surgery is an independent risk factor for reoperation. Guidelines from Europe and the United States currently offer different recommendations: the 2017 European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) advocates for early surgery to prevent irreversible right heart dysfunction [21], whereas the 2020 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend initiating treatment based on symptoms or confirmed right heart insufficiency [22].

Symptoms of severe TR typically manifest only in the later stages, primarily as clinical signs of RV failure with hepatorenal insufficiency. In the absence of symptoms, clinicians are hesitant to recommend, and patients are reluctant to undergo surgery. They often prefer to wait until the disease progresses, facing challenges when requiring large doses of diuretics [23]. A 2021 survey of 1513 cases of isolated TV surgery identified that higher in-hospital mortality was primarily associated with late referrals [24]. The global rates of morbidity and mortality related to this condition are notably high. Isolated TV surgery is ideally performed before the onset of overt symptoms, especially in patients with concurrent heart conditions such as AF [25,26]. However, the approach to elderly patients who are visibly frail poses a significant dilemma.

What are the Options for Treating TR?

The endeavor to compare two primary procedures, traditional open heart surgery and TTVR, faces challenges due to patient selection bias, limiting direct comparisons. Our analysis aims to assess the classification's relevance to transcatheter surgery and to gain a deeper understanding of patient characteristics and prognosis. Prior to PSM, it was observed that patients chosen for TTVR were significantly older and had more comorbidities. While minimally invasive techniques offered shorter endotracheal intubation durations, they were associated with higher mortality. However, after PSM, differences in outcomes between the procedures were not statistically significant, suggesting the need to explore other parameters beyond mortality, such as length of hospital stay, readmission rates, and secondary anatomical or hemodynamic parameters like right ventricular function and pulmonary artery pressure, as criteria for evaluation [27].

Given that heart failure management is a priority, diuretics are indispensable regardless of the chosen intervention [12]. Our recommendation leans towards thoracotomy and valve replacement prior to considering transcatheter surgery. Transcatheter surgery is currently viewed as an option for symptomatic patients at high risk from conventional surgery [28]. With advancements in catheter technology, the indications for this procedure are expected to expand to include earlier stages of the disease and asymptomatic patients.

Conclusions

The five-stage scheme of TR is practically applicable in distinguishing patient prognoses and advocating for early surgical intervention. Although this classification scheme has not yet clarified the differences between traditional and transcatheter surgeries conclusively, it suggests a preference for traditional surgery in patients who are generally in good health.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

Conception and design: HW, LL; Analysis and interpretation: LD; Data collection: JY, RM; Writing the article: JY, RM, LD; Critical revision of the article: HW, LL; Final approval of the article: HW; Statistical analysis: JY,

RM; Overall responsibility: HW, JY, RM & LD are equal to this work. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study was approved by the ethics committee of Shanghai Changhai Hospital, NO. CHEC2021-162, Date: 2021-11-18. Patients sign written informed consent upon admission to the hospital to use some of the data that does not expose patient privacy for scientific purposes.

Acknowledgment

Thanks are extended to all those who contributed to data collection and surgery.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Singh JP, Evans JC, Levy D, Larson MG, Freed LA, Fuller DL, *et al.* Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study). *The American Journal of Cardiology.* 1999; 83: 897–902.
- [2] Antunes MJ, Rodríguez-Palomares J, Prendergast B, De Bonis M, Rosenhek R, Al-Attar N, *et al.* Management of tricuspid valve regurgitation: Position statement of the European Society of Cardiology Working Groups of Cardiovascular Surgery and Valvular Heart Disease. *European Journal of Cardio-Thoracic Surgery.* 2017; 52: 1022–1030.
- [3] Rodés-Cabau J, Taramasso M, O’Gara PT. Diagnosis and treatment of tricuspid valve disease: current and future perspectives. *Lancet.* 2016; 388: 2431–2442.
- [4] Latib A, Grigioni F, Hahn RT. Tricuspid regurgitation: what is the real clinical impact and how often should it be treated? *EuroIntervention.* 2018; 14: AB101–AB111.
- [5] Dreyfus GD, Martin RP, Chan KMJ, Dulguerov F, Alexandrescu C. Functional tricuspid regurgitation: a need to revise our understanding. *Journal of the American College of Cardiology.* 2015; 65: 2331–2336.
- [6] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Fleisher LA, *et al.* 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology.* 2017; 70: 252–289.
- [7] Zack CJ, Fender EA, Chandrashekar P, Reddy YNV, Bennett CE, Stulak JM, *et al.* National Trends and Outcomes in Isolated Tricuspid Valve Surgery. *Journal of the American College of Cardiology.* 2017; 70: 2953–2960.
- [8] Morris K. Revising the Declaration of Helsinki. *Lancet.* 2013; 381: 1889–1890.
- [9] Taramasso M, Vanermen H, Maisano F, Guidotti A, La Canna G, Alfieri O. The growing clinical importance of secondary tricuspid regurgitation. *Journal of the American College of Cardiology.* 2012; 59: 703–710.
- [10] Nemoto N, Lesser JR, Pedersen WR, Sorajja P, Spinner E, Garberich RF, *et al.* Pathogenic structural heart changes in early tricuspid regurgitation. *The Journal of Thoracic and Cardiovascular Surgery.* 2015; 150: 323–330.
- [11] Medvedofsky D, Aronson D, Gomberg-Maitland M, Thomeas V, Rich S, Spencer K, *et al.* Tricuspid regurgitation progression and regression in pulmonary arterial hypertension: implications for right ventricular and tricuspid valve apparatus geometry and patients outcome. *European Heart Journal. Cardiovascular Imaging.* 2017; 18: 86–94.
- [12] Taramasso M, Gavazzoni M, Pozzoli A, Dreyfus GD, Bolling SF, George I, *et al.* Tricuspid Regurgitation: Predicting the Need for Intervention, Procedural Success, and Recurrence of Disease. *JACC. Cardiovascular Imaging.* 2019; 12: 605–621.
- [13] Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, *et al.* Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance. *Journal of the American Society of Echocardiography.* 2017; 30: 303–371.
- [14] Park JB, Lee SP, Lee JH, Yoon YE, Park EA, Kim HK, *et al.* Quantification of Right Ventricular Volume and Function Using Single-Beat Three-Dimensional Echocardiography: A Validation Study with Cardiac Magnetic Resonance. *Journal of the American Society of Echocardiography.* 2016; 29: 392–401.
- [15] Sala A, Lorusso R, Bargagna M, Ascione G, Ruggeri S, Meneghin R, *et al.* Isolated tricuspid valve surgery: first outcomes report according to a novel clinical and functional staging of tricuspid regurgitation. *European Journal of Cardio-thoracic Surgery.* 2021; 60: 1124–1130.
- [16] Moraca RJ, Moon MR, Lawton JS, Guthrie TJ, Aubuchon KA, Moazami N, *et al.* Outcomes of tricuspid valve repair and replacement: a propensity analysis. *The Annals of Thoracic Surgery.* 2009; 87: 83–88; discussion 88–89.
- [17] Russo M, Di Mauro M, Saitto G, Lio A, Berretta P, Taramasso M, *et al.* Outcome of patients undergoing isolated tricuspid repair or replacement surgery. *European Journal of Cardio-Thoracic Surgery.* 2022; 62: ezac230
- [18] Alqahtani F, Berzingi CO, Aljohani S, Hijazi M, Al-Hallak A, Alkhouli M. Contemporary Trends in the Use and Outcomes of Surgical Treatment of Tricuspid Regurgitation. *Journal of the American Heart Association.* 2017; 6: e007597.
- [19] Kilic A, Saha-Chaudhuri P, Rankin JS, Conte JV. Trends and outcomes of tricuspid valve surgery in North America: an analysis of more than 50,000 patients from the Society of Thoracic Surgeons database. *The Annals of Thoracic Surgery.* 2013; 96: 1546–1552; discussion 1552.
- [20] Dreyfus GD, Corbi PJ, Chan KMJ, Bahrami T. Secondary tricuspid regurgitation or dilatation: which should be the criteria for surgical repair? *The Annals of Thoracic Surgery.* 2005; 79: 127–132.

- [21] Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, *et al.* 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *European Heart Journal*. 2017; 38: 2739–2791.
- [22] Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, 3rd, Gentile F, *et al.* 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021; 143: e35–e71.
- [23] Sala A, Lorusso R, Bargagna M, Ruggeri S, Buzzatti N, Scandroglio M, *et al.* Complicated postoperative course in isolated tricuspid valve surgery: Looking for predictors. *Journal of Cardiac Surgery*. 2021; 36: 3092–3099.
- [24] Kawsara A, Alqahtani F, Nkomo VT, Eleid MF, Pislaru SV, Rihal CS, *et al.* Determinants of Morbidity and Mortality Associated with Isolated Tricuspid Valve Surgery. *Journal of the American Heart Association*. 2021; 10: e018417.
- [25] Ingraham BS, Pislaru SV, Nkomo VT, Nishimura RA, Stulak JM, Dearani JA, *et al.* Characteristics and treatment strategies for severe tricuspid regurgitation. *Heart*. 2019; 105: 1244–1250.
- [26] McCarthy PM, Szlapka M, Kruse J, Kislitsina ON, Thomas JD, Liu M, *et al.* The relationship of atrial fibrillation and tricuspid annular dilation to late tricuspid regurgitation in patients with degenerative mitral repair. *The Journal of Thoracic and Cardiovascular Surgery*. 2021; 161: 2030–2040.e3.
- [27] Hahn RT. Current transcatheter devices to treat functional tricuspid regurgitation with discussion of issues relevant to clinical trial design. *Annals of Cardiothoracic Surgery*. 2017; 6: 240–247.
- [28] Taramasso M, Calen C, Guidotti A, Kuwata S, Bieffer HRC, Nietlispach F, *et al.* Management of Tricuspid Regurgitation: The Role of Transcatheter Therapies. *Interventional Cardiology*. 2017; 12: 51–55.