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Tricuspid Regurgitation Does Not Impact Right Ventricular Remodeling After Percutaneous Pulmonary Valve Implantation

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ABSTRACT

OBJECTIVES This study sought to investigate the impact of tricuspid regurgitation (TR) on right ventricular function after percutaneous pulmonary valve implantation (PPVI).

BACKGROUND PPVI provides a less invasive alternative to surgery in patients with right ventricular-to-pulmonary artery (RV-PA) conduit dysfunction. Recovery of the right ventricle has been described after PPVI for patients with pulmonary stenosis and for those with pulmonary regurgitation. Additional TR enforces RV dysfunction by supplemental volume overload. Limited data are available on the potential of the right ventricle to recover in such a specific hemodynamic situation.

METHODS In a matched cohort study, we compared patients who underwent PPVI with additional TR with those without TR.

RESULTS The degree of TR improved in 83% of the patients. In our patients (n = 36) exercise capacity and right ventricular volume index improved similarly 6 months after PPVI in patients with and without important TR. None of them had significant TR in the long-term follow-up of median 78 months.

CONCLUSIONS PPVI improves not only RV-PA-conduit dysfunction, but also concomitant TR. In patients with a dysfunctional RV-PA conduit and TR, the decision whether to fix TR should be postponed after PPVI. (J Am Coll Cardiol Intv 2017;10:701–8)
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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance imaging

PPVI = percutaneous pulmonary valve implantation

PR = pulmonary regurgitation

PS = pulmonary stenosis

PVR = pulmonary valve replacement

RV-PA = right ventricle to pulmonary artery

RVEDVi = right ventricular end-diastolic volume index

RVOT = right ventricular outflow tract

TR = tricuspid regurgitation

Vo_2 peak = peak oxygen uptake

In patients with right ventricular outflow tract (RVOT) conduit dysfunction, percutaneous pulmonary valve implantation (PPVI) is a less invasive therapeutic option than repeated cardiac surgery (1). PPVI proved to be safe and effective in several studies and at present is the preferred treatment option for RVOT conduit dysfunction in many centers (2–5). In prior studies, beneficial effects of PPVI were documented irrespective of the prevailing hemodynamic indication: RVOT stenosis, pulmonary regurgitation (PR), or a combination of stenosis and regurgitation (6,7). Sustained improvements in hemodynamics were shown up to 7 years post-PPVI (8).

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In addition to RVOT dysfunction, some patients referred for PPVI present with moderate to severe tricuspid valve regurgitation (TR). This may be caused by various factors, including a congenitally dysplastic tricuspid valve, RV pressure and/or volume overload, or sequela of preceding surgical procedures. Limited data are available on the potential of the RV to recover in such a specific hemodynamic situation. Current guidelines suggest a surgical approach if RVOT dysfunction is combined with moderate to severe TR (9,10). However, if restoring RVOT function by PPVI improves right heart hemodynamics significantly, the clinical impact of TR may be reduced and surgery may thus be avoidable (11). Therefore, the objective of the present matched cohort study was to investigate the impact of TR on right ventricular function after PPVI.

METHODS

PATIENT SELECTION. Between December 2006 and December 2014, a total of 173 patients underwent PPVI at the German Heart Center Munich. Twenty-two of these patients had moderate or severe TR according to echocardiographic criteria (12) before PPVI and constitute the study cohort (TR cohort, TR patients). Patients were evaluated with a standardized protocol including the following: history, echocardiography, cardiac magnetic resonance imaging (CMR), cardiopulmonary exercise testing, and assessment of New York Heart Association functional class. For every patient with significant TR, a matched control subject was selected with comparable clinical findings but without additional TR (control cohort). According to study protocols, all cases and control subjects were evaluated before PPVI and 6 months after PPVI.

Control subjects were matched to patients with TR according to the following criteria. In detail, we made sure to compare patients: 1) having the same pulmonary valve pathology, either pulmonary stenosis (PS), PR, or a combination of both; 2) with similar indexed right ventricular end-diastolic volume (RVEDVi); and 3) with New York Heart Association functional class state that was the same or differed no more than 1 class. Additionally, the underlying cardiac diagnosis, sex, age at PPVI, and number of previous surgeries were also taken into consideration. PS was defined as a peak invasive right ventricular-to-pulmonary artery (RV-PA) gradient more than 40 mm Hg, and PR was defined as a regurgitant fraction more than 20% by CMR. Patients with mixed valve disease (i.e., meeting both PS and PR criteria) were compared with similar patients with mixed disease. For statistical evaluation, patients with mixed disease were analyzed either with the PS or PR cohorts, depending on which was the dominant pathophysiology.

In 4 patients it was not possible to find a matched pair, in 3 because the RVEDVi differed significantly and in 1 because of a unique congenital heart defect (congenitally corrected transposition of the great arteries). Those 4 patients were excluded from further evaluation. Thus, the study group consisted of 18 patients with pulmonary valve dysfunction and significant TR, who were compared with 18 matched control subjects treated by PPVI who did not have relevant TR.

CARDIOPULMONARY EXERCISE TESTING. All patients underwent a symptom-limited cardiopulmonary exercise test on an electronically braked bicycle in a sitting position according to international guidelines (13). Patients cycled according to a ramped protocol with a 3-min warm-up at 0 W followed by a rampwise increase of load with 10, 15, 20, or 30 W/min with the aim of reaching an exercise duration of 8 to 12 min. They were encouraged to exercise until exhaustion. Oxygen uptake was measured breath by breath by a metabolic cart (Vmax 229, SensorMedics, Viasys Healthcare, Yorba Linda, California). Peak oxygen uptake was defined as the mean oxygen uptake in the 30-s period that was highest throughout the exercise test.

CARDIAC MAGNETIC RESONANCE IMAGING. CMR was performed at 1.5 T (Symphony Maestro Series and Avanto, Siemens Medical Solutions, Erlangen, Germany). Retrospective gated cine CMRs of the heart were acquired in the vertical long-axis, 4-chamber, and short-axis views that included the extent of both ventricles, and 2 long-axis planes of the RVOT for through-plane flow quantification. Aortic and PA flow

data were acquired with a flow-sensitive gradient echo sequence during free breathing. Regurgitant fractions were calculated from forward and backward flow across the valve. For volume measurements of the RV, endocardial contours were traced, excluding papillary muscles, trabeculae, and the moderator band from the blood volume.

STATISTICAL ANALYSIS. Data were analyzed with a standard statistical package (SPSS version 22.0, SPSS Inc., Chicago, Illinois). All continuous variables were expressed as median and minimum-maximum. Pre- versus post-PPVI data were analyzed with the 2-tailed Mann-Whitney *U* test. For continuous data, patients with pulmonary valve dysfunction and additional TR were compared with control subjects using a 2-tailed paired Student *t* test. For statistical analysis of the changes in the degree of TR, the Wilcoxon signed rank test was performed. Statistical significance was inferred when $p < 0.05$.

RESULTS

BASELINE CHARACTERISTICS. The median age of all cases and control subjects included in the study was 21 years (mean, 22.2 ± 7.9 years), the youngest patient being 10 years and the oldest 39 years of age. The group comprised 14 female and 22 male patients. Overall, 18 patients had an underlying cardiovascular diagnosis of tetralogy of Fallot, 9 had pulmonary atresia with ventricular septal defect (n = 9), 8 had truncus arteriosus (n = 8), and 1 had pulmonary atresia with intact ventricular septum (n = 1). Individual patient data are listed in Table 1.

All patients had undergone a median of 2 prior surgical interventions, and all had undergone corrective surgery with RV-PA conduit. Most of the patients were in New York Heart Association functional class II (n = 32), whereas 3 were in functional class I and 1 was class III.

The median peak oxygen uptake ($Vo_{2\ peak}$) was 28.5 ml O_2/kg/min (mean, 27.5 ± 7.4 O_2/kg/min), and ranged from 15 to 44 ml O_2/kg/min. Among patients referred for PPVI because of predominant PR, the median regurgitant fraction calculated by CMR was 33% (21% to 43%). Patients with prevailing PS had a median RV-PA peak systolic pressure gradient at cardiac catheterization of 46 mm Hg (27 to 83 mm Hg). The median central venous pressure (measured in the right atrium) was 8 mm Hg (3 to 17 mm Hg), with no difference between patients with and without TR ($p = 0.29$). The median RVEDVi of all patients included in the study was 100 ml/m^2 (mean, 109.3 ± 34.4 ml/m^2) with a range of 61 to 185 ml/m^2.

PEAK SYSTOLIC PRESSURE GRADIENTS AND PULMONARY REGURGITATION. PPVI was performed successfully in all patients, with no significant procedural adverse events. Patients with pulmonary valve pathology and TR received PPVI at a median age of 22 years (10 to 34 years), which was similar to those without TR, whose median age was 22.5 years (13 to 39 years; $p = 0.19$).

In patients with predominant PR, the regurgitant fraction was significantly reduced after PPVI, from a median of 33% (21% to 43%) to 1% (0% to 3%; $p < 0.001$). In patients with PS, the peak invasive RV-PA systolic pressure gradient was reduced significantly from 46 ± 12 mm Hg to 14 ± 5 mm Hg ($p < 0.001$). Comparing patients with TR with control subjects showed no significant difference in the reduction of PR or PS.

ECHOCARDIOGRAPHIC EVALUATION OF TR. In all patients, echocardiographic data were evaluated for at least 8 years before PPVI. In all of them, TR developed gradually over time, with absent or trivial TR initially that increased to mild and later to moderate or severe. None of them had a sudden increase of TR after surgery.

After PPVI, the degree of TR improved in 15 of 18 (83%) study patients ($p < 0.001$) 6 months after implant. In 3 of 18 (16%) study patients it remained unchanged. Patients in the TR cohort were followed for a median of 6.5 years (8 months to 9.3 years) after PPVI, and at the latest follow-up visit, none had significant TR. In 15 patients, follow-up TR was trivial and in 3 it was mild. In 1 patient whose TR initially improved to trivial, it later become mild in the context of recurrent stenosis of the melody valve. Detailed data are presented in Table 1 and Figure 1.

RIGHT VENTRICULAR END-DIASTOLIC VOLUME INDICES. Patients in the TR cohort had a median RVEDVi before PPVI of 100 ml/m^2 (71 to 182 ml/m^2). After 6 months, RVEDVi decreased significantly to 88 ml/m^2 (60 to 152 ml/m^2; $p < 0.001$). Patients without TR also had a median pre-PPVI RVEDVi of 100 ml/m^2 (61 to 185 ml/m^2), which decreased to 80 ml/m^2 (59 to 162 ml/m^2; $p < 0.001$). Complete results are depicted in Table 1. There was no difference in RVEDVi between patients with and without TR, either at baseline or after PPVI (baseline, $p = 0.63$; after PPVI, $p = 0.20$). There was also no difference between groups in the magnitude of decrease in RVEDVi ($p = 0.57$). In TR patients, RVEDVi decreased a median of 16 ml/m^2 (3 to 65 ml/m^2) and in patients without TR it decreased by a median of 15 ml/m^2 (2 to 78 ml/m^2). The results are listed in Table 2 and depicted in Figure 2.

TABLE 1 Demographic and Clinical Characteristic of All Patients

Patient #	Sex	Diagnosis	Indication for PPVI	Age at PPVI, yrs	NYHA Functional Class Before	Previous Surgeries	CVP a/v/m	RVEDVi, ml/m²		Vo_2 Peak, ml/kg/min		TR			
								Before	After	Before	After	Before	After PPVI	After Follow-Up	Follow-Up, months
1*	Male	TOF	PR	13	2	3	10/12/8	130	119	44	45	Severe	Mild	Trivial	76
2†	Male	TOF	PR	15	1	2	10/10/8	151	107	34	36				
3*	Female	TAC	PR	33	2	3	17/19/17	90	78	21	22	Moderate	Moderate	Mild	85
4†	Female	TAC	PR	33	2	3	9/7/6	103	99	15	20				
5*	Male	TOF	PR	34	2	2	8/10/7	138	73	17	20	Moderate	Trivial	Absent	61
6†	Male	PA, VSD	PR	30	2	2	7/6/5	109	66	33	38				
7*	Male	TOF	PR	33	1	2	6/9/6	128	117	30	32	Moderate	Mild	Trivial	91
8†	Male	TOF	PR	21	2	2	17/16/15	94	78	29	30				
9*	Male	TOF	PR	23	2	3	7/9/6	182	152	25	26	Moderate	Trivial	Trivial	42
10†	Male	TOF	PR	39	2	2	12/11/10	175	126	34	36				
11*	Male	TOF	PR	22	2	2	7/10/8	93	65	22	24	Moderate	Trivial	Trivial	107
12†	Male	PA, VSD	PR	30	2	2	7/6/5	109	60	33	38				
13*	Female	TOF	PR	16	2	2	10/11/9	172	130	37	37	Moderate	Trivial	Mild	80
14†	Female	TOF	PR	18	2	2	10/8/8	185	107	32	44				
15*	Female	TOF	PR	14	2	1	9/10/9	98	95	29	29	Moderate	Moderate	Trivial	86
16†	Female	PA, VSD	PR	16	2	2	12/10/9	94	65	36	35				
17*	Male	PA, VSD	PS	10	2	3	5/8/4	89	86	43	46	Moderate	Absent	Trivial	68
18†	Male	PA, VSD	PS	13	2	3	8/8/6	61	59	26	32				
19*	Male	PA, VSD	PS	23	2	3	7/11/8	113	80	31	34	Moderate	Mild	Trivial	27
20†	Male	PA, VSD	PS	21	2	4	4/4/3	100	90	22	30				
21*	Male	PA, iVS	PS	16	2	2	16/15/12	142	110	36	49	Severe	Severe	Trivial	60
22†	Male	TOF	PS	17	2	2	7/6/5	112	85	30	30				
23*	Female	TOF	PS	25	2	3	7/9/8	134	109	16	28	Moderate	Mild	Trivial	112
24†	Female	PA, VSD	PS	28	3	2	18/15/14	84	73	18	21				
25*	Male	TOF	PS	31	2	3	10/12/10	101	82	19	22	Severe	Moderate	Trivial	88
26†	Male	TOF	PS	36	2	2	9/9/6	100	95	20	24				
27*	Female	TAC	PS	13	2	1	7/9/6	99	91	26	27	Severe	Moderate	Mild	92
28†	Female	TAC	PS	14	2	2	8/7/6	69	67	31	31				
29*	Female	TOF	PS	16	2	2	10/11/8	71	67	21	24	Moderate	Mild	Trivial	60
30†	Female	PA, VSD	PS	17	2	3	10/10/9	71	59	30	31				
31*	Female	TAC	PS	22	2	3	11/12/12	81	60	23	21	Moderate	Trivial	Trivial	93
32†	Female	TAC	PS	20	2	2	10/9/8	93	67	23	23				
33*	Male	TAC	PS	15	2	1	7/10/8	79	71	24	25	Moderate	Trivial	Trivial	8
34†	Male	TAC	PS	15	1	3	12/11/10	84	81	28	30				
35*	Male	TOF	PS	29	2	2	13/14/13	92	89	34	35	Moderate	Trivial	Trivial	62
36†	Male	TOF	PS	26	2	2	8/8/7	108	95	18	35				

*Patients with pulmonary valve dysfunction and additional TR. †Selected matched pairs corresponding in sex, diagnosis group, age at PPVI, and RVEDVi measured by cardiac magnetic resonance imaging. The functional state of the patients is indicated according to NYHA functional classification.

a = "a"-wave, CVP = central venous pressure; m = mean pressure in mm Hg; NYHA = New York Heart Association; PA iVS = pulmonary atresia and intact ventricular septum; PA VSD = pulmonary atresia with ventricular septal defect; PPVI = percutaneous pulmonary valve implantation; PR = pulmonary regurgitation; PS = pulmonary stenosis; RVEDVi = right ventricular end diastolic volume index; TAC = truncus arteriosus communis; TOF = tetralogy of Fallot; TR = degree of tricuspid regurgitation classified according to echocardiographic guidelines in none or trivial, mild, moderate, and severe; v = "v"-wave; Vo_2 peak = peak oxygen uptake.

EXERCISE TESTING. Compared with baseline, functional parameters improved in all patients 6 months after PPVI. Pre-PPVI median $Vo_{2\ peak}$ in index patients and matched pairs was 28.4 ml O_2/kg/min (15.1 to 44 ml O_2/kg/min). This improved significantly to 30 ml O_2/kg/min (20 to 49 ml O_2/kg/min; $p < 0.001$). The median pre-PPVI mean work load was 2.3 W/kg (1 to 3.4 W/kg) and improved significantly to 2.5 W/kg (1.3 to 3.7 W/kg; $p < 0.001$). The difference in Vo_2 between patients with and without TR did not differ at baseline ($p = 0.96$) or after PPVI ($p = 0.41$).

To assess the relationship between baseline TR and functional outcome, the improvement of peak Vo_2 was compared between patients with significant TR and control subjects. In patients with TR, the $Vo_{2\ peak}$ improved from a pre-PPVI median of 25.5 ml O_2/kg/min (16 to 44 ml O_2/kg/min) to 27.5 ml O_2/kg/min (20.4 to 49 ml O_2/kg/min; $p = 0.009$). In control subjects, only the median peak Vo_2 improved from 29.4 (15.1 to 36) to 31 (20 to 43.6) ml O_2/kg ($p = 0.001$). Despite the fact that in both groups the $Vo_{2\ peak}$ improved 6 months after PPVI, the

improvements were similar and not significantly different between groups (p = 0.32). These results are depicted in Figure 2.

Similar results were observed regarding improvement in workload. Before PPVI, the median workload in patients with TR was 2.0 (1.2 to 3.5) W/kg, which increased to 2.2 (1.5 to 3.6) W/kg after PPVI (p = 0.001). In control subjects without TR, median workload increased from 2.5 (1 to 3.4) W/kg to 2.6 (1.3 to 3.7) W/kg, (p = 0.001). As shown in Table 2, there were no significant differences in workload between patients and control subjects either at baseline (p = 0.56) or after PPVI (p = 0.52), and no difference in the amount improvement (p = 0.85).

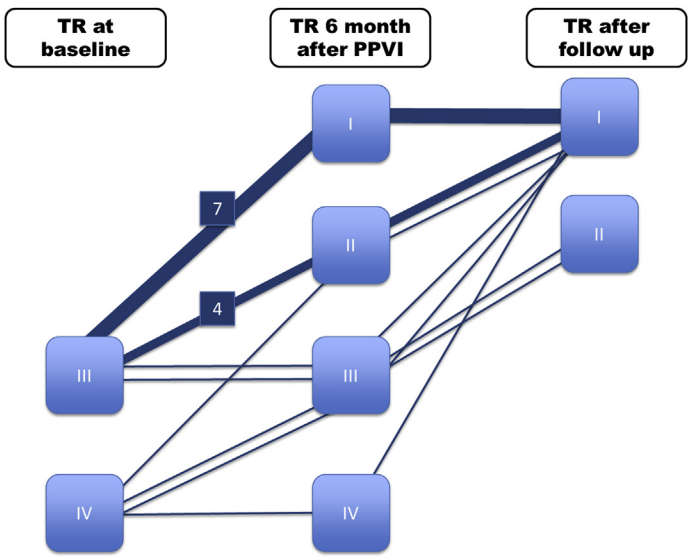
DISCUSSION

This matched cohort study shows that in most patients with RVOT conduit dysfunction and moderate to severe TR, PPVI leads to a sustained reduction in TR. The increase in exercise tolerance and reduction of RVEDVi after PPVI did not differ according to the presence or absence of significant baseline TR.

In the setting of increased afterload from PS or volume overload from PR, the RV undergoes a series of adaptations to maintain stroke volume. The potential of the RV to recover when abnormal loading conditions are relieved has been reported for patients with PS and/or PR (6,14). In addition to dysfunction of the RV-PA conduit, some patients present with important TR, which may be secondary/functional and the result of adaptive mechanisms of the RV (15), a sequela of previous surgical procedures, or related to a primary congenital abnormality of the tricuspid valve. Additional RV volume overload caused by TR can lead to a further rightward shift on the Frank-Starling curve. The potential for recovery of the RV in that specific hemodynamic condition has not been reported so far.

In our study population, exercise capacity and RVEDVi improved equally in patients with and without important TR. Following the current guidelines, surgery is recommended for treatment of RVOT dysfunction with concomitant moderate to severe TR (9,10). Surgery enables addressing both the pulmonary and tricuspid valves directly. The hypothesis of the current study was that treatment of RVOT dysfunction with PPVI, relieving PS, and providing a competent pulmonary valve would improve right heart hemodynamics and mechanics, with consequent reduction in the severity and clinical impact of TR. If this hypothesis were true, surgery could be postponed or potentially avoided altogether.

FIGURE 1 Improvement of TR Over Time



Improvement in the degree of TR in patients with pulmonary valve pathology with additional TR. The **left column** depicts TR at baseline, the **middle column** shows the degree of TR 6 months after percutaneous pulmonary valve implantation, and the **right column** depicts degree of TR after a median follow-up of 6.5 years (8 months to 9.3 years). Each **thin line** represents a patient and indicates stagnation or improvement in the degree of TR in time. The **upper thick line** includes 7 patients, the **lower thick line** 4 patients. **Roman numbers** depict the degree of TR for the left side, **I** representing none or trivial TR, **II** mild, **III** moderate, and **IV** severe TR. PPVI = percutaneous pulmonary valve implantation; TR = tricuspid regurgitation.

DO WE HAVE TO ADDRESS SECONDARY TR?

Symptomatic patients with severe primary tricuspid valve dysfunction need surgery. However, in cases of a secondary TR, there is evidence that treatment of the underlying cause improves tricuspid valve function. For example, patients with severe pulmonary arterial hypertension caused by mitral regurgitation or other left heart disease often show regression of TR and almost one-third of them experience complete resolution of TR following mitral valve surgery without direct intervention on the tricuspid valve (16). Because of its functional physiology, secondary TR may diminish or disappear with improvement of right ventricular function and loading. In the context of right atrial or RV dilation caused by an atrial septal defect, amelioration of functional TR after interventional or surgical repair was described (17). In patients with at least moderate TR, significant improvement in tricuspid valve function occurs after surgical pulmonary valve replacement (PVR), irrespective of concomitant tricuspid valve annuloplasty (18).

In this series, TR gradually developed over years in all patients and was not related to surgery. This

TABLE 2 Hemodynamic and Functional Parameters From Patients With Pulmonary Valve Pathology With and Without Additional TR

		Pulmonary Valve Pathology With TR	Pulmonary Valve Pathology Without TR	p Value
RVEDVi, ml/m^2	Pre	100 (71 to 182)	100 (61 to 185)	0.628
	Post	88 (60 to 152)	80 (59 to 126)	0.203
	p value	*<0.0001*	*0.0002*	
Peak Vo_2, ml/m^2	Pre	25 (16 to 44)	29 (15 to 36)	0.936
	Post	28 (20 to 49)	31 (20 to 41)	0.406
	p value	*0.009*	*0.001*	
Work load, W/kg	Pre	2 (1.8 to 2.4)	2.5 (1.0 to 3.5)	0.563
	Post	2.2 (1.5 to 2.6)	2.6 (1.3 to 3.7)	0.521
	p value	*0.001*	*0.001*	
Absolute change in RVEDVi after PPVI, ml/m^2		16 (3 to 65)	15 (2 to 78)	0.575
Absolute change in peak Vo_2 after PPVI, ml/m^2		1.4 (-2 to 13)	2.6 (-1 to 17)	0.328
Absolute change in work load after PPVI, W/kg		0.16 (-0.2 to 0.7)	0.3 (-0.5 to 0.8)	0.851

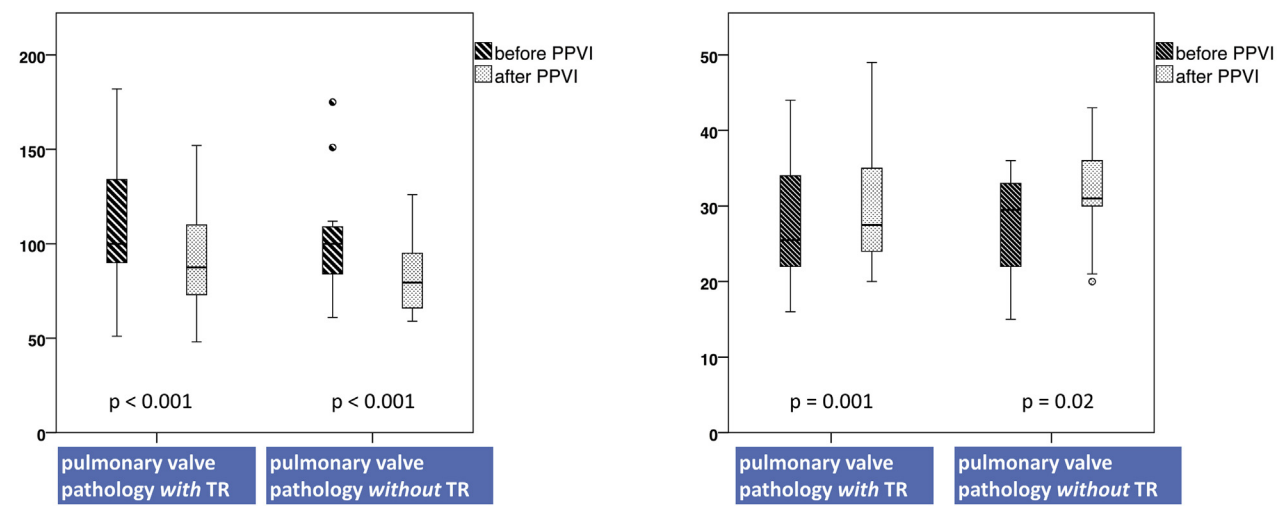
Values are median (range). Pre- and post-interventional values of patients. The minimal and maximal values are stated in parentheses. The p values in *italics* indicate statistic between pre- and post-PPVI values. The p values in nonitalics indicate statistic between patients with pulmonary valve pathology with additional TR and those without TR.

Abbreviations as in Table 1.

suggests that the mechanism might be associated with hemodynamic changes in the pressure or volume loaded RV. After PPVI, TR improved in most patients. The RVEDVi decreased significantly, which may have improved remodeling of the RV. The hemodynamic improvements and RV remodeling seemed to positively influence tricuspid valve function. Indeed, the larger RVEDVi after PPVI in the TR group suggests that the RV remained volume loaded in patients who had concomitant TR at baseline. This seems to be supported by the exercise testing findings, with higher workload and peak Vo_2 in patients without TR. However, even if differences were minimal and in 3 patients (16%) TR did not improve immediately after PPVI, none of the patients had significant TR during long-term follow-up. These results are in concordance with a recent study that documented sustained hemodynamic improvement of tricuspid valve function after PPVI at midterm follow-up (11).

DO PATIENTS WITH RVOT DYSFUNCTION BENEFIT FROM CONCOMITANT SURGERY ON THE TRICUSPID VALVE? The hypothetical advantage of surgery over PPVI in patients with RVOT dysfunction and significant TR is that there is the possibility to repair both dysfunctional valves at the same time. But in some patients with severe TR who undergo tricuspid annuloplasty, significant TR remains (19). Tricuspid valve repair usually is associated with a low perioperative risk (20). However, when reconstruction fails or is not feasible, valve replacement becomes inevitable. Compared with tricuspid valve repair, valve replacement is associated with reduced late

FIGURE 2 Decrease of RVEDVI and Increase of Peak Oxygen Uptake After PPVI



Decrease of the RVEDVi **(left panel)** and increase of the maximal oxygen uptake **(right panel)** after PPVI. The RVEDVi is measured in ml/m^2 and the maximal oxygen uptake in ml/kg/min. In each panel the **dark striped box** presents the data before PPVI and the **light checked box** presents the data after PPVI. The **box plots on the left side of the panel** depict the results of patients with pulmonary valve dysfunction and additional TR. The **box plots on the right side** depict the results of patients without additional TR. RVEDVi = right ventricular end-diastolic volume index; other abbreviations as in Figure 1.

survival (21). Additionally, in patients with repaired tetralogy of Fallot and both RVOT dysfunction and at least moderate TR, significant improvement in RV size and function occurs after PVR with or without tricuspid valve repair. This suggests that tricuspid valve repair at the time of PVR may not be superior to PVR alone (22).

Bokma et al. (23) compared the results of PVR alone with those with concomitant tricuspid annuloplasty in patients with repaired tetralogy of Fallot and severe TR. Irrespective of early post-operative TR reduction, patients with severe preoperative TR were at high risk for adverse clinical events after PVR in long-term follow-up. This may reflect the fact that the presence of TR is a marker of more advanced disease and an indication for PPVI or PVR to prevent irreversible RV damage. However, meticulous evaluation is needed to rule out patients with dysplastic tricuspid valves, because addressing just the pulmonary valve is a potentially deficient strategy in such patients.

WHEN SHOULD WE TREAT RVOT DYSFUNCTION? The optimal timing for PVR is still under debate because no controlled, randomized studies are available. In 1 study, RV size did not return to normal after PVR in patients with a RVEDVi more than 170 ml/m^2 (24). Oosterhof et al. (25), reported that RV volume returned to normal if PVR was performed before the RVEDVi reached 160 ml/m^2. Another large study reported that RV remodeling was possible in patients <17.5 years of age with a RVEDVi <150 ml/m^2 (26). In contrast to these data, it was shown that in young patients with a mean age of 14 years, the RVEDVi normalized after PVR even if RVEDVi exceeded 200 ml/m^2 before surgery (27). This suggests that the potential of the RV to remodel decreases with age and that there is not completely fixed "point of no return" for RV dilation. In our patients, PPVI was performed at a mean RVEDVi of 111 ml/m^2 at a mean age of 21 years. Compared with published surgical series, the patients included in our study were older and had less severe RV dilation. This may be explained in part by the method of assessing the RVEDV in CMR. Exclusion of papillary muscles, trabeculae, and the moderator band from the RV volume automatically results in smaller volume indices. However, PPVI has improved functional outcome even in patients with preserved RV function and underlines the earlier timing of PPVI (28).

STUDY LIMITATIONS. This is a retrospective matched cohort study with a relatively small number of patients, and thus the findings cannot be generalized. Also, the study might be underpowered and accordingly subject to type II error. In addition, the patients in this series with significant TR generally had modest functional impairment and RV enlargement at baseline, and do not represent the more severe end of the clinical spectrum of patients with RVOT dysfunction and RV volume overload related to PR and TR. Accordingly, the findings of this study may not reflect expected outcomes in patients with more severe RV dilation and/or symptoms of right heart failure.

CONCLUSIONS

This study shows that in patients with RVOT conduit dysfunction and moderate to severe TR, PPVI leads to improvement in TR in most cases. The beneficial effects of PPVI, including improved clinical symptoms and exercise tolerance, along with RV remodeling, were similar in patients with and without significant baseline TR. This study supports the idea of primary catheter intervention in cases of RVOT dysfunction and secondary TR. However, if significant TR persists, close clinical surveillance is indicated to prevent irreversible damage of the RV.

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PERSPECTIVES

WHAT IS KNOWN? PPVI is a less invasive therapeutic option in patients with RVOT conduit dysfunction than repeated cardiac surgery. Current guidelines suggest a surgical approach if RVOT dysfunction is combined with moderate to severe TR.

WHAT IS NEW? In patients who underwent PPVI with additional TR, degree of TR improved in 83% 6 months after the intervention. None of them had significant TR in the long-term follow-up.

WHAT IS NEXT? In patients with a dysfunctional RV-PA conduit and additional TR, the decision whether to fix TR should be postponed after PPVI if TR is secondary in nature.

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