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## Clinical outcomes of tricuspid valve repair accompanying left-sided heart disease

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## Retrospective Study

**Clinical outcomes of tricuspid valve repair accompanying left-sided heart disease**

Kasra Azarnoush, Ahmad S Nadeemy, Bruno Pereira, Massoud A Leesar, Céline Lambert, Alaa Azhari, Vedat Eljezi, Nicolas Dauphin, Etienne Geoffroy, Lionel Camilleri

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**Author contributions:** Azarnoush K and Nadeemy AS designed and performed the research and wrote the paper; Pereira B and Lambert C did the statistic and data evaluation; Dauphin N and Geoffroy E performed all echocardiography concerning study patients; Leesar MA, Azhari A, Eljezi V and Camilleri L supervised the report and the manuscript and gave the final approval.

**Institutional review board statement:** The study was reviewed and approved by the Clermont-Ferrand University Hospital research unit, the “Délégation à la Recherche Clinique et à l’Innovation (DRCI)” and all statistical analyses were overseen by an independent Biostatistics unit.

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**Conflict-of-interest statement:** All authors declare having no conflicts of interest.

**Data sharing statement:** The statistical methods and original anonymous dataset are available on request from the corresponding author at [kazarnoush@chu-clermontferrand.fr](mailto:kazarnoush@chu-clermontferrand.fr).

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**Abstract****AIM**

To determine whether the need for additional tricuspid valve repair is an independent risk factor when surgery is required for a left-sided heart disease.

**METHODS**

One hundred and eighty patients ( $68 \pm 12$  years, 79 males) underwent tricuspid annuoplasty. Cox proportional-hazards regression model for multivariate analysis was performed for variables found significant in univariate analyses.

**RESULTS**

Tricuspid regurgitation etiology was functional in 154 cases (86%), organic in 16 cases (9%), and mixed in

10 cases (6%), respectively. Postoperative mortality at 30 days was 11.7%. Mean follow-up was 51.7 mo with survival at 5 years of 73.5%. Risk factors for mortality were acute endocarditis [hazard ratio (HR) = 9.22 (95%CI: 2.87-29.62),  $P < 0.001$ ], ischemic heart disease requiring myocardial revascularization [HR = 2.79 (1.26-6.20),  $P = 0.012$ ], and aortic valve stenosis [HR = 2.6 (1.15-5.85),  $P = 0.021$ ]. Significant predictive factors from univariate analyses were double-valve replacement combined with tricuspid annuloplasty [HR = 2.21 (1.11-4.39),  $P = 0.003$ ] and preoperatively impaired ejection fraction [HR = 1.98 (1.04-3.92),  $P = 0.044$ ]. However, successful mitral valve repair showed a protective effect [HR = 0.32 (0.10-0.98),  $P = 0.046$ ]. Additionally, in instances where tricuspid regurgitation required the need for concomitant tricuspid valve repair, mortality predictor scores such as Euroscore 2 could be shortened to a simple Euroscore-tricuspid comprised of only 7 inputs. The explanation may lie in the fact that significant tricuspid regurgitation following left-sided heart disease represents an independent risk factor encompassing several other factors such as pulmonary arterial hypertension and dyspnea.

### CONCLUSION

Tricuspid annuloplasty should be used more often as a concomitant procedure in the presence of relevant tricuspid regurgitation, although it usually reveals an overly delayed correction of a left-sided heart disease.

**Key words:** Tricuspid regurgitation; Patient outcome assessment; Valvular annuloplasty; Infective endocarditis; Mitral valve annuloplasty

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**Core tip:** Tricuspid valve repair with flexible ring is easy to achieve in patients undergoing heart surgery. Predictor scores such as Euroscore 2 could be shortened to a simple Euroscore-tricuspid of only 7 inputs. A significant tricuspid regurgitation following a left-sided heart disease is an independent risk factor that encompasses several other factors such as pulmonary arterial hypertension and dyspnea. Patients with functional damage of the right side of the heart and significant functional tricuspid regurgitation have poor mid-term results with high mortality. A concomitant tricuspid regurgitation usually reveals a delayed correction of a left-sided heart disease.

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### INTRODUCTION

The concomitant correction of functional tricuspid regur-

gitation secondary to left heart disease requiring surgery remains underused<sup>[1]</sup> despite recent data showing late development of severe tricuspid regurgitation in patients with mild regurgitation at the time of cardiac procedures (e.g., mitral valve surgery)<sup>[2]</sup>. Several factors including pulmonary arterial hypertension, right ventricular dilatation, increased tricuspid annulus diameter and the occurrence of right-sided heart failure promote persistent or even deteriorating functional tricuspid insufficiency<sup>[3,4]</sup>. Associated tricuspid regurgitation is present in almost 50% of patients undergoing mitral-valve surgery<sup>[5]</sup>. Most patients presenting with significant tricuspid regurgitation suffer from functional regurgitation due to dilatation of the tricuspid annulus, caused by dilatation of the right ventricle<sup>[6]</sup>.

Rare organic tricuspid insufficiencies may be secondary to iatrogenic injury (*i.e.*, pacing leads), or of rheumatic, infectious, congenital or carcinoid origin<sup>[7]</sup>.

Data on concomitant tricuspid valve annuloplasty are rare and usually focus on different techniques for repair. A recent review seemingly demonstrated evidence for tricuspid annuloplasty to be a low-risk procedure<sup>[8]</sup>. However, as highlighted in the present work, a concomitant tricuspid regurgitation reveals a delayed correction of left-sided heart disease. Our data demonstrate that standard Euroscore 2 mortality risk factors such as gender, pulmonary hypertension, renal impairment or weight of the intervention should no longer be taken into account when significant tricuspid regurgitation appears prior to surgery of left-sided heart disease and the need for tricuspid repair becomes an independent mortality risk factor.

The present study aimed to confirm that the need of concomitant tricuspid annuloplasty according to guidelines represents a far too late treatment. Patients should be addressed to heart surgery centers for an early correction of the left-side heart disease before the need of additional tricuspid valve repair procedure.

### MATERIALS AND METHODS

All patients undergoing concomitant tricuspid valve annuloplasty between January 2005 and December 2009 were included in this retrospective, single-center study. The study was approved by the local ethics committee and all patients gave their written informed consent for the procedure as well as for inclusion in this retrospective study<sup>[9]</sup>.

All surgeries were performed using full median sternotomy and extracorporeal circulation with cardiac arrest using blood cardioplegia. Tricuspid annuloplasty was performed either with a De Vega tricuspid repair<sup>[10]</sup>, a flexible Sovering® ring (Sorin Biomedica Cardio S.r.l., Saluggia, Italy) sized 26 to 36 mm<sup>[11]</sup>, or a flexible Bex® linear reducer (Gamida, France)<sup>[12]</sup>, respectively. If necessary, annuloplasty was combined with concomitant procedures to the tricuspid valve such as resection of vegetations in case of endocarditis, implantation of artificial chords or tricuspid pillar reinsertion in case of prolapse.

**Table 1** Characteristics and cardiovascular risk factors of the study patients

	<i>n</i> (%)
Age (yr)	68.3 ± 12.4
Gender	
Female	101 (56)
Male	79 (44)
Dyspnea (New York Heart Association)	
Class I	7 (4)
Class II	25 (14)
Class III	125 (69)
Class IV	23 (13)
Cardiac rhythm	
Sinus rhythm	77 (43)
Atrial fibrillation	87 (48)
Branch block	40 (22)
Pacemaker	16 (9)
Risk factors	
Arterial hypertension	79 (44)
Hypercholesterolemia	77 (43)
Tobacco	44 (24)
Diabetes	42 (23)
Lower limb or supra-aortic obstructive arteriopathy	20 (11)
Pulmonary disease	25 (14)
Cerebrovascular accident or transient ischemic attack	19 (11)
Rheumatic valve disease	40 (22)
Myocardial infarction	12 (7)
Pacemaker implantation	16 (9)
Reoperation	26 (14)
Other heart disease	
Aortic regurgitation	19 (11)
Aortic stenosis	30 (17)
Combined aortic stenosis/regurgitation	15 (8)
Mitral regurgitation	99 (55)
Mitral stenosis	21 (12)
Combined mitral stenosis/regurgitation	21 (12)
Pulmonary valve regurgitation	1 (0.6)
Coronary artery disease	28 (16)
Acute endocarditis	9 (5)
Interventricular or interatrial septal defect	3 (1.7)

The patients' health status was obtained through a questionnaire submitted to the cardiologist, to the attending physician or, in the absence of the latter, by interviewing the patient or his/her relatives by phone (if the patient was deceased).

### Statistical analysis

Data are presented as the mean ± SD for continuous data and as the number of patients and associated percentages for categorical parameters. Cox proportional-hazards regression model was performed to evaluate the impact of several covariates on mortality in a multivariate context and define prognostic factors (using a stepwise backward and forward algorithm, from variables with a  $P < 0.10$  in univariate analyses) according to the results of univariate analysis and clinical relevance.

All analyses were conducted using Stata v12® (Stata Corp, College Station, United States). The tests were two-sided, with a type I error set at  $\alpha = 0.05$  (except for multiple comparisons).

## RESULTS

Between January 2005 and December 2009, a total 180 consecutive patients underwent tricuspid valve annuloplasty in our institution. During the same period, another 3 patients underwent isolated tricuspid valve replacement and were not included in the present study. Among the 180 included patients, there were 79 males (44%) and 101 females (56%). Age ranged from 12 to 89 years; mean age was  $68.3 \pm 12.4$  years (Table 1).

Tricuspid valve regurgitation etiology was classified as functional in 154 cases (86%), organic in 16 cases (9%) and mixed in 10 cases (6%). In instances of functional tricuspid regurgitation, the main cause was degenerative mitral valve disease. In instances of organic tricuspid regurgitation, the predominant pathologies were rheumatism disease and infectious endocarditis, 9 of which required urgent surgery for acute endocarditis (Table 1).

Ninety-seven patients (45%) suffered from at least one heart failure episode, 22 with left-sided HF, 15 with right-sided HF, and 60 with global heart failure, respectively. Eighty-five patients (47%) suffered from persistent atrial fibrillation preoperatively. Further cardiovascular risk factors of the study patients are summarized in Table 1, along with preoperative echocardiographic findings in Table 2.

Tricuspid annuloplasty with a prosthetic ring was performed in 176 patients; a Sovering® ring was used in 156 cases and a Bex® linear reducer in 20 cases. In 20 cases, annuloplasty was combined with concomitant procedures for tricuspid valve: Valve repair (leaflet slit or cleft closure), vegetation resection, implantation of a Gore-Tex® cord, and one tricuspid pillar reinsertion for iatrogenic tricuspid incompetence as a consequence of pacemaker lead removal. Four 4 De Vega tricuspid repairs were performed while the remaining procedures consisted of the following: Aortic valve replacement in 29 cases (16%), mitral valve replacement in 67 cases (37%), double mitro-aortic valvular replacement in 42 cases (23%), mitral valve repair in 38 cases (21%), pulmonary valve replacement in one case (0.6%), coronary artery bypass grafting in 26 cases (14%), and other procedures in 21 cases. Only 9 patients (5%) underwent surgery for isolated tricuspid regurgitation. These patients presented with preoperative grade III or IV tricuspid incompetence. Three of these patients had a previous history of mitral or aortic valvular surgery, with tricuspid insufficiency appearing within two years postoperatively. Two of these patients had a preoperative pulmonary artery hypertension with peak gradients over 60 mmHg at their first operation. The other five patients did not present any associated left-sided heart disease.

Mean hospital stay was  $17.8 \pm 19.3$  d (range 2 to 165 d). Postoperative complications were reoperation for bleeding in 15 cases (8%) and one postoperative stroke. A total of 21 patients (11.7%) died within 30 d.

**Table 2** Preoperative and postoperative characteristics of the study patients

	mean $\pm$ SD	n (%)
Preoperative parameter		
Left ventricular ejection fraction (%)	58.6 $\pm$ 12.5	
Systolic pulmonary arterial pressure (mmHg)	58.0 $\pm$ 16.7	
Tricuspid regurgitation		
I		9 (5)
II		69 (38)
III		70 (39)
IV		32 (18)
Left ventricular end-diastolic diameter (mm)	52.7 $\pm$ 9.5 (29-74)	
Left ventricular end-systolic diameter (mm)	34.4 $\pm$ 9.3 (17-63)	
Postoperative parameter		
Left ventricular ejection fraction (%)	54.4 $\pm$ 12.2 (10-82)	
Systolic pulmonary arterial pressure (mmHg)	38.6 $\pm$ 10.6 (19-76)	
Tricuspid regurgitation		
0- I		150 (83)
II		28 (15)
III		1 (0.6)
IV		1 (0.6)
Left ventricular end-diastolic diameter (mm)	50.4 $\pm$ 7.4	
Left ventricular end-systolic diameter (mm)	35.2 $\pm$ 8.3	

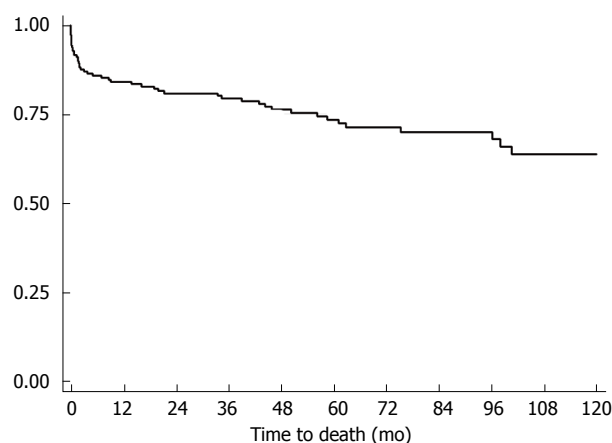
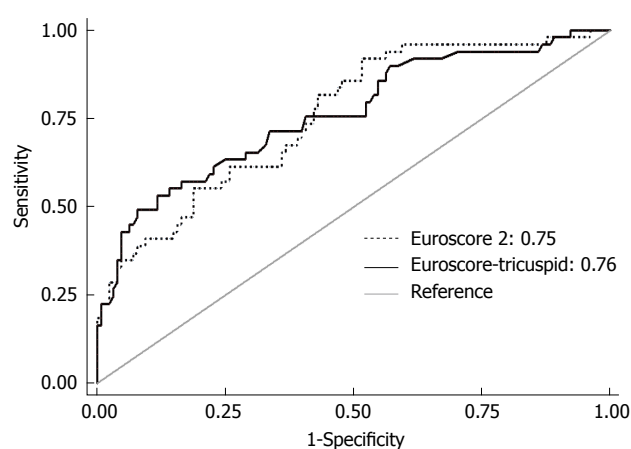
The main causes of death were multi-organ failure in 20 cases, two of whom were from massive bleeding, and one unexplained sudden death.

All patients underwent early postoperative echocardiography, demonstrating marked reduction in both tricuspid insufficiency and in systolic pulmonary artery pressure (Table 2).

Among hospital survivors, two patients (1%) were lost at follow-up, the initial analysis thus resulting in a 99% follow-up. Data from these two patients were subsequently collected in 2014. One patient living in Kathmandu returned for a control cardiology visit in our university hospital and the second patient had a control consultation in the thoracic surgery department in Clermont-Ferrand, allowing us to complete the initial follow-up. Mean follow-up was 51.7  $\pm$  39 mo with 5-year survival at 73.5% and 10-year survival at 63.8% (Figure 1). The main cause of death during the follow-up was heart failure. Only one tricuspid valve repair failed. Eight patients had a cerebrovascular event during the study period and seven patients presented with a late complete atrioventricular block requiring pacemaker implantation.

Univariate and multivariate analyses and parameters affecting global mortality (in-hospital and post-discharge) are detailed in Tables 3 and 4.

Of note, there was no significant correlation between death and several Euroscore factors such as gender, pulmonary hypertension, NYHA dyspnea level, chronic lung disease, renal impairment or weight of the intervention (Table 3). From multivariate analyses (Table 4), the adverse factors for mortality were the presence

**Figure 1** Overall patient survival.**Figure 2** ROC curve comparing Euroscore 2 and Euroscore-tricuspid.

of acute endocarditis, ischemic heart disease that required myocardial revascularization, and aortic valve stenosis, respectively. In contrast, a successful mitral valve repair appeared to have a protective effect.

When taking into account a tricuspid valve regurgitation requiring an additional tricuspid valve repair accompanying a left-sided heart disease surgery, the 18 predictive risk factors of Euroscore 2 could be reduced to a Euroscore-tricuspid of only 7 factors with an at least equivalent statistical power (Figure 2). This new Euroscore-tricuspid would require only the following patient data: Age, ischemic heart disease, insulin-treated diabetes, previous cardiac surgery (redo intervention), active endocarditis, critical preoperative state and left ventricle function less than 50%.

## DISCUSSION

Both the current American and European guidelines recommend correction of relevant functional tricuspid insufficiency if other cardiac diseases are corrected surgically<sup>[4,7]</sup> since functional tricuspid regurgitation, a frequent finding in patients undergoing cardiac surgery for other reasons<sup>[5]</sup>, has proven to increase over time when not corrected during first surgery<sup>[2]</sup>, mainly due to



**Table 3** Univariate analyses: Parameters affecting global mortality

Variable	n (%)	Univariate HR	P
Gender (male)	79 (44)	1.38 [0.77–2.44]	0.27
Age ( $\geq$ 75 yr)	63 (35)	1.75 [0.98–3.11]	0.06
Tobacco use	44 (24)	1.16 [0.60–2.24]	0.66
Pulmonary disease	25 (14)	1.58 [0.74–3.40]	0.24
Pacemaker	16 (9)	2.40 [1.12–5.13]	0.02
Branch block	40 (22)	1.88 [1.01–3.47]	0.04
Previous heart failure	75 (42)	1.67 [0.94–2.95]	0.08
Ejection fraction ( $>$ 50%)	132 (73)	0.49 [0.25–0.98]	0.044
Hypertension	79 (44)	1.81 [1.01–3.20]	0.04
Diabetes on insulin	8 (4)	2.33 [0.83–6.51]	0.11
Aortic regurgitation	19 (11)	0.52 [0.16–1.67]	0.27
Aortic disease	15 (8)	1.29 [0.51–3.26]	0.59
Mitral regurgitation	99 (55)	1.01 [0.56–1.79]	0.98
Mitral stenosis	21 (12)	0.96 [0.38–2.44]	0.93
Mitral disease	21 (12)	0.55 [0.19–1.54]	0.26
Dyslipidemia	77 (43)	0.88 [0.49–1.57]	0.67
NIDD	34 (19)	1.31 [0.64–2.64]	0.45
Cerebrovascular accident	19 (11)	1.44 [0.60–3.40]	0.41
Myocardial infarction	12 (7)	1.70 [0.67–4.30]	0.26
New York Heart Association (III/IV)	148 (82)	1.99 [0.78–5.04]	0.14
Redo vs Tridux	26 (14)	1.49 [0.74–3.00]	0.26
Double valve replacement associated with tricuspid repair	43 (24)	2.21 [1.11–4.39]	0.024
Sinus rhythm	77 (43)	0.74 [0.41–1.35]	0.33
Sovering ring	156 (87)	1.10 [0.49–2.46]	0.81
Bex device	20 (11)	1.16 [0.52–2.60]	0.71
Systolic pulmonary artery pressure ( $>$ 59 mmHg)	98 (54)	1.06 [0.60–1.88]	0.83
Systolic pulmonary artery pressure ( $>$ 49 mmHg)	31 (17)	1.16 [0.56–2.40]	0.69
Tricuspid annulus diameter ( $>$ 40 mm)	20 (11)	0.31 [0.07–1.27]	0.10
Postoperative ejection fraction ( $>$ 50%)	98 (66)	2.58 [1.31–5.08]	0.006

HR: Hazard ratio.

**Table 4** Prognostic factors for mortality in multivariate analyses

Variable	n (%)	Univariate		Multivariate	
		HR	P	HR	P
Aortic stenosis	30 (17)	2.69 [1.24–5.42]	0.011	2.60 [1.15–5.85]	0.021
Coronary disease	28 (16)	4.12 [2.06–8.21]	$<$ 0.001	2.79 [1.26–6.20]	0.012
Mitral-valve repair	38 (21)	0.27 [0.08–0.88]	0.03	0.32 [0.10–0.98]	0.046
Infective endocarditis	9 (5)	5.06 [1.7–14.62]	0.003	9.22 [2.87–29.62]	$<$ 0.001

HR: Hazard ratio.

progressive annular dilatation<sup>[3]</sup>. However, although factors influencing the natural course of tricuspid regurgitation over time<sup>[4]</sup> and even during long-term follow-up of over 5 years<sup>[13]</sup> as well as its deleterious effect on mortality<sup>[14]</sup> are well known, its concomitant correction has yet to be performed to an adequate extent<sup>[1]</sup>. In the present study, the conducting of a successful mitral valve repair was found to be a protective factor when tricuspid annuloplasty was performed in patients with significant mitral regurgitation.

Acute endocarditis, associated ischemic heart disease and double valve replacement combined with tricuspid regurgitation were the main risk factors for hospital mortality in this study. Surprisingly, there was no correlation between elevated pulmonary arterial pressure, advanced age, preexisting arrhythmias and mid-term mortality results as conversely reported by

others<sup>[15]</sup>.

The 11.7% hospital mortality rate observed herein, mainly driven by multi-organ failure, is a reflection of the high rate of concomitant procedures. Other studies have reported hospital mortality rates of up to 35% in patients undergoing tricuspid valve repair as a concomitant procedure to other cardiac surgery<sup>[16,17]</sup>.

The use of a flexible ring represented the technique of choice in the present series. Easy implantation, avoidance of a suture close to the conduction system, measured reduction of the tricuspid annulus and preservation of the valve's normal physiological shape are among the related advantages of this approach<sup>[18]</sup>. For dilatation of the tricuspid annulus, annuloplasty alone provides excellent results in the absence of valvular or subvalvular disease<sup>[3]</sup>; however, it is no longer effective in correcting tricuspid regurgitation if there is also damage

of the leaflets and of the subvalvular apparatus, and/or in instances where additional procedures are required<sup>[18,19]</sup>. Accordingly, less-than-moderate tricuspid regurgitation prior to discharge after tricuspid annuloplasty during redo valve surgery additionally proved to be an independent risk factor for better long-term outcome in terms of survival in a recent retrospective analysis<sup>[20]</sup>. Furthermore, concomitant tricuspid annuloplasty using flexible bands offered improved durability as compared to suture annuloplasty for preventing postoperative tricuspid regurgitation progression in two retrospective comparative analyses<sup>[21,22]</sup>. In the current series, 20 patients underwent a concomitant valvular or subvalvular procedure, without any added mortality or morbidity.

Recent clinical studies have demonstrated that moderate to severe residual tricuspid regurgitation still persists in 10% of patients who have undergone surgical repair<sup>[18]</sup>. Tricuspid regurgitation is related to the degree of limited leaflet motion and to the severity of the dilatation of the tricuspid annulus. The severity of preoperative tricuspid regurgitation, together with right ventricular dysfunction, contributes to postoperative residual insufficiency. Risk factors for recurrent tricuspid regurgitation are preoperative severe regurgitation, tricuspid repair without a prosthetic ring or with an oversized ring (large tricuspid valve), pacemaker catheters that pass through the tricuspid valve, mitral valve replacement rather than mitral repair, left ventricular dysfunction associated or not with advanced remodelling, cardiomegaly and atrial fibrillation<sup>[19]</sup>.

Finally and surprisingly, we found that mortality predictor scores such as Euroscore 2 could be shortened to a simple Euroscore-tricuspid of only 7 inputs. From our standpoint, the explanation may reside in the fact that significant tricuspid regurgitation following a left-sided heart disease is an independent risk factor encompassing several other factors such as pulmonary arterial hypertension and dyspnea. Such finding has been reported in several studies of other diseases with regard to aortic and mitral valve diseases which also corroborate the present data embodying multiple diseases at once<sup>[23-25]</sup>.

The present study demonstrates the efficacy and durability of tricuspid annuloplasty with an open flexible ring. This procedure may be performed in patients with severe left-sided valve disease. Patients with functional damage of the right side of the heart combined with significant functional tricuspid regurgitation have poor mid-term results along with high mortality. A concomitant tricuspid regurgitation typically reveals a delayed correction of left-sided heart disease.

## COMMENTS

### Background

The concomitant correction of functional tricuspid regurgitation secondary to left heart disease requiring surgery remains underused and an associated functional tricuspid regurgitation typically reveals a delayed correction of left-sided heart disease.

### Research frontiers

Functional tricuspid valve regurgitation concerns patients who are referred

to heart surgery for left-sided heart disease too late. Results of this study contribute to clarify these patients' clinical situation.

### Innovations and breakthroughs

In this study, when a tricuspid regurgitation required the need for concomitant tricuspid valve repair, mortality predictor scores such as Euroscore 2 could be shortened to a simple Euroscore-tricuspid comprised of only 7 inputs. The explanation may lie in the fact that significant tricuspid regurgitation following left-sided heart disease represents an independent risk factor encompassing several other factors such as pulmonary arterial hypertension and dyspnea.

### Applications

The present study demonstrates the efficacy and durability of tricuspid annuloplasty with an open flexible ring.

### Peer-review

The study aimed the need of concomitant tricuspid annuloplasty for an early correction of the left-side heart disease. The author conducted retrospective multivariate analysis for significant variables in univariate analyses in 180 cases with tricuspid annuloplasty. The 5-10 years follow-up observation find out the risk factors for mortality were acute endocarditis, ischemic heart disease requiring myocardial revascularization, and aortic valve stenosis. Significant predictive factors from univariate analyses were double-valve replacement combined with tricuspid annuloplasty and preoperatively impaired erection fraction. The author concluded that tricuspid annuloplasty should be used more often as concomitant procedure if relevant tricuspid regurgitation is present. The study suggests that the predictor scores could be shorten to a simple Euroscore-tricuspid of only 7 inputs. Functional tricuspid regurgitation may be frequently found in patients undergoing cardiac surgery from other reasons. It will become more severe over time if not corrected during first surgery. It is significant to have a investigation on the outcomes of tricuspid valve repair accompanying left-sided heart disease surgery. This manuscript retrospectively investigated this topic, discussed the advantages of the correction surgery at the same time, analyzed the risk factors and concluded to simplify using the predictive factors.

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