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Tricuspid valve surgery improves cardiac output and exercise performance in patients with Ebstein's anomaly

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ABSTRACT

Background: Clinical, hemodynamic and functional effects of tricuspid valve surgery in patients with Ebstein's anomaly are not well understood.
Methods: Sixteen patients (median age of 27.7 years) were examined before and eight months after surgery by means of echocardiography, cardiovascular magnetic resonance (CMR) and cardiopulmonary exercise testing.
Results: Peak work load (1.87 to 2.0 W/kg; p = 0.026), maximum oxygen uptake (21 to 22 ml/kg/min; p = 0.034) as well as cardiac output (2.7 to 2.9 l/min/m^2; p = 0.035) increased postoperatively. The reduction of tricuspid regurgitation led to a higher pulmonary stroke volume (29 to 42 ml/m^2, p = 0.005) and augmented the left ventricular (LV) volume (55 to 63 ml/min/m^2; p = 0.001) with a trend to better ejection fraction (61 to 64%; p = 0.083). Right ventricular (RV) volume index (124 to 108 ml/m2; p = 0.034) and ejection fraction (50 to 42%; p = 0.036) decreased on CMR. Echocardiographic measurements of RV function also decreased (tricuspid annular plane systolic excursion 2.3 to 1.7; p = 0.002; isovolumic acceleration 0.98 to 0.65; p = 0.004; and 2-d longitudinal global strain −19.3 to −16.25; p = 0.006).
Conclusion: Tricuspid valve surgery improves exercise capacity in patients with Ebstein's anomaly. The reduction of tricuspid regurgitation decreases the volume of the right ventricle and increases pulmonary antegrade flow. As a result LV volume and cardiac output increase. This hemodynamic benefit occurs despite the preload dependent reduction in RV volume and ejection fraction.

1. Introduction

Following Ebstein's 1866 description of a post-mortem patient with cyanosis and tricuspid valve anomaly [1], another 100 years would pass until the first angiographic [2] and later echocardiographic [3] diagnoses of Ebstein's anomaly in living patients were made. Due to the wide variation in right ventricle and right atrioventricular (AV) junction morphology, the pathomorphology of the tricuspid valve (TrV) has remained a focus of scientific interest for many years.[4–6] Since the 1960s, surgical interventions on the TrV with either repair [7,8] or replacement [9] have evolved continually and effective treatment options for this rare congenital malformation have become available.

Despite establishment of the technical success of these surgical interventions, there remains only limited data regarding the beneficial effect of surgery on long-term outcome in these patients. Recently, Müller et al. [10] showed an increase in peak oxygen uptake and work capacity in 21 patients after TrV surgery. The hemodynamic component of that improvement has not yet been examined.

We therefore decided to perform a prospective cohort study on patients before and after a surgical intervention on the TrV. Patients were assessed by means of conventional echocardiography, tissue Doppler imaging, 2-d speckle tracking, cardiovascular magnetic resonance (CMR) and cardiopulmonary exercise testing (CPET). The aim was to describe in detail changes in cardiac output, RV and LV volumes and function and their relation to peak oxygen uptake.

2. Methods

2.1. Patient population

Sixteen (8 male, 8 female) of 26 consecutive patients who underwent TrV surgery due to Ebstein´s disease at our institution from August 2005 to October 2009 were prospectively included in the study. Ten patients were not eligible for CMR study because of young age (below 8 years) or presence of a cardiac pacemaker and therefore were not included in this study. Median age at surgery was 27.7 years, (range from 8.2 to 69.1 years).

The anatomic severity of Ebstein´s anomaly was classified based on echocardiographic appearance as described by Dearani et al. [11]. Abnormality was graded as mild, moderate or severe primarily based on the amount of displacement of the leaflets, the degree of tethering of the anterior leaflet and the degree of right ventricular dilatation. The Ebstein

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anomaly was classified as mild in one patient, as moderate in twelve patients and as severe in three patients.

All patients underwent a standardized work-up before surgery, consisting of an echocardiographic examination including myocardial Doppler and speckle tracking imaging, CMR and CPET. This was repeated at a median interval of 8 months after the operation.

All but one patient was either in functional class I or II. Four patients had a history of previous cardiac surgery (TrV repair n = 3, TrV replacement n = 1). The surgical procedure consisted of a mono- or bicuspid valve restoration (n = 10) with annuloplasty but without plication as has been described by Sebening and Augustin [8]. In this technique the leaflets are not delaminated and relocated but mobilized and the ring is stabilized at the true anatomical atrio-ventricular junction according to the surgeon's judgement. Biological valves were used in 6 patients, where valvuloplasty alone could not produce a sufficient reduction in tricuspid regurgitation. Any interatrial communication was closed during the operation.

The study was approved by the Ethical Committee of the Technische Universität München and all data were handled in accordance with the 1975 Helsinki declaration. Informed consent was obtained in all cases.

2.2. Echocardiography

Transthoracic echocardiography was performed using the Vivid 7 ultrasound system (General Electric, Vingmed, Horten, Norway) using standard views according to guidelines. All data were stored digitally for offline analysis. Measurements of M-mode and tissue Doppler parameters were made in 3 cardiac cycles and the average was used for statistical analysis. Grading of the tricuspid regurgitation (grade 1 = trivial, 2 = mild, 3 = moderate, 4 = severe) was based on the width of colour regurgitation jet at the valve level (vena contracta), the extent of the regurgitation jet in the right atrium and its size and volume, as recommended by the American Society of Echocardiography [12].

Colour tissue Doppler images were recorded from the apical 4-chamber view at frame rates of > 180 fps. The colour coded myocardial velocities reflecting longitudinal function were measured at the basal segment of RV and LV free walls below the atrio-ventricular valve insertion as previously described [13]. Echopac Software (General Electric, Vingmed, Horten, Norway) was used to analyse the colour coded velocities and myocardial deformation. Isovolumic acceleration (IVA), systolic velocity (s), E and A (diastolic velocities) were measured. Circumferential function of LV was recorded in a parasternal short axis view. The analysis of deformation was done after careful timing of the beginning of systole (aortic valve opening), end of systole (aortic valve closure) and beginning of diastole (mitral valve opening) by pulsed Doppler analysis of aortic and mitral flow curves. Frame rates for speckle tracking loops ranged from 60 to 85 fps.

Tricuspid annular plane systolic excursion (TAPSE) was measured by 2-dimensional echocardiography–guided M-mode recordings from the apical 4-chamber view, with the cursor placed at the free wall of the tricuspid annulus [14]. Although there are only limited data on the application of TAPSE in patients with Ebstein's anomaly it is a legitimate longitudinal measure of RV-function because the attachment of the anterior leaflet to the atrio-ventricular junction is unchanged following this surgery.

2.3. Cardiovascular Magnetic Resonance

A standard 1.5 Tesla CMR scanner (MAGNETOM Avanto, Siemens Healthcare, Erlangen, Germany) was used. Ventricular volumes were measured as previously described [15] and confirmed by others [16].

In short, patients were imaged in the supine position, using a 12-element cardiac phased array coil with breath holding in expiration and vectorcardiographic electrocardiogram gating. Axial slices were acquired from the coronal and sagittal localizing images by planning a stack of orthogonal slices to cover the heart from a level just below the diaphragm to the pulmonary bifurcation. The axial multiphase steady state free precession images were acquired with retrospective electrocardiogram triggering, a slice thickness of 4.5, 6, or 8 mm, (depending on body weight), 25 phases/cardiac cycle, 1 slice per 8- to 12-second breath hold, and an acquisition matrix of 192 x 192. The RV and LV volumes were calculated from the axial data sets using standard analysis software (Argus, Siemens Healthcare Erlangen, Germany). End-diastole and end-systole for the right and left ventricles were defined separately. End diastole was defined visually as the phase with the largest volume. End-systole was defined visually as the phase with the smallest volume. Endocardial contours of the RV and LV were traced manually in every slice in which the myocardium of the ventricle was visible. All area distal to the free leaflets of the tricuspid valve was accepted as ventricular volume. The papillary muscles and trabeculae were considered a part of the myocardium and were excluded from the volume. Contour tracing was aided by reviewing the multiple phase scans in the movie mode. The program computed the end-diastolic volume and end-systolic volume according to the defined endocardial borders of the RV and LV in all end-diastolic and end-systolic slices.

Flow in the aorta and pulmonary artery were measured as previously described [17] using phase velocity CMR. In brief, a conventional phase-sensitive gradient echo sequence was used in a double-oblique plane perpendicular to the ascending aorta at the level of the sinotubular junction and the main pulmonary artery. The following acquisition parameters were used: repetition time 25 ms, echo time 6 ms, slice thickness 6 mm, flip angle 30°, receiver bandwidth 31.25 kHz, rectangular field of view 260–330 mm, matrix 256 x 256, number of excitations 3. The highest flow velocity to be encoded was set to 2.5 m/s. Data were reconstructed to provide 30 magnitudes (anatomic) and phase (velocity-mapped) images per cardiac cycle.

2.4. Cardiopulmonary exercise test

All patients underwent a symptom limited cardiopulmonary exercise test on an upright bicycle ergometer as previously described [18]. ECG and pulse oximetry were monitored continuously. Breath by breath gas exchange analysis was performed using a metabolic chart (Vmax 229, SensorMedics, Cardinal Health Inc. Dublin, Ohio). Peak VO_2 was defined as the highest mean uptake during any 30-second time interval in the test. Ventilatory efficiency was represented by slope in the ventilation / carbon dioxide elimination curve (V_E/V_{CO2} slope) (this measurement was confined to the linear part of the curve and excluded values beyond the respiratory compensation point). Lower values of the V_E/V_{CO2} slope represent more effective ventilation.

2.5. Statistical analysis

Data are expressed in median values and interquartile ranges (IQRs) for skewed variables. Data analysis was performed using the SPSS 16.0 statistical package (SPSS Inc., Chicago, IL, USA). Non-parametric Wilcoxon tests were performed to detect significant differences between parameters before and after surgical procedure.

A probability value of < 0.05 was considered to be statistically significant.

3. Results

Following surgery, both tricuspid regurgitation (p = 0.001) and tricuspid ring diameters (p = 0.002) decreased significantly while LV diastolic diameters (measured using echocardiography) increased (p = 0.07). TAPSE, used as a longitudinal parameter of RV function, declined significantly after surgery. Table 1 shows pre- and post-operative values of conventional echocardiographic parameters.

As shown in Table 2 patients after tricuspid valve repair or tricuspid valve replacement showed significantly improved exercise performance. Peak workload, peak oxygen uptake and V_E/V_{CO2} slope improved following surgery. Moreover postoperative oxygen saturations were higher both at rest and during maximum exercise.

End diastolic RV volumes as measured by CMR volumetry were enlarged in all patients before the intervention and were reduced significantly by surgery (Table 3a). The smaller postoperative RVs showed a decrease in global function as measured by ejection fraction, whereas end diastolic LV volume (measured using MR) increased after surgery and there was an accompanying trend towards better global

Table 1
Conventional Echocardiography.

	Preoperative	n	Postoperative	n	p-value
LVDd (mm)	37(33 – 41)	16	42(36 – 47)	16	0.07
LVEF (%)	71(58 – 74)	16	72(65 – 77)	16	0.17
TI (Grade 1–4)*	4(3 – 4)	16	2(1 – 3)	16	0.001
TrV diameter (mm)	55(44 – 64)	16	37(33 – 44)	16	0.002
TrV diast inflow (mm Hg)	2(2 – 2)	15	2.5(2 – 3.75)	16	0.144
TAPSE (cm)	2.3(1.8 – 3.5)	16	1.7(1.4 – 1.8)	16	0.002

Data are presented as median (25th, 75th percentile). *TI is presented as median (range). LVDd = left ventricular diastolic diameter; LVEF = left ventricular ejection fraction; TI = tricuspid insufficiency; TrV = tricuspid valve; TAPSE = tricuspid annular plane systolic excursion.

Table 2
Cardiopulmonary exercise test.

	Preoperative	n	Postoperative	n	p-value
Work load(W/kg)	1.9(1.4 – 2.2)	16	2.0(1.8 – 2.5)	16	0.026
VO_2 max (ml/min/kg)	21(16 – 23)	16	22(19 – 29)	16	0.034
V_E/V_{CO2} slope	33(31 – 46)	15	29(28 – 32)	16	0.003
SpO_2 Rest (%)	98(95 – 99)	16	99(98 – 100)	16	0.007
SpO_2 Exercise (%)	93(83 – 98)	16	97(98 – 100)	16	0.009
RER	1.06(1.00 – 1.23)	16	1.07(1.02 – 1.13)	16	0.796

Data are presented as median (25th, 75th percentile).
VO_2 = maximum oxygen uptake; V_E/V_{CO2} = ventilatory equivalent; RER = respiratory exchange rate.