Characterization of tricuspid regurgitation and its prognostic implications

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Chapter 4

Long-term impact of preventive tricuspid valve annuloplasty on right ventricular remodeling

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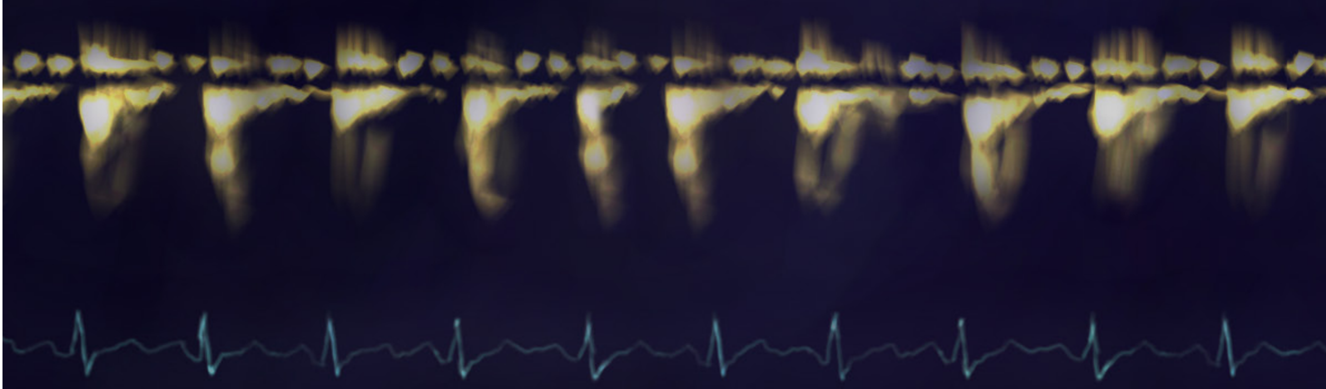

ABSTRACT

Background: In patients with primary mitral regurgitation (MR), concomitant tricuspid valve (TV) annuloplasty at the time of left-sided valve surgery is indicated in case of a dilated TV annulus ≥40 mm independent of the presence or severity of tricuspid regurgitation (TR). However, the long-term impact on right ventricular (RV) adverse remodeling is less well established and the benefit of preventive TV annuloplasty remains controversial. The aim of the study was to assess differences in long-term RV adverse remodeling and the development of significant TR in those patients.

Methods: In total, 98 patients (mean age 65±11 years, 85% male) with significant primary MR and TV annulus dilatation ≥40 mm without significant TR who underwent mitral valve (MV) repair with or without concomitant TV annuloplasty were included. Of the 98 patients, 28 patients underwent isolated MV repair without TV annuloplasty and 70 patients received concomitant TV annuloplasty at the time of MV surgery.

Results: The RV basal diameter (p=0.03), RV long axis diameter (p=0.04), RV end-diastolic area (p<0.01) and RV end-systolic area (p=0.03) showed less adverse remodeling at follow-up in patients with concomitant TV annuloplasty compared to patients without TV annuloplasty. Additionally, 4 patients (14%) in the subgroup without TV annuloplasty developed significant TR during follow-up in contrast to 0 patients in the subgroup with TV annuloplasty (p=0.001).

Conclusion: Concomitant preventive TV annuloplasty during mitral valve surgery in patients with primary MR, no significant TR and a tricuspid annulus (≥40 mm), prevented RV adverse remodeling and the development of significant TR at long-term follow-up.

INTRODUCTION

Secondary tricuspid regurgitation (TR) in patients with concomitant left-sided valve disease was initially thought to decrease or even resolve once surgery had corrected the primary left-sided problem (1). However, patients with increased right ventricular (RV) afterload due to left-sided heart valve disease may develop a vicious circle of tricuspid valve (TV) annulus dilatation, worsening TR and adverse RV remodeling (2). Studies have shown that a conservative approach of a dilated TV annulus without significant TR (<2+) during left-sided valve surgery does not stop the progression of this process: up to one-third of patients develop late significant TR after mitral valve (MV) surgery if the dilated annulus is not addressed (3). Significant TR and the associated RV adverse remodeling is associated with poor prognosis (4). Additionally, surgical intervention in patients with late isolated TR can be a high-risk procedure with high morbidity and mortality (5). Accordingly, current guidelines recommend concomitant TV annuloplasty at the time of left-sided valve surgery in patients with a dilated TV annulus of ≥40 mm independent of the presence or severity of TR (6). Although various studies have confirmed reduction of TR after this procedure, the long-term impact on RV adverse remodeling and clinical outcomes is less well established and the benefit of preventive TV annuloplasty remains controversial (7-10). Therefore, the aim of the current study was to assess differences in long-term RV adverse remodeling and clinical outcomes in patients with significant primary mitral regurgitation (MR) and TV annulus dilatation ≥40 mm without significant TR who underwent MV surgery with versus without concomitant preventive TV annuloplasty.

4

METHODS

Patients who underwent MV repair for primary MR due to fibro-elastic deficiency or Barlow's disease with or without concomitant TV annuloplasty at the Leiden University Medical Center (Leiden, The Netherlands) between 2000-2017 were included. TV annuloplasty was performed by inserting an annular ring in the position of the TV annulus. The following exclusion criteria were used: unavailable echocardiogram pre-operative or at long-term follow-up (≥2 years), pre-operative TR grade ≥3 (significant TR), pre-operative TV annulus diameter <40 mm and age <18 years. Patients were divided into 2 groups 1) patients who did not undergo concomitant TV annuloplasty ("no TV annuloplasty") and 2) patients who underwent concomitant TV annuloplasty ("TV annuloplasty"). Pre-operative demographic and clinical characteristics of patients were collected from the hospital information system (HIX 6.1; ChipSoft BV, Amsterdam, The Netherlands) and the patient electronic record used by the cardiology department (EPD-Vision®; Leiden University Medical Center, Leiden, The Netherlands). The following information was obtained: demographic characteristics, cardiovascular risk factors, concomitant cardiovascular disease, concomitant surgical procedures and clinical follow-up data. The following endpoints were assessed: all-cause mortality and adverse events after surgery which included the implantation of a pacemaker or implantable cardioverter-defibrillator, new onset of atrial fibrillation, surgical intervention on the mitral or tricuspid valve, hospitalization for heart failure, myocardial infarction, out-of-hospital cardiac arrest and stroke. Date of death was verified by reviewing the hospital records, which are connected to the governmental death registry database. For retrospective analysis of clinically acquired data and anonymously handled the Institutional Review Board waived the need of written patient informed consent.

Standard transthoracic 2D echocardiography was performed in all patients before surgery and at long-term follow-up (≥2 years) using commercially available ultrasound devices (Vivid 5, Vivid 7, System 5 and E9, GE Healthcare, Vingmed, Horten, Norway). Conventional 2D, M-mode, pulsed and continuous wave and color Doppler images were acquired in parasternal and apical views with the patients in left lateral decubitus position. Data were digitally stored and analyzed offline using EchoPAC (version 112, 202 and 203 GE Medical Systems, Horten, Norway). The right atrial maximum dimension, TV annular diameter and RV dimensions and areas were measured on the focused RV 4-chamber apical view (11, 12). In addition, the fractional area change was derived from the RV end-diastolic and end-systolic areas traced on the focused RV 4-chamber apical view (12). The RV systolic pressure was determined using the peak velocity of the TR jet (12). Left ventricular dimensions (end-diastolic and end-systolic diameter) were assessed from the parasternal long-axis view and were used to calculate fractional shortening (11). From the apical 2- and 4-chamber views, the left ventricular end-diastolic and end-systolic volumes were measured using the Simpson's biplane method; left ventricular ejection fraction was subsequently calculated (11). The maximum left atrial diameter was assessed in the parasternal long-axis view at end-systole. Left atrial volumes were measured at end-systole in the apical 2- and 4-chamber views using the Simpson's biplane method and indexed for body surface area (left atrial volume index) (11). MR and TR were graded according to current guidelines using a multi-parametric approach (13, 14). Additionally, TR was quantitatively assessed according to current recommendations (13).

Categorical variables are expressed as absolute numbers and percentages. Continuous variables are presented as mean±standard deviation (SD) when normally distributed and as median with interquartile range (IQR) when not normally distributed. The Kolmogorov-Smirnov test and the Shapiro Wilk test were used to assess for normality of data distribution. The chi-square test, unpaired Student's T-test, Mann-Whitney U test and Kruskal-Wallis test were used for the analysis of the continuous and categorical clinical and echocardiographic variables as appropriate. Repeated-measure analysis-of-variance (ANOVA) was used to analyze the trend of right and left cardiac chamber dimensions, volumes and function during follow-up and to investigate the effect of preventive TV annuloplasty on adverse RV remodeling. Multiple pairwise comparisons within groups were performed with the paired Student's T-test, Wilcoxon signed-rank test or McNemar test as appropriate. Kaplan-Meier analysis was performed to evaluate the differences in all-cause mortality and the Log-rank test was used to compare the 2 groups. The chi-square test was used to analyze the other end-points. To evaluate the reproducibility for the TV annular measurements, the intra-class correlation coefficient (ICC) was calculated for inter- and intra-observer agreement in 10 randomly selected patients. Statistical analysis was performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). For all tests, a 2-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 98 patients met the inclusion criteria; 28 of these patients underwent isolated MV repair without TV annuloplasty and 70 patients received concomitant TV annuloplasty at the time of MV surgery. Clinical characteristics at the time of MV surgery of all patients and for the 2 subgroups (with and without concomitant TV annuloplasty) are summarized in Table 1. The mean age of the overall population at the time of surgery was 65±11 years and 83 patients (85%) were men. More than half of the patients had pre-existing atrial fibrillation (55%) for which most patients underwent a maze procedure during surgery. In per-group analysis, no statistically significant differences were noted between patients with and without concomitant TV annuloplasty except in preoperative logistic EuroSCORE (3.0% [1.7-4.5] vs. 1.3% [0.8-3.4], respectively; p<0.001) as expected due to the additional TV annuloplasty. The echocardiographic characteristics at the time of MV surgery of all patients and according to the 2 subgroups are summarized in Table 2. Approximately two-third (68%) of the patients had MR grade 4 before surgery. Consequently, the left atrium was severely dilated in the overall population (LA diameter 48±9 mm and LA volume index 56 [45-76] ml/mm^2). Per design of the study, the TV annulus was dilated in all patients (43±3 mm) at baseline. Additionally, RV basal diameter was dilated (50±5 mm) compared to the normal range (25-41 mm)(11), while RV midventricular diameter (32±6 mm) and longitudinal diameter (78±10 mm) were within the normal range (19-35 mm and 59-83 mm, respectively) (11). Both subgroups with and without preventive TV annuloplasty were comparable at baseline in terms of echocardiographic characteristics,

Table 1. Baseline clinical characteristics

Variable	Total population (n=98)	TV annuloplasty (n=70)	No TV annuloplasty (n=28)	P-value
Age at surgery (years)	65±11	66±10	63±13	0.172
Men	83 (85%)	62 (89%)	21 (75%)	0.092
NYHA Class				0.251
I	19 (19%)	15 (21%)	4 (14%)	
II	57 (58%)	42 (60%)	15 (51%)	
III	21 (21%)	13 (19%)	8 (29%)	
IV	1 (1%)	0 (0%)	1 (4%)	
Atrial fibrillation	53 (55%)	38 (54%)	15 (56%)	0.910
Diabetes mellitus	2 (2%)	2 (3%)	0 (0%)	0.366
Hypertension	42 (43%)	30 (43%)	12 (43%)	1.000
Chronic obstructive pulmonary disease	5 (5%)	4 (6%)	1 (4%)	0.663
Smoker	39 (40%)	32 (46%)	7 (25%)	0.052
Coronary artery disease	29 (30%)	22 (31%)	7 (26%)	0.596
Out of hospital cardiac arrest	3 (3%)	2 (3%)	1 (4%)	0.853
Pacemaker/ICD	5 (5%)	2 (3%)	3 (11%)	0.099
eGFR, ml/min/1.73m^2	81±25	82±25	79±24	0.536
Logistic EuroSCORE (%)	2.8 (1.4-3.8)	3.0 (1.7-4.5)	1.3 (0.8-3.4)	**<0.001**
Maze procedure	41 (42%)	31 (44%)	10 (36%)	0.437

Values are mean±SD, median (IQR) or n (%).
eGFR = estimated glomerular filtration rate; ICD = implantable cardioverter-defibrillator; NYHA = New York Heart Association

although pre-operative RV function was more preserved in patients without TV annuloplasty compared to those with TV annuloplasty (RV fractional area change 38% [33-44] vs. 33% [22-45], respectively; p=0.05). The ICC for repeated measurements of the TV annular diameter at baseline by the same observer (intra-observer agreement) was excellent (ICC=0.96), the ICC for measurements between two different observers (inter-observer agreement) was also good (ICC=0.89).

Supplementary Tables 1 and 2 summarize the echocardiographic characteristics at baseline and long-term follow-up for the subgroup with TV annuloplasty and the subgroup without TV annuloplasty, respectively. The median time between baseline and follow-up echocardiography in the overall population was 6.4 (3.9-9.3) years. The median follow-up duration was not significantly different between patients with and without concomitant TV

Table 2. Baseline echocardiographic characteristics

Variable	Total population (n=98)	TV annuloplasty (n=70)	No TV annuloplasty (n=28)	P-value
Heart rate (bpm)	70 (60-83)	70 (61-82)	73 (60-83)	0.452
Atrial fibrillation	34 (35%)	27 (39%)	7 (25%)	0.144
RV basal diameter (mm)	50±5	50±5	50±5	0.777
RV mid diameter (mm)	32±6	32±6	31±5	0.470
RV long axis diameter (mm)	78±10	78±11	77±9	0.467
RV end-diastolic area (cm^2)	27 (23-30)	27 (22-31)	26 (24-28)	0.345
RV end-systolic area (cm^2)	17 (14-21)	17 (14-22)	15 (13-17)	0.146
RV fractional area change (%)	36 (24-45)	33 (22-45)	38 (33-44)	**0.050**
RA maximum diameter (mm)	56±8	57±7	56±9	0.796
TR vena contracta (mm)	3.7±2.2	3.7±2.3	3.7±2.3	0.938
TR PISA radius (cm)	0.39±0.21	0.40±0.21	0.36±0.21	0.479
TR EROA (mm^2)	6.5 (2.7-10.2)	6.4 (2.4-9.7)	9.3 (3.8-12.7)	0.312
TR regurgitant volume (ml/ beat)	4.6 (2.3-9.1)	4.5 (2.0-8.3)	5.2 (2.9-9.8)	0.584
TR gradient (mmHg)	29 (21-34)	30 (23-40)	28 (16-31)	0.056
TR velocity (m/sec)	2.7±0.6	2.8±0.5	2.5±0.6	**0.021**
TV annulus (mm)	43±3	43±3	42±2	**0.023**
TR grade				0.333
0	11 (11%)	8 (11%)	3 (11%)	
1	52 (53%)	34 (49%)	18 (64%)	
2	35 (36%)	28 (40%)	7 (25%)	
LA diameter (mm)	48±9	48±8	48±10	0.922
LA volume index (ml/mm^2)	56 (45-76)	56 (46-74)	56 (38-88)	0.760
LV end-diastolic diameter (mm)	57±7	58±7	56±6	0.400
LV end-systolic diameter (mm)	36±7	37±8	35±6	0.222
LV fractional shortening (%)	37±9	37±10	38±9	0.409
LV end-diastolic volume (ml)	146 (116-174)	146 (116-174)	144 (111-175)	0.917
LV end-systolic volume (ml)	53 (42-67)	55 (44-69)	49 (38-61)	0.200
LV ejection fraction (%)	62±9	61±9	65±8	0.084
MR grade				0.303
3	31 (32%)	20 (29%)	11 (39%)	
4	67 (68%)	50 (71%)	17 (61%)	

Values are mean±SD, median (IQR) or n (%).
EROA = effective regurgitant orifice area; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; PISA = proximal isovelocity surface area; RA = right atrium; RV = right ventricle; TR = tricuspid regurgitation; TV = tricuspid valve

annuloplasty (6.1 [3.9-9.4] years vs. 6.7 [3.8-9.1] years, respectively; p=0.89). As expected after MV repair, a significant reduction in MR severity and LA size was observed in both subgroups (p<0.01 for all). In patients who underwent concomitant TV annuloplasty, no significant RV dilatation was observed at follow-up in contrast to the patients who did not undergo concomitant TV annuloplasty, who did develop RV dilatation. In patients without TV annuloplasty, the RV midventricular diameter, longitudinal diameter, end-diastolic and end-systolic areas were significantly larger at follow-up (p<0.01 for all). Additionally, 4 patients (14%) in the subgroup without TV annuloplasty developed significant TR during follow-up in contrast to zero patients (0%) in the subgroup with TV annuloplasty (p=0.001). Only in patients who underwent TV annuloplasty, was there a significant reduction (vs baseline) in right atrial diameter observed (baseline right atrial diameter 57±7 mm; follow-up 52±7 mm; p<0.01), with significant reduction in TR grade (93% of patients having no residual TR or TR grade 1, p<0.01). To evaluate whether concomitant TV annuloplasty had an impact on the change in different echocardiographic parameters over time, repeated measure ANOVA was performed (Table 3 and Figure 1). This analysis showed that concomitant TV annuloplasty was associated with less adverse RV remodeling. The RV basal diameter (p=0.03), RV long axis diameter (p=0.04), RV end-diastolic area (p<0.01) and RV end-systolic area (p=0.03) showed less adverse remodeling at follow-up in patients with concomitant TV annuloplasty compared to patients without TV annuloplasty. RV function was more preserved at baseline in patients without TV annuloplasty, but did not change over time in both subgroups, showing no interaction between TV annuloplasty and RV function (p=0.49). As expected, TV annuloplasty was not associated with changes over time in left-sided echocardiographic variables.

Clinical outcome data of the total population, and of the patients with versus without concomitant TV annuloplasty are shown in Table 4. During the median follow-up of 6.4 (3.9-9.3) years, 9 patients (13%) with TV annuloplasty and 7 patients (25%) without TV annuloplasty died. Kaplan–Meier analysis showed no significant differences in survival rates between patients with and without TV annuloplasty (log-rank chi-square 0.56; p=0.45). The most frequent adverse events during follow-up were the need of a pacemaker or implantable cardioverter-defibrillator (21%) and new onset atrial fibrillation (10%). No significant differences in incidence of these or other outcomes between patients with versus without TV annuloplasty were observed.

DISCUSSION

The main finding of the current study was that in patients with significant primary MR and a dilated tricuspid annulus (≥40 mm) without significant TR (<2+) at baseline who

Table 3. Changes over time in echocardiographic parameters after mitral valve repair with versus without tricuspid valve annuloplasty

	Baseline	Follow-up	P-value
RV basal diameter (mm)			**0.032**
TV annuloplasty	50±5	49±8	
No TV annuloplasty	50±5	52±7	
RV mid diameter (mm)			0.079
TV annuloplasty	32±6	33±6	
No TV annuloplasty	31±5	36±7	
RV long axis diameter (mm)			**0.038**
TV annuloplasty	78±11	81±9	
No TV annuloplasty	77±9	84±8	
RV end-diastolic area (cm^2)			**0.004**
TV annuloplasty	27 (22-31)	27 (23-32)	
No TV annuloplasty	26 (24-28)	30 (26-35)	
RV end-systolic area (cm^2)			**0.033**
TV annuloplasty	17 (14-22)	17 (14-23)	
No TV annuloplasty	15 (13-17)	18 (15-22)	
RV fractional area change (%)			0.489
TV annuloplasty	33 (22-45)	33 (26-42)	
No TV annuloplasty	38 (33-44)	37 (31-47)	
RA maximum diameter (mm)			0.109
TV annuloplasty	57±7	52±7	
No TV annuloplasty	56±9	55±6	
TR gradient (mm)			0.264
TV annuloplasty	30 (23-40)	19 (15-24)	
No TV annuloplasty	28 (16-31)	22 (17-26)	
LV end-diastolic volume (ml)			0.135
TV annuloplasty	146 (116-174)	136 (113-160)	
No TV annuloplasty	144 (111-175)	118 (99-142)	
LV end-systolic volume (ml)			0.453
TV annuloplasty	55 (44-69)	61 (51-75)	
No TV annuloplasty	49 (38-61)	53 (46-69)	
LV ejection fraction (%)			0.330
TV annuloplasty	61±9	52±8	
No TV annuloplasty	65±8	53±7	
LA volume index (ml/mm^2)			0.835
TV annuloplasty	56 (46-74)	43 (30-59)	
No TV annuloplasty	56 (38-88)	41 (32-58)	

Values are mean±SD or median (IQR). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; TR = tricuspid regurgitation; TV = tricuspid valve

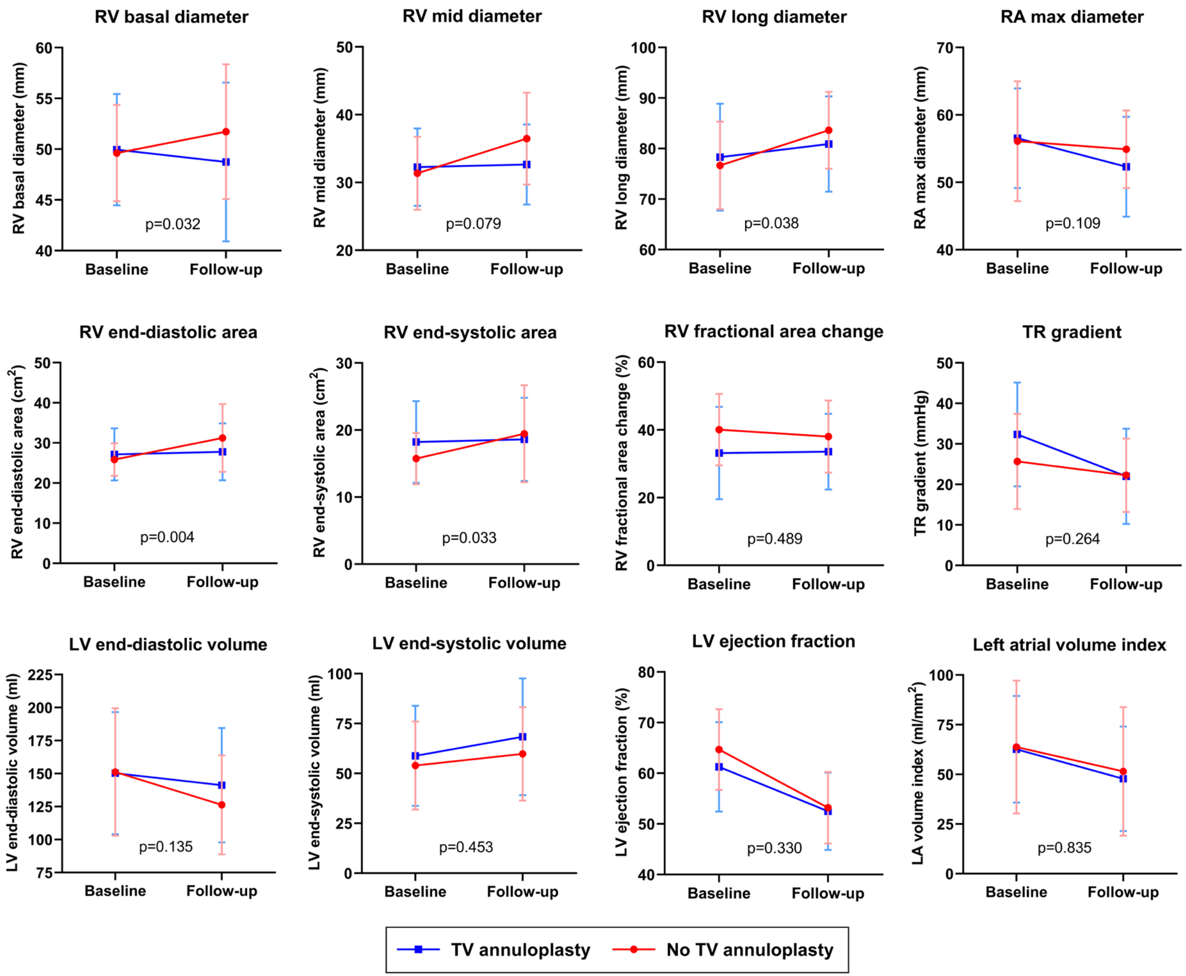

Figure 1. Changes over time in echocardiographic parameters after MV repair with (blue line) or without TV annuloplasty (red line)

LV = left ventricular; RA = right atrial; RV = right ventricular; TR = tricuspid regurgitation; TV = tricuspid valve

Table 4. Outcome data of the overall population of patients who underwent mitral valve surgery and the subgroups with and without tricuspid valve annuloplasty

Variable	Total population (n=98)	TV annuloplasty (n=70)	No TV annuloplasty (n=28)	P-value
All-cause mortality	16 (16%)	9 (13%)	7 (25%)	0.142
Surgical reintervention MV	8 (8%)	6 (9%)	2 (7%)	0.816
Surgical reintervention TV	1 (1%)	0 (0%)	1 (4%)	0.112
Heart failure hospitalization	8 (8%)	6 (9%)	2 (7%)	0.816
Myocardial infarction	2 (2%)	1 (1%)	1 (4%)	0.498
Out of hospital cardiac arrest	2 (2%)	1 (1%)	1 (4%)	0.498
Cerebrovascular accident	6 (6%)	2 (3%)	4 (14%)	0.087
Pacemaker/ implantable cardio-verter-defibrillator	21 (21%)	13 (19%)	8 (29%)	0.276
New onset atrial fibrillation	10 (10%)	6 (9%)	4 (14%)	0.399

Values are n (%).
MV = mitral valve; TV = tricuspid valve

underwent MV surgery, preventive TV annuloplasty was effective in preserving RV size and preventing the development of significant TR at long-term follow-up.

Previous studies have demonstrated that patients with RV dilatation who underwent TV annuloplasty during MV surgery were protected from development of significant TR and associated adverse RV remodeling in the first years after surgery (7, 15, 16). Bertrand et al. (15) showed that TV annuloplasty during MV surgery prevented postoperative RV dilatation in patients with a dilated TV annulus, although this effect was more pronounced in patients with moderate TR at baseline. Benedetto et al. (7) and Van de Veire et al. (16) reported RV reverse remodeling and prevention of TR progression in patients with less than moderate TR at 1 and 2 years after preventive TV annuloplasty at the time of MV surgery. In contrast, a recent randomized controlled trial analyzing 106 patients with less than severe TR demonstrated no impact of concomitant TV annuloplasty during MV surgery on RV dimensions during a median follow-up of 3.8 (3-5.6) years (8). However, these patients were not selected based on the presence of a dilated TV annulus, which suggests that TV annuloplasty may not be necessary to prevent RV dilatation in patients with normal preoperative TV annulus dimensions. Furthermore, secondary TR may slowly progress and TV annuloplasty does not reverse RV dilatation in secondary TR, but may only slow down the remodeling process that causes and results from TR (17). Therefore, the follow-up time in the previous studies may not be sufficient to analyze the effect of TV annuloplasty on subsequent development of TR and adverse RV remodeling. The current study is the first to assess late adverse RV remodeling with a median follow-up of 6.4 (3.9-9.3) years in patients with primary MR. The results confirm and extend previous findings by demonstrating that concomitant TV annuloplasty during MV surgery was effective in preventing TR progression and adverse RV remodeling at long-term follow-up. Regarding RV systolic function, no significant changes between baseline and long-term follow-up were demonstrated in patients with TV annuloplasty as well as in patients without TV annuloplasty in the current study. Previous studies showed conflicting results. Chikwe et al. (18) investigated longitudinal changes in qualitatively assessed RV function up to 5 years after surgery in 645 patients who underwent MV repair (for degenerative MR) with or without TV annuloplasty in the presence of significant TR or a dilated tricuspid annulus (≥40 mm). After initial deterioration of RV function postoperatively in both groups, a more rapid recovery and improvement of RV function was observed in patients who underwent TV annuloplasty. Desai et al. (19) found similar late improvement of RV function in patients with preoperative severe TR. Patients with non-significant TR did not receive TV annuloplasty in this study. In contrast, others studies have demonstrated no impact of TV annuloplasty on RV function at follow-up as measured qualitatively (20) and by fractional area change (8, 21), which is concordant with the findings in the current study. Explanation for these varying results may relate to differences in patient population, baseline RV function or pulmonary artery pressures. Isolated MV surgery reduces pulmonary pressures and RV afterload, whereas correcting TR increases RV afterload, which may impair RV function but may also conceal changes in RV myocardial contractility. RV-pulmonary artery coupling could be a more useful parameter to accurately assess RV function, but non-invasive measurements of RV-pulmonary artery coupling still need further validation (22).

Badhwar et al. (9) reported that the addition of TV annuloplasty to MV surgery was associated with an increased risk of 30-day mortality in a large cohort of patients from The Society of Thoracic Surgeons Adult Cardiac Database. Most likely, the more advanced heart disease in the TV annuloplasty group accounted for this increased 30-day mortality, since adjustment for baseline characteristics neutralized the negative impact of TV annuloplasty on 30-day mortality. Moreover, multiple studies assessing long-term follow-up demonstrated no increased mortality in patients undergoing preventive TV annuloplasty (8, 10, 18, 20). Similarly, in the current study no significant differences were observed in all-cause mortality and morbidity during long-term follow-up in patients with versus without TV annuloplasty. The sample size of the current study and some previous studies may be too small to demonstrate significant differences in clinical outcomes.

However, the current results demonstrate that TV annuloplasty was effective in preventing the development of significant TR, which is an independent predictor of worse survival in general (4) and after MV surgery. Since TV annuloplasty in patients with a dilated TV annulus is not associated with incremental risk of mortality while reoperation of late significant TR is associated with high morbidity and mortality (5), a more widespread use of preventive TV annuloplasty might be justifiable. Large prospective studies are needed to clarify the clinical benefit of preventive TV annuloplasty during mitral valve surgery and to establish selection criteria for patients who may benefit most from preventive TV annuloplasty. A recent international randomized controlled trial assigned 401 patients with severe degenerative MR and grade ≤2 TR who underwent MV surgery to receive a procedure with or without TV annuloplasty. After a follow-up period of 2 years, the patients who underwent concomitant TV annuloplasty had less frequent progression to severe TR. The occurrence of major adverse events and the overall survival were similar in the groups with and without TV annuloplasty (23).

The current study is a retrospective cohort study from a single tertiary center with limitations inherent to its design. Due to the strict inclusion criteria, the sample size was relatively small. As the event rate of clinical outcomes was low, the current study was possibly underpowered to detect statistically significant differences. Because we were interested in the long-term outcome of TV annuloplasty, we excluded patients without available follow-up more than 2 years after surgery, inducing a selection bias. Furthermore, 2-dimensional transthoracic echocardiography may not be ideal for assessment of TV annulus dimensions, whereas 3-dimensional echocardiography may provide more accurate measurements of the tricuspid annulus.

In conclusion, the present study demonstrated that concomitant TV annuloplasty during MV surgery in patients with primary MR, no significant TR and a tricuspid annulus (≥40 mm), prevented adverse RV remodeling and the development of significant TR at long-term follow-up. Conversely, patients with isolated MV surgery and a dilated TV annulus who did not undergo TV annuloplasty showed significant RV dilatation with progression of TR. These results underscore that preventive TV annuloplasty may be effective in reducing late development of TR and RV dilatation. No effect of concomitant TV annuloplasty on outcomes was demonstrated, which may relate to the limited sample size. Larger randomized controlled trials with long-term follow-up are needed to provide further insight whether the preventive TV annuloplasty approach is associated with improved clinical outcomes.

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Supplementary Table 1. Echocardiographic characteristics at baseline and long-term follow-up of the subgroup of patients with concomitant tricuspid valve annuloplasty

Variable	Baseline	Follow-up	P-value
Heart rate (bpm)	70 (61-82)	69 (61-80)	0.916
Atrial fibrillation	27 (39%)	27 (39%)	1.000
RV basal diameter (mm)	50±5	49±8	0.224
RV mid diameter (mm)	32±6	33±6	0.665
RV long axis diameter (mm)	78±11	81±9	**0.031**
RV end-diastolic area (cm^2)	27 (22-31)	27 (23-32)	0.562
RV end-systolic area (cm^2)	17 (14-22)	17 (14-23)	0.296
RV fractional area change (%)	33 (22-45)	33 (26-42)	0.914
RA maximum diameter (mm)	57±7	52±7	**<0.001**
TR vena contracta (mm)	3.7±2.3	1.7±2.0	**<0.001**
TR PISA radius (cm)	0.40±0.21	0.25±0.28	**0.004**
TR EROA (mm^2)	6.4 (2.4-9.7)	0 (0-9.6)	0.092
TR RVol (ml/beat)	4.5 (2.0-8.3)	0 (0-6.5)	**0.029**
TR gradient (mmHg)	30 (23-40)	19 (15-24)	**0.006**
TV annulus (mm)	43±3	30±5	**<0.001**
TR grade			**<0.001**
0	8 (11%)	33 (47%)	
1	34 (49%)	32 (46%)	
2	28 (40%)	5 (7%)	
LA diameter (mm)	48±8	43±8	**<0.001**
LA volume index (ml/mm^2)	56 (46-74)	43 (30-59)	**<0.001**
LV end-diastolic diameter (mm)	58±7	55±7	**0.002**
LV end-systolic diameter (mm)	37±8	37±9	0.794
LV fractional shortening (%)	37±10	33±11	**0.009**
LV end-diastolic volume (ml)	146 (116-174)	136 (113-160)	0.138
LV end-systolic volume (ml)	55 (44-69)	61 (51-75)	**0.007**
LV ejection fraction (%)	61±9	52±8	**<0.001**
MR grade			**<0.001**
0	0 (0%)	25 (36%)	
1	0 (0%)	35 (50%)	
2	0 (0%)	8 (11%)	
3	20 (29%)	2 (3%)	
4	50 (71%)	0 (0%)	

Values are mean ±SD, median (IQR) or n (%). P-value by paired Student's T-test or Wilcoxon signed-rank test for Gaussian and non-Gaussian distributed continuous variables, respectively. P-value by McNemar test for categorical variables. EROA = effective regurgitant orifice area; IQR = interquartile range; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; PISA = proximal isovelocity surface area; RA = right atrium; RV = right ventricle; RVol = regurgitant volume; SD = standard deviation; TR = tricuspid regurgitation; TV = tricuspid valve

Supplementary Table 2. Echocardiographic characteristics at baseline and long-term follow-up of the subgroup of patients without concomitant tricuspid valve annuloplasty

Variable	Baseline	Follow-up	P-value
Heart rate (bpm)	73 (60-83)	69 (63-76)	0.696
Atrial fibrillation	7 (25%)	7 (25%)	1.000
RV basal diameter (mm)	50±5	52±7	0.196
RV mid diameter (mm)	31±5	36±7	**0.001**
RV long axis diameter (mm)	77±9	84±8	**0.001**
RV end-diastolic area (cm^2)	26 (24-28)	30 (26-35)	**0.002**
RV end-systolic area (cm^2)	15 (13-17)	18 (15-22)	**0.006**
RV fractional area change (%)	38 (33-44)	37 (31-47)	0.456
RA maximum diameter (mm)	56±9	55±6	0.318
TR vena contracta (mm)	3.7±2.3	3.1±2.8	0.416
TR PISA radius (cm)	0.36±0.21	0.34±0.25	0.711
TR EROA (mm^2)	9.3 (3.8-12.7)	6.0 (3.3-11.8)	0.272
TR RVol (ml/beat)	5.2 (2.9-9.8)	3.7 (0.8-8.1)	0.117
TR gradient (mmHg)	28 (16-31)	22 (17-26)	0.085
TV annulus (mm)	42±2	42±5	0.973
TR grade			**<0.001**
0	3 (11%)	3 (11%)	
1	18 (64%)	12 (43%)	
2	7 (25%)	9 (32%)	
3	0 (0%)	4 (14%)	
LA diameter (mm)	48±10	43±9	**< 0.001**
LA volume index (ml/mm^2)	56 (38-88)	41 (32-58)	**< 0.001**
LV end-diastolic diameter (mm)	56±6	53±6	**0.012**
LV end-systolic diameter (mm)	35±6	36±8	0.184
LV fractional shortening (%)	38±9	32±10	**0.004**
LV end-diastolic volume (ml)	144 (111-175)	118 (99-142)	**0.007**
LV end-systolic volume (ml)	49 (38-61)	53 (46-69)	0.118
LV ejection fraction (%)	65±8	53±7	**<0.001**
MR grade			**<0.001**
0	0 (0%)	9 (32%)	
1	0 (0%)	15 (54%)	
2	0 (0%)	2 (7%)	
3	11 (39%)	2 (7%)	
4	17 (61%)	0 (0%)	

Values are mean ±SD, median (IQR) or n (%). P-value by paired Student's T-test or Wilcoxon signed-rank test for Gaussian and non-Gaussian distributed continuous variables, respectively. P-value by McNemar test for categorical variables. EROA = effective regurgitant orifice area; IQR = interquartile range; LA = left atrium; LV = left ventricle; MR = mitral regurgitation; PISA = proximal isovelocity surface area; RA = right atrium; RV = right ventricle; RVol = regurgitant volume; SD = standard deviation; TR = tricuspid regurgitation; TV = tricuspid valve

4