

Analyses for Prevalence and Outcome of Tricuspid Regurgitation in China: An Echocardiography Study of 134,874 Patients

Lifan Yang^a Haiyan Chen^b Wenzhi Pan^a Lihua Guan^a Xiaochun Zhang^a
Lei Zhang^a Qinchun Jin^a Daxin Zhou^a Xianhong Shu^b Junbo Ge^a

^aDepartment of Cardiology, Shanghai Institute of Cardiovascular Disease, Zhongshan Hospital, Fudan University, Shanghai, China; ^bDepartment of Echocardiology, Shanghai Institute of Cardiovascular Disease, Zhongshan Hospital, Fudan University, Shanghai, China

Keywords

Tricuspid regurgitation · Echocardiography · Prevalence · Outcome

Abstract

Background: The aim of this study is to investigate the prevalence and outcome of tricuspid regurgitation (TR) in the Chinese population. **Methods:** The echocardiography database, including 134,874 patients at our heart center from 2010 to 2012, was retrospectively analyzed. **Results:** The rates of mild, moderate, and severe TR were 2.96, 2.22, and 1.39%, respectively. Of these patients, 4.86% had primary TR, 91.41% had functional TR, and 3.73% had unexplained TR. The rate of TR was increased in elders (odds ratio: 1.038 for 1 year's increment; 95% confidence interval: 1.037–1.040; $p < 0.001$) and females (odds ratio: 1.386; 95% confidence interval: 1.327–1.448, $p < 0.001$). The major etiologies of TR were left-sided valve heart disease (VHD) and dilated cardiomyopathy. The survival rate of severe TR patients with pulmonary artery hypertension (PAH) was lower than in those without PAH ($p < 0.0001$). There was a positive association between the prevalence of TR and impaired left ventricular ejection fraction. Compared to the non-left-sided VHD

group, the left-sided VHD group had a better prognosis among severe TR patients. The 5-year survival rates were 79.69, 71.12, and 77.01% in the groups of left-sided VHD, non-left-sided VHD, and all patients. **Conclusions:** Patients with severe TR have a bad prognosis, especially those with non-left-sided VHD and those with PAH.

© 2019 S. Karger AG, Basel

Introduction

Tricuspid regurgitation (TR) means backflow of blood into the atrium when leaflets of the tricuspid valve do not coapt properly during ventricular systole. TR is frequent, and the detection rate is 80% in the population [1]. The pathogenesis is intricate because of the heterogeneity of etiology, and much research indicates that TR severity is related to pulmonary artery hypertension (PAH) and impaired left ventricular ejection fraction (LVEF) [2, 3]. Moderate to severe TR has usually been reported with a

Dr. Haiyan Chen and Dr. Wenzhi Pan contributed equally to this work with Dr. Lifan Yang.

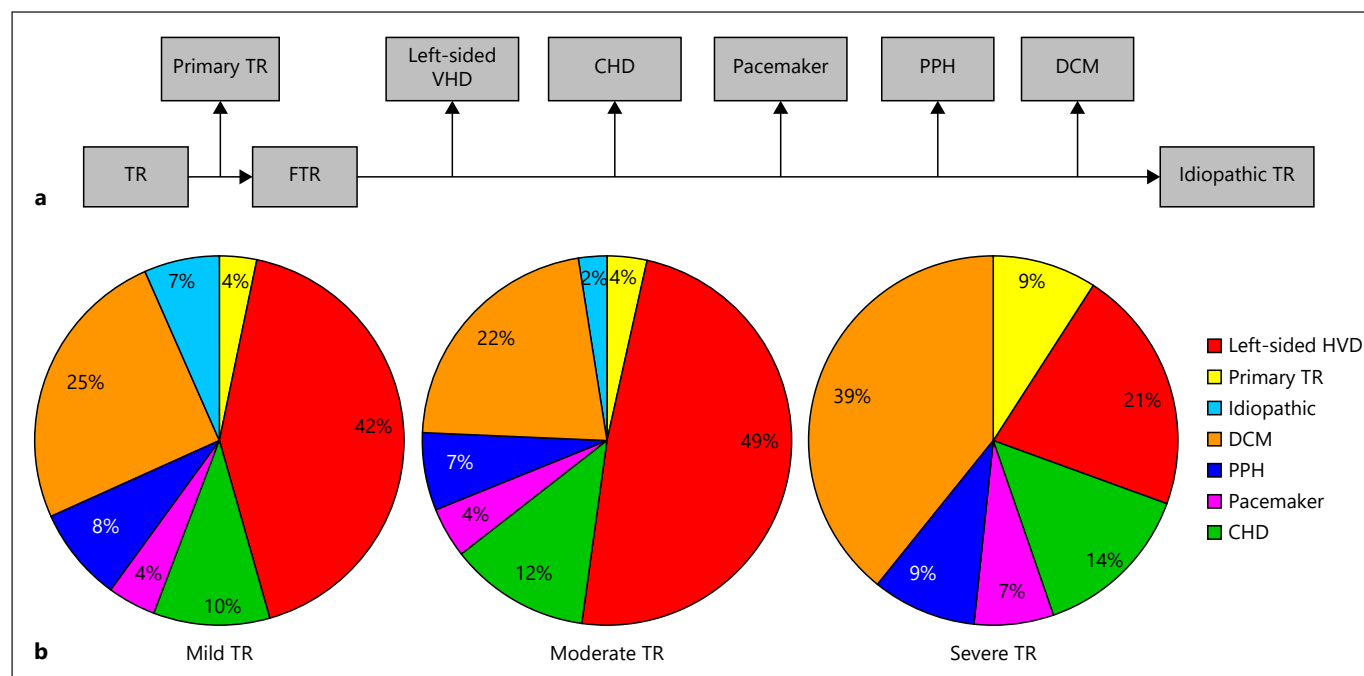


Fig. 1. **a** Analysis flowchart for etiological classification of TR. **b** Pie graphs of etiologies of TR.

poor prognosis [4]. The most effective treatment of TR is surgery, but little data indicates long-term survival of surgery. Furthermore, the mortality from surgery appears to be 8–9% [5]. With the development of interventional treatment for TR [6], tricuspid valve regurgitation has become a focus of interest in the world. Until now, little has been known about the prevalence and prognosis of TR in China. Therefore, the aim of this study was to examine the prevalence and outcome of TR in a large population.

Methods

The study was a retrospective analysis of a patient population. The detection rate of TR was surveyed in the whole population and subgroups. The etiologies of TR were analyzed. Finally, the 5-year survival rate of patients with severe TR was investigated. Clinical follow-up was obtained by telephone interviews. The time and diagnosis of death was determined by medical records and death certificates. The follow-up period started from the first echocardiography examination.

Patient Population

The study retrospectively analyzed the echocardiography database of the patients referred to Zhongshan Hospital, Fudan University, from January 2010 to December 2012. The database was described in our previous study [7]. Briefly, 82.16% of the patients were outpatients and 17.84% were inpatients. Patients who were

younger than 20 years or had poor echocardiographic images were excluded. The study was approved by the Biomedical Research Ethics Committee of the Zhongshan Hospital affiliated with Fudan University (B2013-105). The ethics committee waived the informed consent for retrospective analysis. Although this analysis was based on the echocardiography database, the major clinical diagnoses of the patients (such as post-heart surgery, cardiomyopathy, pacemaker implantation, etc.) could also be collected because these were also recorded in the echocardiography database at our center.

Echocardiography

Two-dimensional transthoracic echocardiograms (IE33/IU22, Philips) were used in the study. A total of 6 echocardiography doctors who had passed echocardiography certification performed echocardiography in the research. If echocardiographic examination was done more than once during the period of study, we used the first examination only. LVEF was measured by Simpson's method. At our center, qualitative TR assessment was mainly based on the central jet area, tricuspid valve leaflet anatomy, vena contracta, and hepatic venous flow pattern, according to recent American Society of Echocardiography guideline criteria (apical 4-chamber, parasternal right ventricular inflow, parasternal short axis, and subcostal views) [8]. Those with a jet area less than 5 cm² were graded as mild TR (+); and those with a jet area more than 10 cm², hepatic vein systolic blunting, and right ventricular, right atrium, and inferior vena cava dilated were classified as severe TR (3 to 4+). The signs of moderate TR (2+) were greater than mild but not enough to propose severe TR. Echocardiography was mainly used to determine the etiology of TR in our study.

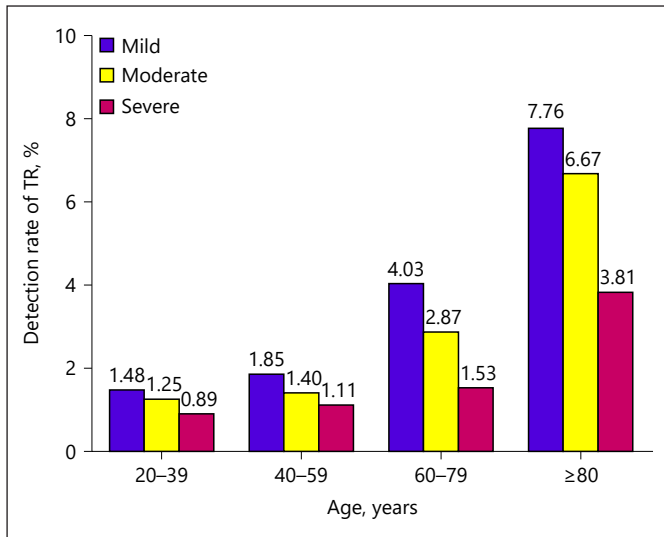


Fig. 2. Detection rates of different TR severity in different age groups.

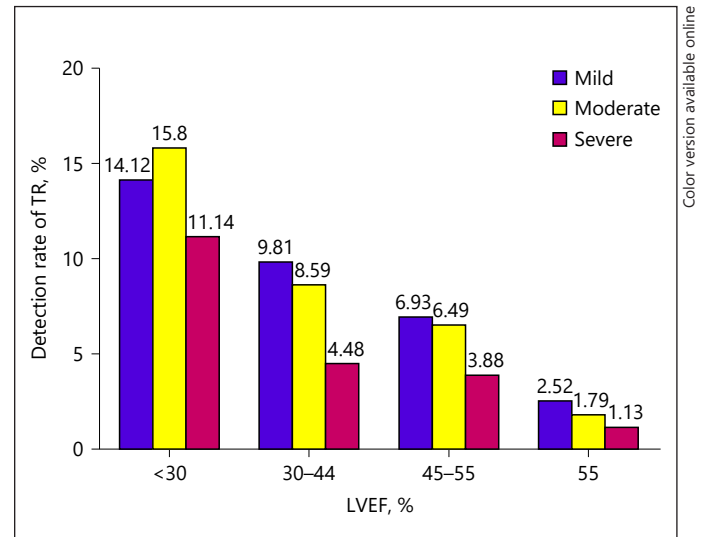


Fig. 3. Detection rates of different TR severity in groups divided by LVEF.

Etiology of TR

Mild, moderate, and severe TR was included in the study. Trace TR was excluded because it does not have clinical significance. The etiology of TR is complex because of confounding comorbidities. Patients were classified into 3 groups based on echocardiograms, including primary TR, functional TR (FTR), and unexplained TR, and the analysis flowchart is provided in Figure 1a. First, we collected primary TR cases that were attributed to structural abnormalities of the tricuspid valve, such as Ebstein's anomaly, rheumatic valve disease, carcinoid heart disease, and trauma. Thus, the FTR group remained. As commonly known, the major cause of FTR is left-sided valve heart disease (VHD) [9], so those cases were assigned to the second group. Many reports showed that the etiology of TR included atrial fibrillation, pacemaker leads, PAH, and dilated cardiomyopathy (DCM) [10, 11]. We continuously isolated congenital heart disease (CHD), postoperative pacemaker, primary pulmonary hypertension (PPH), and DCM in the aforementioned order. The former cause was adopted if the patient had 2 causes. Last, if the mentioned causes were not found, we classified those patients as having unexplained TR.

Patients with DCM presented with enlargement of the heart chamber and worse ventricular function resulting from hypertension, coronary heart disease, and myocarditis as well as from metabolic dysfunction, alcoholism, and other etiological cardiomyopathy in our study. Left-sided VHD indicated more than mild damage or post-surgery of mitral or aortic valves. CHD represented the congenital abnormality of structures of the heart without deformity of the tricuspid valve. Presence of a pacemaker indicated the patients who had an implant with a right ventricular pacing or defibrillating lead. PPH indicating idiopathic PAH (class I PAH according to the Nice classification) referred to the absence of secondary causes. PAH was defined as pulmonary systolic pressure more than 40 mm Hg, which was confirmed by the Bernoulli equation ($\Delta P = 4 \times v^2$), the maximal velocity of the TR jet area, allowing calculation of the pressure gradient between the right atrium and the right ventricle [12].

Idiopathic TR meant that no cause of the regurgitation could be identified [13]. The diagnosis of the etiology was based on the echocardiographic database recording the major clinical diagnosis of patients and was rechecked by the echocardiography report of the patients; this could provide tremendous information about the etiology.

Statistical Analysis

Statistical analyses were performed using SPSS version 22 (SPSS, Inc., Chicago, IL, USA), and continuous and categorical variables were presented as mean values \pm standard deviations and percentages, respectively. The rates of disease were compared by the χ^2 test. Logistic regression analyses were used to study the risk factors of TR. Survival curves were compared by the log-rank test. Cox regression analyses were used to study predictors of mortality from TR. Differences were considered statistically significant at the two-sided $p < 0.05$ level.

Results

A total of 134,878 cases were included in our study, and 8,872 patients had mild, moderate, or severe TR. The prevalence of TR in patients was as follows: 3,987 (2.96%) patients had a mild degree of TR (+), 3,015 (2.22%) patients had moderate TR (2+), and 1,870 (1.39%) patients had severe TR (3+/4+).

Age and Gender Related to the Prevalence of TR

The average age of TR and normal patients was 63.73 ± 15.75 and 55.60 ± 15.31 years, respectively. The detection rates of TR in different age groups are shown in Figure 2. The rate of TR rose significantly with increasing age (odds

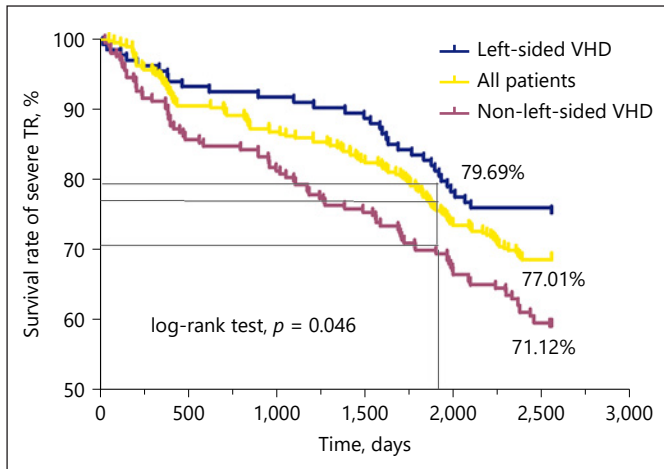


Fig. 4. Survival rates in all severe TR, left-sided VHD, and non-left-sided VHD subgroups. The 1-, 2-, 3-, 4-, and 5-year survival rates in all severe TR cases were 95.11, 91.95, 88.50, 82.76, and 77.01%. The survival rate in the left-sided VHD subgroup was higher than that in the non-left-sided VHD subgroups.

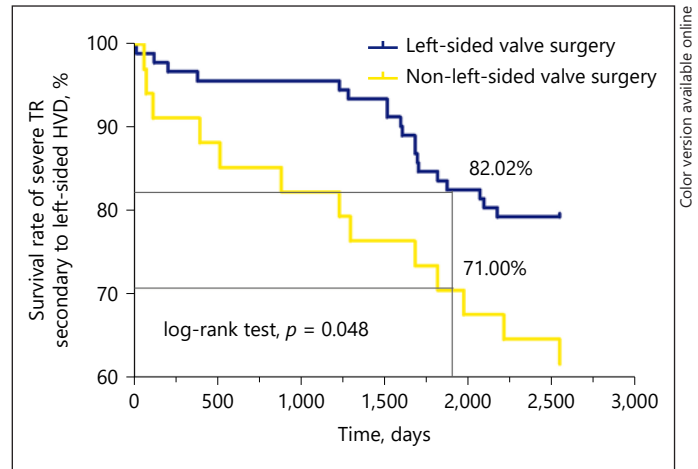


Fig. 5. Comparison of survival rates between left-sided valve surgery and non-left-sided valve surgery subgroups.

ratio [OR]: 1.038 for 1 year's increment; 95% confidence interval: 1.037–1.040; $p < 0.001$) and in females (OR: 1.386; 95% confidence interval: 1.327–1.448, $p < 0.001$).

Prevalence of TR in Different Etiologies

Generally, 431 patients (4.86%) had primary TR, 8,441 patients (91.41%) had FTR, and 331 patients (3.73%) had unexplained TR. The etiologies of TR are given in Figure 1b. The main etiologies of mild TR, moderate TR, and severe TR were left-sided VHD (42.0%), left-sided VHD (48.6%), and DCM (39.1%), respectively. The causes of severe FTR were DCM (39.1%), left-sided VHD (21.3%), CHD (14.2%), PPH (9.0%), and a pacemaker (6.9%). The causes of moderate FTR were left-sided VHD (48.6%), DCM (21.8%), CHD (12.4%), PPH (6.8%), and a pacemaker (4.4%).

Prevalence of PAH in TR

The prevalence of PAH in different etiologies of FTR is given in Table 1. Generally, the detection rates of PAH in primary TR and FTR were 45.71 and 52.23%, respectively. For primary TR, the prevalence of PAH in the mild, moderate, and severe TR groups was 16.71, 12.53, and 16.47% ($p > 0.05$), respectively. For FTR, the proportions of PAH in the mild, moderate, and severe TR groups were 44.92, 54.19, and 55.31%, respectively ($p < 0.001$). Left-sided VHD (23.25%) and DCM (21.23%) had the highest proportions of PAH in the moderate and severe FTR groups, respectively.

Table 1. Prevalence of pulmonary artery hypertension in different etiologies of FTR

| | Mild | Moderate | Severe |
|-------------------|-------|----------|--------|
| Left-sided VHD, % | 14.25 | 23.25 | 10.70 |
| CHD, % | 5.64 | 8.52 | 11.18 |
| Pacemaker, % | 1.23 | 1.89 | 3.16 |
| DCM, % | 14.07 | 13.76 | 21.23 |
| PPH, % | 9.73 | 6.77 | 9.04 |
| Total, % | 44.92 | 54.19 | 55.31 |

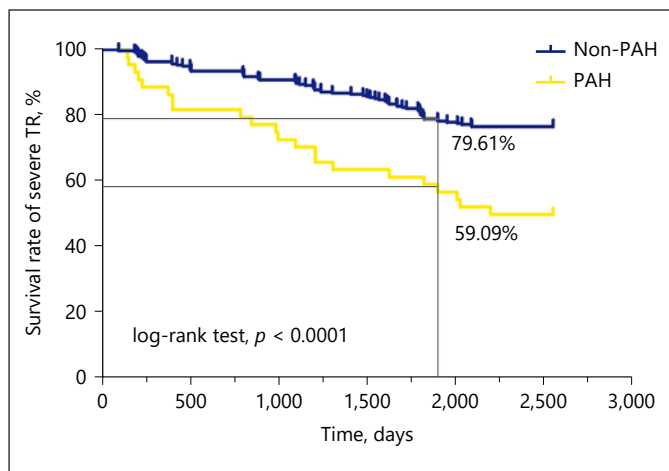
FTR, functional tricuspid regurgitation; VHD, valve heart disease; CHD, congenital heart disease; DCM, dilated cardiomyopathy; PPH, primary pulmonary hypertension.

Prevalence of TR in the Groups Divided by LVEF

The rates of TR in different severities in groups divided by LVEF are provided in Figure 3. The rates of severe TR in subjects with LVEF $< 30\%$, LVEF 30–44%, LVEF 45–55%, and LVEF $> 55\%$ were 11.14, 4.48, 3.88, and 1.13% ($p < 0.001$), respectively.

Survival Rates in Severe TR

Of 1,870 patients, we could stay in touch with 1,535 patients in the severe TR group, so the loss rate was 17.91%. The survival rate of patients with severe TR and its subgroups was analyzed. The 5-year survival rates were 79.69, 71.12, and 77.01% in the left-sided VHD group, non-left-sided VHD group, and all patients, respectively (Fig. 4). For severe TR, the survival rate in the



Color version available online

Fig. 6. Comparison of survival rates between PAH and non-PAH subgroups.

left-sided VHD group was higher than that in the non-left-sided VHD group.

In the left-sided VHD group, the survival rate in the left-sided valve surgery subgroup was higher than in the non-left-sided valve surgery subgroup (82.02 vs. 71.00%, $p = 0.048$; Fig. 5). In addition, the survival rate of severe TR patients with PAH was lower than in those without PAH (59.09 vs. 79.61%, $p < 0.0001$; Fig. 6).

Discussion

This is the first large-scale investigation to study the prevalence and outcome of TR in China, involving a total of 134,874 patients. The primary findings of the study are as follows: (1) the detection rates of mild TR (+), moderate TR (2+), and severe TR (3+/4+) were 2.96, 2.22, and 1.39%, respectively; (2) the rate of TR increased with age ($p < 0.001$, OR: 1.038), in females ($p < 0.001$, OR: 1.386), and with impaired LVEF; (3) the primary etiologies of TR were left-sided VHD and DCM; and (4) patients with severe TR had a bad prognosis, especially those with non-left-sided VHD or those with PAH.

The prevalence of mild TR, moderate TR (2+), and severe TR (3+/4+) was 2.96, 2.22, and 1.39%, respectively, in our study, while the Framingham Heart Study found that TR was detectable in 82.0% of men and in 85.7% of women among the general population in 1999 [1]. Behm et al. [14] found that TR was present in 80–90% of normal individuals in 2004. Our study did not include trace TR, which may be the reason for the inconsistency in the

prevalence of TR between our study and the other 2 studies. The time of study and the difference in subjects' races and in the operators who performed the echo studies may also have influenced the results.

The prevalence in our study, showing that 91.41, 4.86, and 3.73% of patients had FTR, primary TR, and idiopathic TR, agreed with Mutlak et al.'s [15] study, in 2007, indicating that 90.5 and 9.5% of patients had FTR and primary TR, respectively, whereas Behm et al.'s [14] study, in 2004, showed that 85.5 and 14.5% of patients had FTR and primary TR, respectively, and Ong et al.'s [16] study, in 2014, demonstrated that 79.7, 11.3, and 9% of patients had FTR, primary TR, and idiopathic TR, respectively. The differences in the results may be attributed to the population of TR or different compositions of the cohorts.

The previous studies found that female gender was associated with the prevalence of TR [16]. Our study supports this result and found that the prevalence of TR increased with age, which means that older people had greater odds of developing TR.

Findings on moderate TR, mainly resulting from left-sided VHD (48.6%), were consistent with many previous reports [17, 18]. The major cause of severe FTR was DCM (39.1%). This meant that left-sided VHD, the primary cause of moderate TR, was no longer the first cause as TR progressed. Some researchers indicated that severe TR was mainly related to pacemaker lead induction [9, 19, 20], whereas our study indicated that the rate of severe TR in subjects with implantation of a postoperative pacemaker was only 6.9%. Reasons for this might be the types of pacemakers used and the varied proficiency of the operators for pacemaker implantation procedures [13].

The rates of PAH in primary TR and secondary TR were 45.71 and 52.23%, respectively, in our study. PAH can cause right-ventricular enlargement and then lead to TR. On the contrary, severe TR can also cause PAH: significant TR has worse right-ventricular function, and this can cause elevation of left-ventricular filling pressures, which can cause elevation of pulmonary vein pressure and, finally, PAH [2]. In our study, for FTR, the rates of PAH in the groups of mild, moderate, and severe TR were 44.92, 54.19, and 55.31%, respectively ($p < 0.001$). This indicated that the prevalence rate of PAH was related to FTR severity, which was consistent with other studies [3, 21].

Studies showed that most TR cases result mainly from left-sided VHD and impaired LVEF (<50%) [9, 22]. Our study had a consistent result, which revealed that the prevalence of TR increased with impaired LVEF ($p < 0.001$), but Bar et al. [23] had a conflicting finding. They found that the poor prognosis of TR was associated with

preserved LVEF and PAH. Heart failure with preserved LVEF was characterized by impaired left-ventricular diastolic function, resulting from the rise in left-ventricular filling pressure, leading to a rise of PAH [2], so more attention should be paid to left-ventricular diastolic function in further research.

The 5-year survival rate of severe TR was 77.01% in our study, which was similar to the study of Topilsky et al. [24], which found a 5-year TR survival rate of 77.6%. Compared with left-sided valve heart surgery, the non-surgery subgroup had a worse prognosis. Although Bar et al. [23] thought that TR with left-sided heart valve procedures was not an independent correlate of survival and they could not identify any preoperative predictors [25], many other researchers found that preoperative TR severity and right-ventricular dysfunction were independently associated with survival after left-heart valve procedures [3, 26–28]. It is easily understood that PAH was a crucial predictor of long-term mortality from severe TR in our study.

Limitations

Our study has several limitations. First, the present study was undertaken at a single center, which may lead to a selection bias. However, our center is 1 of the 3 largest heart centers in China and treats patients from all over the nation. The sample size was large; thus, the results are representative. Second, the analysis was based on a patient population referred to our department, not on a community population. Thus, the rate of TR does not reflect the true epidemiological incidence. However, the results can still indicate that TR is relatively common in the patient population. Third, the data for the study mainly came from the echocardiography database. We may have obtained an incorrect etiology based only on echocardiography with a lack of clinical information. However, the major clinical diagnoses of the patients could also be collected in the echocardiography database at our center and were rechecked by the echocardiography reports.

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). *Am J Cardiol*. 1999 Mar;83(6):897–902.
- 2 Mascherbauer J, Kammerlander AA, Zotter-Tufaro C, Aschauer S, Duca F, Dalos D, et al. Presence of 'isolated' tricuspid regurgitation should prompt the suspicion of heart failure with preserved ejection fraction. *PLoS One*. 2017 Feb;12(2):e0171542.
- 3 Chen L, Larsen CM, Le RJ, Connolly HM, Pislaru SV, Murphy JG, et al. The prognostic significance of tricuspid valve regurgitation in pulmonary arterial hypertension. *Clin Respir J*. 2018 Apr;12(4):1572–1580.
- 4 Takahashi Y, Izumi C, Miyake M, Imanaka M, Kuroda M, Nishimura S, et al. Actual management and prognosis of severe isolated tricuspid regurgitation associated with atrial fibrillation without structural heart disease. *Int J Cardiol*. 2017 Sep;243:251–7.
- 5 Al-Hijji M, Fender EA, El Sabbagh A, Holmes DR. Current Treatment Strategies for Tricuspid Regurgitation. *Curr Cardiol Rep*. 2017 Sep;19(11):106.
- 6 Latib A, Mangieri A. Transcatheter Tricuspid Valve Repair: New Valve, New Opportunities, New Challenges. *J Am Coll Cardiol*. 2017 Apr; 69(14):1807–10.

Forth, the recent ESC/EACTS guidelines [29] stress the importance of tricuspid disease especially in patients with significant mitral valve disease, and the time for intervention of TR should be considered early. Our research found that severe TR patients with left-sided valve surgery have a better prognosis than those who did not accept left-sided valve surgery, which demonstrates the benefits of left-sided valve intervention. However, we did not explore interventions for TR because of a lack of clinical information in our echocardiography database.

Conclusion

TR is a relatively common heart disease. The elderly and females have a higher possibility to develop it. Our data provided comprehensive etiology factors for TR. Patients with severe TR have a bad prognosis, especially those with non-left-sided VHD or those with PAH.

Statement of Ethics

The study was approved by the Biomedical Research Ethics Committee of the Zhongshan Hospital affiliated with Fudan University (B2013-105). The ethics committee waived the informed consent for retrospective analysis.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

The study has received funding from the Shanghai Science and Technology Commission "Science and Technology Innovation Action Plan" Biomedical Science and Technology Support Project Guide (16441908100 and 16441901502).

- 7 Li J, Pan W, Yin Y, Cheng L, Shu X. Prevalence and correlates of mitral regurgitation in the current era: an echocardiography study of a Chinese patient population. *Acta Cardiol.* 2016 Feb;71(1):55–60.
- 8 Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, et al.; American Society of Echocardiography. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr.* 2003 Jul;16(7):777–802.
- 9 Yiu KH, Chen Y, Liu JH, Lin Q, Liu M, Wu M, et al. Burden and contributing factors associated with tricuspid regurgitation: a hospital-based study. *Hosp Pract (1995).* 2017 Dec;45(5):209–14.
- 10 Messing B, Porat S, Imbar T, Valsky DV, Anteby EY, Yagel S. Mild tricuspid regurgitation: a benign fetal finding at various stages of pregnancy. *Ultrasound Obstet Gynecol.* 2005 Nov;26(6):606–9.
- 11 Cheng R, Azarbal A, Currier J, Thomson LE, Hamilton MA, Esmailian F, et al. Tricuspid Regurgitation, the Forgotten Valvular Lesion-A Contemporary Review of Etiology, Prevalence, and Management Options. *Rev Cardiovasc Med.* 2015;16(3):171–81.
- 12 Schneider M, Pistrutto AM, Gerges C, Gerges M, Binder C, Lang I, et al. Multi-view approach for the diagnosis of pulmonary hypertension using transthoracic echocardiography. *Int J Cardiovasc Imaging.* 2018 May;34(5):695–700.
- 13 Fender EA, Zack CJ, Nishimura RA. Isolated tricuspid regurgitation: outcomes and therapeutic interventions. *Heart.* 2018 May;104(10):798–806.
- 14 Behm CZ, Nath J, Foster E. Clinical correlates and mortality of hemodynamically significant tricuspid regurgitation. *J Heart Valve Dis.* 2004 Sept;13(5):784–9.
- 15 Mutlak D, Lessick J, Reisner SA, Aronson D, Dabbah S, Agmon Y. Echocardiography-based spectrum of severe tricuspid regurgitation: the frequency of apparently idiopathic tricuspid regurgitation. *J Am Soc Echocardiogr.* 2007 Apr;20(4):405–8.
- 16 Ong K, Yu G, Jue J. Prevalence and spectrum of conditions associated with severe tricuspid regurgitation. *Echocardiography.* 2014 May;31(5):558–62.
- 17 Chan V, Burwash IG, Lam BK, Auyeung T, Tran A, Mesana TG, et al. Clinical and echocardiographic impact of functional tricuspid regurgitation repair at the time of mitral valve replacement. *Ann Thorac Surg.* 2009 Oct;88(4):1209–15.
- 18 Sagie A, Freitas N, Chen MH, Marshall JE, Weyman AE, Levine RA. Echocardiographic assessment of mitral stenosis and its associated valvular lesions in 205 patients and lack of association with mitral valve prolapse. *J Am Soc Echocardiogr.* 1997 Mar;10(2):141–8.
- 19 Delling FN, Hassan ZK, Piatkowski G, Tsao CW, Rajabali A, Markson LJ, et al. Tricuspid Regurgitation and Mortality in Patients With Transvenous Permanent Pacemaker Leads. *Am J Cardiol.* 2016 Mar;117(6):988–92.
- 20 Al-Bawardy R, Krishnaswamy A, Rajeswaran J, Bhargava M, Wazni O, Wilkoff B, et al. Tricuspid regurgitation and implantable devices. *Pacing Clin Electrophysiol.* 2015 Feb;38(2):259–66.
- 21 Huttin O, Voilliot D, Mandry D, Venner C, Juillièrè Y, Selton-Suty C. All you need to know about the tricuspid valve: tricuspid valve imaging and tricuspid regurgitation analysis. *Arch Cardiovasc Dis.* 2016 Jan;109(1):67–80.
- 22 Neuhold S, Huelsmann M, Pernicka E, Graf A, Bonderman D, Adlbrecht C, et al. Impact of tricuspid regurgitation on survival in patients with chronic heart failure: unexpected findings of a long-term observational study. *Eur Heart J.* 2013 Mar;34(11):844–52.
- 23 Bar N, Schwartz LA, Biner S, Aviram G, Ingbir M, Nachmany I, et al. Clinical Outcome of Isolated Tricuspid Regurgitation in Patients with Preserved Left Ventricular Ejection Fraction and Pulmonary Hypertension. *J Am Soc Echocardiogr.* 2018 Jan;31(1):34–41.
- 24 Topilsky Y, Nkomo VT, Vatury O, Michelena HI, Letourneau T, Suri RM, et al. Clinical outcome of isolated tricuspid regurgitation. *JACC Cardiovasc Imaging.* 2014 Dec;7(12):1185–94.
- 25 Toyama K, Ayabe K, Kar S, Kubo S, Minamishima T, Rader F, et al. Postprocedural Changes of Tricuspid Regurgitation After MitraClip Therapy for Mitral Regurgitation. *Am J Cardiol.* 2017 Sep;120(5):857–61.
- 26 Kammerlander AA, Marzluft BA, Graf A, Bachmann A, Kocher A, Bonderman D, et al. Right ventricular dysfunction, but not tricuspid regurgitation, is associated with outcome late after left heart valve procedure. *J Am Coll Cardiol.* 2014 Dec;64(24):2633–42.
- 27 Antunes MJ, Rodríguez-Palomares J, Prendergast B, De Bonis M, Rosenhek R, Al-Attar N, et al.; ESC Working Groups of Cardiovascular Surgery and Valvular Heart Disease. Management of tricuspid valve regurgitation: Position statement of the European Society of Cardiology Working Groups of Cardiovascular Surgery and Valvular Heart Disease. *Eur J Cardiothorac Surg.* 2017 Dec;52(6):1022–30.
- 28 Mohammed SF, Hussain I, AbouEzzeddine OF, Takahama H, Kwon SH, Forfia P, et al. Right ventricular function in heart failure with preserved ejection fraction: a community-based study. *Circulation.* 2014 Dec;130(25):2310–20.
- 29 Falk V, Baumgartner H, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur J Cardiothorac Surg.* 2017 Oct;52(4):616–64.