Original Article

Echocardiographic right ventricular evaluation in cardiac surgery patients undergoing mitral valve reconstruction: a single center prospective observational study

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Background: Mitral valve (MV) regurgitation (MR) is the second most frequent indication for valvular surgery in Europe. Right ventricular (RV) dysfunction is a common finding after cardiac surgery and might persist for years. The RV-function after MV surgery has been controversially discussed. We therefore aimed to evaluate early RV-performance in patients undergoing MV surgery.

Methods: Between 09/2020 and 06/2022, ninety-two patients presenting with MR undergoing MV surgery were consented and prospectively included for evaluation. Echocardiographic evaluation was performed one day before surgery, one week after surgery and three months later. Primary endpoints reported RV-function changes including tricuspid annular plane systolic excursion (TAPSE), RV systolic prime (S') and fractional area change (FAC). Secondary endpoints included stability of MV repair, changes in left ventricular functions and early mortality.

Results: Mean patients' age was 59.1±11.4 years. Fifty-five (59.7%) patients were male. Most of patients presented with severe (n=88; 95.7%) MR. Mean systolic pulmonary artery pressure was 35.6±15.7 mmHg. Moderate or severe pulmonary arterial hypertension (PAH) was present in 60 (65.2%) patients. Patients underwent either isolated MV surgery (n=67; 72.8%) or combined with tricuspid valve surgery (n=25; 27.2%). Minimal invasive surgery was performed in 26.1% (n=24) of the patients. Postoperative short-term follow-up at 3 months reported RV-dysfunction in 44.5% (n=41) of the patients as indicated by reductions in TAPSE & RV S' from 21.2±4.7 to 14±3.3 mm (P<0.001) and from 14.7±4.3 to 9.7±2.8 cm/s (P<0.001) respectively. The FAC reduction from 42.9%±9.6% to 42.2%±9.9% was non-significant (P=0.593) and no need for redo mitral or tricuspid valve surgery was reported. Finally, the presence and severity of preoperative PAH played significant roles for the incidence of RV dysfunction, P=0.021 and P=0.047, respectively. Minimal invasive surgical procedure significantly reduced the incidence of postoperative RV-dysfunction (P=0.013).

Conclusions: Study early results report a significant reduction of RV-function after MV surgery as measured by TAPSE, & RV S', even when the FAC remains unchanged. Even though, this finding has limited prognostic implications during an uneventful surgical course.

Keywords: Right ventricular function; Doppler echocardiography; mitral valve regurgitation (MR); mitral valve surgery; pulmonary arterial hypertension (PAH)

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Submitted Nov 09, 2023. Accepted for publication Jan 12, 2024. Published online Apr 03, 2024.
doi: 10.21037/jtd-23-1727
View this article at: https://dx.doi.org/10.21037/jtd-23-1727

Introduction

Mitral valve (MV) regurgitation (MR) is the second most frequent indication for valve surgery in Europe (1). Its prevalence is increasing, despite the reduced incidence of rheumatic disease (2), probably due to heart failure and left ventricular dysfunction (3,4). Right ventricular (RV) dysfunction is a common finding in patients with chronic MR presenting for surgical treatment (5). Recently, different studies have investigated and reported RV performance after MV surgery (6-9). Since the reduction of the RV systolic function might persist for years after surgery (10), this RV-dysfunction seems to be a negative prognostic marker following cardiac surgery (5,11) and has been indicated to be a strong predictor for reduced survival (12).

Cardiac magnetic resonance (CMR) is the gold standard investigation to assess RV function (13). Limitations in the availability, portability, costs, and time requirements made its use in the clinical routine unpractical. On the other hand, several studies have shown that echocardiography [especially the three dimensional (3D) one] could determine the RV volumes and function in a comparable manner with CMR, this has been steadily improved over the past couple of years (14-20). Based on the above-mentioned limitations, the 3D echocardiographic data are adequate to determine the RV volumes and ejection fraction. Therefore, recent guidelines suggest to reserve 3D methods for serial volume and ejection fraction determinations when available (21). That's why echocardiographers have been using other parameters to describe the RV-function easily and in a reproducible way, mainly via measuring tricuspid annular plane systolic excursion (TAPSE), RV systolic prime (S') and fractional area change (FAC) instead of volume and ejection fraction measured by 3D echocardiography. To be noted, that there are still limitations of using the 2D and Doppler echocardiography to quantify the RV systolic function.

Therefore, in this study we aimed to evaluate early RV performance after MV surgery using focused echocardiography in a prospective manner and examined the impact of pulmonary arterial hypertension (PAH), its severity and its treating medications as well as minimal invasive surgery on the incidence of RV-dysfunction in those patients. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1727/rc).

Highlight box

Key findings

- A significant reduction of right ventricular (RV)-function was reported after mitral valve (MV)-surgery which persists during early follow-up.

What is known and what is new?

- A reduction of RV-function is usually observed after MV-surgery due to different factors such as pericardiotomy, decreased coronary blood flow, inflammatory effects post-cardiopulmonary bypass or as a result of a complex interaction between the remodeled and enlarged left ventricle.
- Preoperative RV-dysfunction, severe preoperative tricuspid regurgitation, severe pulmonary hypertension (PH), prolonged ventilation and minimal invasive surgery were observed as potential confounding variables which may impact the incidence of postoperative RV-dysfunction in the current study.

What is the implication, and what should change now?

- This finding has limited prognostic implications during an uneventful surgical course.
- Minimal invasive MV-surgery & proper management of PH could reduce the incidence of RV-dysfunction.
- Meticulous future screening to report mid- to long-term results is still warranted.
- Further studies with larger cohort and longer follow-up are still under investigation to provide more clinical outcomes.

Methods

Study design and patient population

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study obtained a review board approval according to the ethics committee of University Hospital Essen (Ref# 20-9403-BO), and informed consent was obtained from all individual participants. The study is a single-center prospective observational one including patients presenting with MR undergoing MV surgery at our department, almost over a two-year period between 09/2020 through 06/2022. Exclusion criteria were: patients <18 years, those who refused to participate in the study, patients presenting for emergency surgery, and those who sign the consent to participate into the study and draw their consent later on. Within the aforementioned time period, 335 patients presenting with MV pathology at our institution were screened for study participation. In total, 135 patients fulfilled inclusion & exclusion criteria and agreed to participate in this study. However, primary analysis records of 34 patients had to be excluded due to inadequate echocardiographic image quality and 9 patients did not come for follow-up as agreed before study participation. Finally, data from 92 patients could be included in the final analysis of our study.

Transthoracic & transesophageal echocardiography (TTE & TEE)

TTE was performed one day before surgery, postoperative (pre-discharge) and three months after surgery, to evaluate the heart valves, right and left ventricular functions. All TTE & TEE exams were performed by experienced cardiothoracic anesthesiologists who are certified by the National Board of Echocardiography. A standardized resting TTE examination triggered with electrocardiography (ECG) was performed pre- and postoperatively with the GE Vivid S70 ultrasound system (GE HealthCare GmbH, Solingen, Germany). Intraoperative TEE examination to assess valve pathology, repair or prothesis function and biventricular function was included. RV-function and dimensions were assessed according to the American Society of Echocardiography (ASE) guidelines for assessment of the right heart in adults (13). RV-function was assessed using TAPSE, RV S' and FAC with abnormal levels considered as less than 16 mm, 10 cm/s and 35%, respectively (13).

Moreover, TAPSE is defined as the distance traveled between end-diastole and end-systole at the lateral corner of the tricuspid annulus. TAPSE was recorded from a 2-dimensional guided RV-focused apical four-chamber view at the free wall of the RV with M-mode. FAC is the area different between RV end-diastolic and end-systolic areas measured through ideally RV-focused apical view. The border should be traced carefully to exclude the heavy trabeculations inside the right ventricle. RV S' is evaluated by tissue Doppler which measure the longitudinal velocity of the tricuspid annulus in RV-focused apical four-chamber view. This velocity has been named the systolic wave prime or systolic excursion velocity. In the current study, a RV-dysfunction was defined when at least two of these three echocardiographic indices were significantly reduced according to the ASE guidelines (13). RV peak systolic pressures (RVSP) were estimated from peak tricuspid regurgitation (TR) velocities by the simplified Bernoulli equation in addition to right atrial (RA) pressure: RVSP = 4 × TR velocity × 2 + RA pressure. RA pressures were estimated from an interrogation of the inferior vena cava and pulse wave Doppler of the hepatic vein (13). In the absence of RV outflow obstruction (RVOT) the RVSP was considered to be equal to the systolic pulmonary arterial pressure (SPAP). The TEE was performed in every patient after intubation during the whole procedure.

Pulmonary artery catheter (PAC)

In our department, it is standard operating procedure (SOP) for all patients undergoing MV surgery to receive a PAC following the induction of anesthesia. PAC was used to report hemodynamic values including: pulmonary artery systolic and diastolic pressures (SPAP & DPAP), central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), systemic and pulmonary vascular resistance (SVR & PVR). Mean PAP was calculated with the equation [DPAP + 1/3(SPAP–DPAP)] (22). Cardiac output (CO) was determined using the thermodilution technique (22). Stroke volume (SV) was calculated as CO divided by heart rate (HR) [CO/HR]. Indexes of CO, SV, SVR and PVR variables were calculated via dividing each value with the body surface area (BSA) yielding cardiac index (CI), stroke volume index (SVI), systemic vascular resistance index (SVRI) and pulmonary vascular resistance index (PVRI). To be noted that the PCWP measurement was performed under general anesthesia, which in turn underestimate the presence of post-capillary PAH, however, the echocardiographic reported dilated left atrium in the majority of patients (88, 95.7%) gave us an indirect information for presence of post-capillary PAH.

Pulmonary hypertension (PH) is defined as a mean pulmonary artery pressure (mPAP) of ≥20 mmHg as per the ESC guidelines, typically measured using PAC. In our study, we opted to use systolic pulmonary artery pressure (sPAP) to assess PH severity due to its common measurement via echocardiography, especially in cases of tricuspid valve regurgitation. The severity of PH holds significance in the EuroSCORE, which provides easy and known classification of the severity of PH. During induction of anesthesia, we meticulously measured the mPAS, sPAP, and dPAP in every patient using PAC. Interestingly, while the sPAP values obtained via PAC were not significantly higher, they closely resembled the sPAP values obtained

Table 1 Baseline data

Variables	Patients (n=92)
Demographics	
Age, years	59.1±11.4
Gender, male	55 (59.7)
BMI, kg/m^2	26.8±4.9
Risk factors & comorbidities	
Preoperative cardiac arrhythmia	22 (23.9)
NYHA III–IV	39 (42.4)
Preoperative endocarditis	9 (9.8)
Prior cardiac surgery	9 (9.8)
Anticoagulation (OACs or DOACs)	32 (34.8)
Preoperative creatinine level, mg/dL	0.9±0.2
Preoperative impaired kidney function	6 (6.5)
History of smoking	31 (33.7)
COPD	9 (9.8)
Pulmonary arterial hypertension	
None (sPAP 0–30 mmHg)	32 (34.8)
Moderate (sPAP 31–55 mmHg)	50 (54.3)
Severe (sPAP >55 mmHg)	10 (10.9)
Preoperative mitral valve pathology	
Mild MVR	1 (1.1)
Moderate MVR	3 (3.3)
Severe MVR	88 (95.7)
Mild mitral stenosis	8 (8.7)
MVR etiology	
Leaflet prolapse	69 (75)
Ischemic mitral valve	13 (14.1)
Myxomatous mitral valve	1 (1.1)
Endocarditis	9 (9.8)
Preoperative tricuspid valve pathology	
Mild TVR	61 (66.3)
Moderate TVR	16 (17.4)
Severe TVR	9 (9.8)
Other cardiac pathologies	
Presence of mild AVR	21 (22.8)
Coronary artery disease	6 (6.5)
Operation risk scores	
Logistic EuroSCORE	4 (2.1–7.6)
EuroSCORE II	1.7 (0.8–2.4)
STSROM	0.7 (0.4–1.4)
STSROMM	6.8 (5.0–11.8)

Data are presented by mean ± SD or number (%) or median (interquartile range). BMI, body mass index; NYHA, New York Heart Association functional classification; OACs, oral anticoagulants; DOACs, direct oral anticoagulants; COPD, chronic obstructive pulmonary disease; sPAP, systolic pulmonary artery pressure; MVR, mitral valve regurgitation; TVR, tricuspid valve regurgitation; AVR, aortic valve regurgitation; EuroSCORE, European System for Cardiac Operative Risk Evaluation; STSROM, Society of Thoracic Surgery Risk of Mortality; STSROMM, Society of Thoracic Surgery Risk of Mortality or Morbidity; SD, standard deviation.

via preoperative echocardiography. Prior to surgery, we did not employ a PAC in the patient. Consequently, we relied on the EuroSCORE classification of PH and categorized the patients into three groups, as reported in *Table 1*: those without systolic PH, those with moderate systolic PH (31–55 mmHg), and those with severe PH (>55 mmHg). The mean sPAP measured intraoperatively via TEE was 38.7±10.5 mmHg, while the preoperative echocardiography recorded a mean sPAP of 35.6±15.7 mmHg. Notably, it is intriguing to note the higher mean sPAP values during the intraoperative phase, potentially influenced by various factors such as anesthesia, ventilation, volume status, and catecholamine intake.

Surgical approach and myocardial protection during cardiac surgery

At our center, surgical access is mainly surgeon depended. Experienced surgeons tend to perform minimally invasive MV-surgery via lateral mini-thoracotomy. Additionally, other factors played a role in choosing the surgical access such as patients' BSA, previous cardiac surgery, concomitant procedure other than tricuspid valve surgery, peripheral artery disease (PAD) etc. All patients were operated using cardiopulmonary bypass, central cannulation in cases of conventional surgery and peripheral cannulation (via femoral vessels) was performed in cases of minimal invasive surgery, all patients received a left ventricular vent placed into the left atrium. All patients received antegrade cold crystalloid cardioplegia (Custodiol, Köhler Chemie, Alsbach, Germany) via aortic root to allow cardiac arrest, the amount of the administrated cold crystalloid cardioplegia used was similar in both conventional and minimal invasive techniques. Additionally, systemic mild hypothermia (minimum of 32 ℃) was applied during surgery.

Statistical analysis

Statistical analysis was performed using the SPSS-software (version 27.0. IBM Crop., Armonk, NY, USA). Continuous data were expressed as means and standard deviation (SD) or medians with the 25th–75th interquartile ranges (IQR), as appropriate, and categorical data were expressed as percentages and frequencies. Differences between preoperative and postoperative echocardiographic measurements were compared by *t*-test. Additionally, the correlation between the incidence of postoperative RV-dysfunction and the presence of either preoperative PAH, severity of PAH, usage of anti-pulmonary hypertensive agents or a minimal invasive procedure were examined using the simple cross tables test and demonstrated using clustered bar charts, where Chi-square (χ^2) test or Fisher's exact test (if the expected cell frequencies were <5) were used to estimate the significance of the correlation. All reported P values are two-sided and a value of P<0.05 was considered statistically significant. Moreover, the RV and pulmonary artery pressure indexed value were calculated to navigate the predictive role of RV PA coupling (23). Additionally, potential perioperative risk factors for incidence of postoperative RV-dysfunction using multivariate Regression proportional hazards modelling were examined. Variables from the multivariate modelling exhibiting significance (<0.05) or trend for significance (up to 0.1) were considered to define independent predictors of postoperative RV-dysfunction.

Results

Baseline and preoperative characteristics

Preoperative patients' characteristics, risk factors and comorbidities are described in *Table 1*. A total of 92 patients could be included in final analysis. Mean age was 59.1±11.4 years and more than half of the patients were male (n=55, 59.7%), most of patients presented with severe MR (n=88, 95.7%), mainly due to leaflet prolapse (n=69, 75%). Concomitant moderate to severe tricuspid valve regurgitation was present in 25 (27.2%) patients. Moderate to severe PAH was reported in 60 (65.2%) patients. Preoperative echocardiographic data are reported in detail in *Table 2*. Impaired left ventricular function (<50% ejection fraction) was present in 12 (13%) patients and was accompanied by RV-dysfunction in 6 (6.5%) patients. Nine patients (9.8%) had chronic obstructive pulmonary disease (COPD) classified as GOLD I–II, indicating that the COPD stage was not severe among these individuals. Their ventilation time was not prolonged. This in turn, did not impact the incidence of postoperative RV-dysfunction similar to those didn't have any COPD at all.

Intraoperative and early postoperative results

Each patient received transesophageal echocardiographic examination and right sided heart catheterization using PAC. Date recorded of both tools were collected and reported in *Table 3* after induction of anesthesia. The mean estimated left ventricular ejection fraction (LVEF) was 55.2%±6.2% and the mean SPAP measured by PAC was 38.7±10.5 mmHg. Most of patients underwent elective procedure and nine patients required an urgent procedure due to endocarditis. Patients underwent either isolated MV surgery (n=67; 72.8%) or combined with tricuspid valve repair (n=25; 27.2%), where successful MV repair was performed in all patients. Minimal invasive valve surgery was performed in 24 (26.1%) patients. Mean aortic cross-clamp was 56.3±20.5 minutes. Other perioperative outcomes are displayed in detail in *Table 4*. Early postoperative results are summarized in *Table 5* and reported that 32 (34.7%) patients required RV medical support using Iloprost®, nitrous oxide and/ or tadalafil. Need for reintubation was reported in 3 (3.3%) patients which was due to pneumonia in 2 (2.2%) of them. One patient required cardiopulmonary reanimation due to heart failure and received extracorporeal membrane oxygenator (ECMO) for 7 days. Revision for bleeding was observed in 9 (9.8%) patients and 30-day mortality was reported to be 3.3% (n=3 patients). The cause of the 30-day mortality was attributed to multiorgan failure resulting from sepsis due to MV endocarditis. Finally, coupling the RV PA indexed values in our study did not show RV PA uncoupling. Preoperative analysis FAC/RVSP =42.9%/35.6 mmHg resulted in a 1.20%/mmHg value while postoperative analysis FAC/RVSP =42.2%/29.06 mmHg

Table 2 Preoperative transthoracic echocardiographic data

Variables	Patients (n=92)
Left ventricular function	
LVEF (%)	55.9±8.9
Impaired left ventricular function (LVEF <50%)	12 (13.0)
MAPSE, mm	16.7±4.7
E/E’ ratio	10.1±5.1
LV S’, cm/s	11±2.9
LV EDD index, mm/m^2	33.4±0.7
LV ESD index, mm/m^2	20.4±0.6
LAD, mm	46.7±0.7
Mitral valve function	
Eccentric jet	64 (69.6)
Vena contracta, mm	9±6
EROA, cm^2	0.5±0.2
Regurgitant volume, mL	59.9±16.4
E-max, m/s	1±0.4
E/A ratio	1.9±1.6
Deceleration time, msec	213.7±81.1
Right ventricular function	
Preoperative right ventricular dysfunction	6 (6.5)
FAC, %	42.9±9.6
TAPSE, mm	21.2±4.7
RV S’, cm/s	14.7±4.3
Tricuspid valve function	
Emax, m/s	0.6±0.2
Amax, m/s	0.5±0.2
E/A ratio	1.5±1
Deceleration time, msec	205.9±78.3
Pulmonary artery pressure	
Mean sPAP, mmHg	35.6±15.7

Data are presented as mean ± SD or number (%) or median (interquartile range). LVEF, left ventricular ejection fraction; MAPSE, mitral annular plane systolic excursion; LV S’, left ventricle systolic prime; LV EDD, left ventricular end-diastolic dimension; LV ESD, left ventricular end-systolic dimension; LAD, left atrial diameter; EROA, effective regurgitation orifice area; FAC, fractional area change; TAPSE, tricuspid annular plane systolic excursion; RV S’, right ventricle systolic prime; sPAP, systolic pulmonary artery pressure; SD, standard deviation.

Table 3 Intraoperative data after anesthesia induction

Variables	Patients (n=92)
Transesophageal echocardiographic data	
Emax, m/s	0.99 (0.82–1.1)
Amax, m/s	0.42 (0.3–0.5)
E/A ratio	2.3±0.9
Deceleration time, msec	219.2±74.6
E’ septal, cm/s	8.2±2.8
E’ lateral, cm/s	9.3±3.5
E/E’ ratio	11.9±5.8
LVEF (%)	55.2±6.2
Eccentric jet	64 (69.6)
Vena contracta, mm	8±5
EROA, cm^2	0.49±0.2
Regurgitant volume, mL	57.7±14.2
Pulmonary artery catheter data	
sPAP, mmHg	38.7±10.5
mPAP, mmHg	25.6±8.9
dPAP, mmHg	17.3±6.6
CVP, mmHg	11.6±9.1
Heart rate, bpm	62.6±15.4
MAP, mmHg	74.9±13.2
SpO_2, %	98.7±1.6
Heart index, L/min/m^2	1.8±0.6
Cardiac output, L/min	3.6±1.1
Wedge pressure, mmHg	14 (9–16)
SVRI, dyn·s·cm^{-5}·m^2	2,894±1,120.7
PVRI, dyn·s·cm^{-5}·m^2	529.1±308.9

Data are presented as mean ± SD or number (%) or median (interquartile range). LVEF, left ventricular ejection fraction; EROA, effective regurgitation orifice area; sPAP, systolic pulmonary artery pressure; mPAP, mean pulmonary artery pressure; dPAP, diastolic pulmonary artery pressure; CVP, central venous pressure; MAP, mean arterial pressure; SVRI, systemic vascular resistance index; PVRI, pulmonary vascular resistance index; SD, standard deviation.

Table 4 Operative outcomes

Variables	Patients (n=92)
Urgency	
Elective	83 (90.2)
Urgent	9 (9.8)
Surgical procedure	
Isolated mitral valve repair	67 (72.8)
Concomitant with tricuspid valve repair	25 (27.2)
Surgical details	
Minimal invasive	24 (26.1)
Conventional surgery	68 (73.9)
HLM time, minutes	88.6±29.8
Aortic cross-clamp time, minutes	56.3±20.5
Lowest body temperature, ℃	33.7±2.1
Usage of anti-pulmonary hypertension medication	
Only Iloprost	23 (25.0)
NO and Iloprost	5 (5.4)
Intraoperative foreign blood transfusion	
Mean amount of foreign blood transfusion, units	0 (0–2)

Data are presented as mean ± SD or number (%) or median (interquartile range). HLM, heart-lung machine; NO, nitrous oxide; SD, standard deviation.

Table 5 Early postoperative outcomes

Variables	Patients (n=92)
Respiratory system	
Time prior the 1st extubation attempt, hours	6 [5–9]
Need for NIV-CPAP	27 (29.3)
Need for NIV-BIPAP	4 (4.3)
Need for reintubation	3 (3.3)
Postoperative pneumonia	2 (2.2)
Cardiac system	
Postoperative CPR	1 (1.1)
Postoperative pacemaker	2 (2.2)
Postoperative ECMO	1 (1.1)
Need for norepinephrine	92 (100.0)
Need for dobutamine	83 (90.2)
Need for epinephrine	41 (44.6)
Need for milrinone	3 (3.3)
Revision for bleeding	9 (9.8)
Postoperative right ventricle support	32 (34.7)
Iloprost	31 (33.7)
NO	1 (1.1)
Tadalafil	19 (20.7)
Postoperative blood components transfusion	
Mean amount of foreign blood transfusion, units	1 [0–2]
ICU stay, days	2 [2–4]
Hospital-stay, days	11 [8–15]
Mortality at 28 days	3 (3.3)

Data are presented as number (%) or median [interquartile range]. NIV, non-invasive ventilation; CPAP, continuous positive airway pressure; BIPAP, bilevel positive airway pressure; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; NO, nitrous oxide; ICU, intensive care unit.

resulted in a value of 1.45%/mmHg. Both preoperative and postoperative values were >0.71%/mmHg. It seems that the patients had an adequate RV/PA coupling and could maintain flow across the pulmonary vascular system for a given RV afterload

Patients exhibiting preoperative or intraoperative RV-dysfunction alongside an increase in intraoperative sPAP measured by PAC were administered Iloprost. Those experiencing a decline in oxygenation intra- or postoperatively received additional nitric oxide (NO) therapy. Moreover, individuals who sustained elevated systolic PAP measured by PAC despite Iloprost administration postoperatively were provided with tadalafil.

Follow-up results

Table 6 reports the changes in right and left ventricular functions three months after surgery. These values were compared with the preoperative values, which is reported in detail in *Table 7*. A significant reduction in RV function after MV repair could be observed. In 41 (44.5%) patients postoperative RV systolic dysfunction was reported as indicated by reduction in TAPSE & RV S' measurements from 21.2±4.7 to 14±3.3 mm (P<0.001) and from 14.7±4.3 to 9.7±2.8 cm/s (P<0.001), respectively. The change in FAC measurements from 42.9%±9.6% to 42.2%±9.9%

Table 6 Postoperative follow-up transthoracic echocardiographic outcomes

Variables	Patients (n=92)
Left ventricular function	
LVEF, %	51.4±9.2
MAPSE, mm	14.5±4.7
E/E' ratio	15.2±2.2
LV S', cm/s	9.6±2.2
LV EDD index, mm/m^2	31.7±0.6
LV ESD index, mm/m^2	19.4±0.7
LAD, mm	44.7±0.7
Mitral valve function	
Emax, m/s	1.2±0.3
Amax, m/s	0.7±0.3
E/A ratio	1.8±0.8
Deceleration time, msec	280.8±90.9
Vmax, m/s	1.22±0.34
Pmax, mmHg	6.33±3.23
Pmean, mmHg	2.3±1.18
Right ventricular function	
Postoperative right ventricular dysfunction	41 (44.5)
FAC, %	42.2±9.9
TAPSE, mm	14±3.3
RV S', cm/s	9.7±2.8
RVSP (sPAP), mmHg	29.1±10.7
Tricuspid valve function	
Emax, m/s	0.8±0.4
Amax, m/s	0.7±0.6
E/A ratio	1.4±0.5
Deceleration time, msec	213.6±55.8
Vmax, m/s	1.1±0.26
Pmax, mmHg	5.56±2.49
Pmean, mmHg	1.77±0.51

Data are presented as mean ± SD or number (%). LVEF, left ventricular ejection fraction; MAPSE, mitral annular plane systolic excursion; LV S', left ventricle systolic prime; LV EDD, left ventricular end-diastolic dimension; LV ESD, left ventricular end-systolic dimension; LAD, left atrial diameter; FAC, fractional area change; TAPSE, tricuspid annular plane systolic excursion; RV S', right ventricle systolic prime; RVSP, right ventricular systolic pressure; sPAP, systolic pulmonary artery pressure; SD, standard deviation.

Table 7 Comparison of preoperative and follow-up echocardiographic right- and left ventricular functions

Variables	Preoperative TTE	Follow-up TTE	P value
FAC, %	42.9±9.6	42.2±9.9	0.593
RV S', cm/s	14.7±4.3	9.7±2.8	<0.001
TAPSE, mm	21.2±4.7	14±3.3	<0.001
LVEF, %	55.9±8.9	51.4±9.2	0.001
MAPSE, mm	16.7±4.7	14.5±3.8	0.002

Data are presented as mean ± SD. TTE, transthoracic echocardiography; FAC, fractional area change; RV S', right ventricle systolic prime; TAPSE, tricuspid annular plane systolic excursion; LVEF, left ventricular ejection fraction; MAPSE, mitral annular plane systolic excursion; SD, standard deviation.

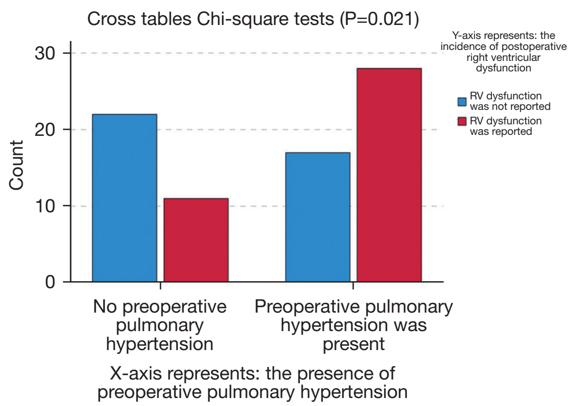

Figure 1 Clustered bar charts illustrating correlation between the incidence of RV-dysfunction and the presence of preoperative pulmonary arterial hypertension. The Y-axis represents the incidence of postoperative RV-dysfunction. The X-axis represents the presence or absence of preoperative pulmonary arterial hypertension. RV, right ventricular.

shows no difference (P=0.593). Left ventricular function was postoperatively reduced as well as reported via (I) reduced ejection fraction from 55.9%±8.9% to 51.4%±9.2% (P=0.001) and (II) reduced mitral annular plane systolic excursion (MAPSE) from 16.7±4.7 to 14.5±3.8 mm (P=0.002), after MV repair. Short term follow-up at 3 months reported no need for redo mitral or tricuspid valve surgery. Finally, the presence and severity of preoperative PAH played a significant role for the incidence of RV-dysfunction, P=0.021 and P=0.047, respectively (*Figures 1,2*). Minimal invasive surgical procedure significantly reduced the

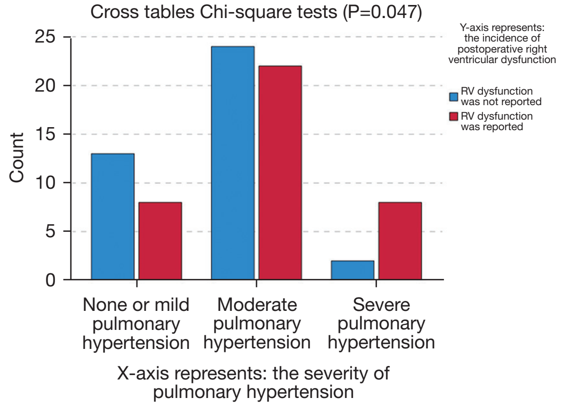

Figure 2 Clustered bar charts illustrating correlation between the incidence of RV-dysfunction and the severity of pulmonary arterial hypertension. The Y-axis represents the incidence of postoperative RV-dysfunction. The X-axis represents the presence of none-to-mild, moderate or severe preoperative pulmonary arterial hypertension. RV, right ventricular.

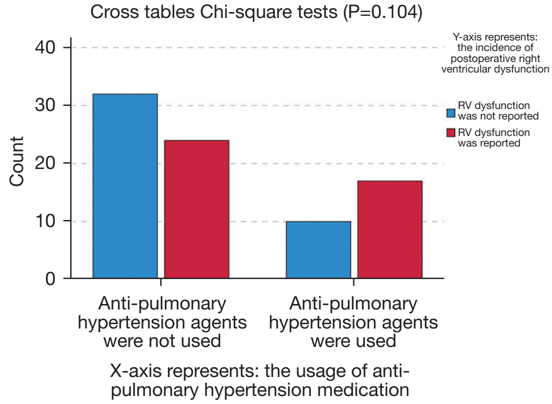

Figure 4 Clustered bar charts illustrating correlation between the incidence of RV-dysfunction and the perioperative use of anti-pulmonary hypertension medication. The Y-axis represents the incidence of postoperative RV-dysfunction. The X-axis represents the perioperative usage of an anti-pulmonary hypertensive medication. RV, right ventricular.

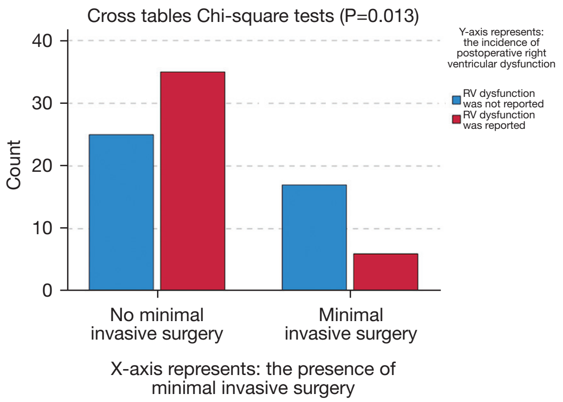

Figure 3 Clustered bar charts illustrating correlation between the incidence of RV-dysfunction and the use of a minimal invasive surgical procedure. The Y-axis represents the incidence of postoperative RV-dysfunction. The X-axis represents whether the procedure was performed via a minimal invasive or a conventional way. RV, right ventricular.

incidence postoperative RV-dysfunction (P=0.013, *Figure 3*). The usage of anti-PH medications tends to reduce the incidence of RV-dysfunction; however, this did not reach statistical significance (P=0.104, *Figure 4*).

Multivariate regression analysis

Table 8 reports the multivariate regression analysis were variables exhibiting significance (<0.05) or tend for significance (up to 0.1) were considered to define independent predictors of postoperative RV-dysfunction. These potential perioperative risk factors for RV-dysfunction were examined. Of those, five variables (severity of TR, preoperative RV-dysfunction, preoperative pulmonary artery pressure, type of surgical procedure and ventilation time) exhibited significance or tend for significance. This multivariate-analysis reported presence of preoperative RV-dysfunction (OR, 1.117; 95% CI: 1.017–1.226; P=0.021) and prolonged mechanical ventilation times (OR, 1.12; 95% CI: 0.996–1.258; P=0.058), as independent predictors of postoperative RV-dysfunction. Additionally, preoperative severe TR (OR, 1.214; 95% CI: 0.971–1.518; P=0.089), preoperative severe PAH (OR, 1.038; 95% CI: 0.997–1.08; P=0.07), and minimal invasive surgery (OR, 0.885; 95% CI: 0.774–1.011; P=0.073) are important factors which influence the incidence of postoperative RV-dysfunction.

Discussion

The main findings of the current study are: (I) echocardiography is an important tool for RV function assessment, (II) patients presenting with MR undergoing surgery suffer from a perioperative deterioration of the RV function, (III) this deterioration persists for at least three months after surgery, (IV) preoperative PAH especially

Table 8 Multivariate regression analysis

Variable	OR	95% CI	P value
Age	0.967	0.922–1.014	0.167
Male sex	1.127	0.943–1.346	0.188
Severity of mitral regurgitation	0.951	0.876–1.033	0.236
Severity of tricuspid regurgitation	1.214	0.971–1.518	0.089
Preoperative right ventricular dysfunction	1.117	1.017–1.226	0.021
Left ventricular ejection fraction	1.056	0.989–1.128	0.101
Preoperative systolic pulmonary artery pressure	1.038	0.997–1.08	0.07
Severity of pulmonary hypertension	1.073	0.91–1.266	0.399
Minimal invasive surgery	0.885	0.774–1.011	0.073
Cardiopulmonary bypass time	0.981	0.946–1.018	0.304
Aortic cross clamp time	1.004	0.954–1.056	0.884
Postoperative systolic pulmonary artery pressure	1.026	0.97–1.086	0.363
Postoperative anti-pulmonary hypertension agent	1.018	0.862–1.204	0.831
Mechanical ventilation time	1.12	0.996–1.258	0.058

OR, odds ratio; CI, confidence interval.

severe grades impact the incidence of RV-dysfunction and (V) minimal invasive MV repair procedures seem to protect RV functions.

Postoperative RV-dysfunction is common after MV repair and could be accompanied by a LV dysfunction, which may persist for years, which in turn may influence patients' long-term outcome. In this prospective analysis, all patients received MV repair via different surgical strategies even those presenting with MV endocarditis (24,25). Data reporting RV functions after MV surgery are controversial. In earlier report from Le Tourneau *et al.*, RV-dysfunction is a common finding in patients with chronic MR presenting for surgical treatment (5). However, they reported a quick improvement of the RV function after MV repair (5). On the opposite, our current study reports a considerable incidence of RV-dysfunction after MV repair, which persists for at least three months after surgery. Similar to the current results, Sun and colleagues also demonstrated a persisting RV-dysfunction in MV surgery (26). There are numerous studies that have discussed the short- and long-term RV-dysfunction after MV surgery. For instance, Ragnarsson *et al.* reported a worse RV function after MV surgery during the long-term echocardiographic examination (7). The study of Sugiura and colleagues observed similar results to the current study reporting a reduction in RV function after MV surgery during the short-term follow-up (8). Keller *et al.* reported acute changes of global and longitudinal RV function after open chest MV surgery, attributing this finding to factors such as pericardiotomy, decreased coronary blood flow, and inflammatory effects post-cardiopulmonary bypass (9). Others reported that RV-dysfunction is the result of a complex interaction between the remodeled and enlarged left ventricle, septal performance and sPAP in mitral regurgitation or other cardiovascular diseases (27-29).

In this study, two-dimensional echocardiography was used to evaluate both ventricular functions in the preoperative phase, the early postoperative phase (before discharge) and later on within the 3-month follow-up, where a reduction in the RV function was observed. The reduction in RV function measured by TAPSE and RV S' could be explained by the reduction in the RV longitudinal pattern or function. The RV has a preponderance of longitudinal fibers, therefore, a greater proportion of contractility of the RV occurs from the base to the apex. The reduction in the RV longitudinal pattern has previously been described with several conventional echocardiographic indices (30). Within our results the reduction in FAC was not significant. A possible explanation of this could be attributed to the fact, that FAC reflects the change in all heart fibers, the radial and longitudinal ones by measuring the area change in the RV between systole and diastole. Another explanation could be that the FAC measurement is much more difficult to obtain than TAPSE or RV S', since it is not such easy to have a clear endocardial border to trace. Moreover, TAPSE and S' do obtain indices of RV longitudinal function, which make a greater proportion of contractility of the RV. These measurements are easy to assess, not time consuming and reproducible, that's why the use of 2D and Doppler echocardiography in RV-function evaluation after MV repair should not be neglected, in spite of the known limitations in the use of two-dimensional and Doppler echocardiographic evaluations.

TAPSE has been validated against RVEF by biplane Simpson method and RV FAC (31,32). Based on the guidelines for the echocardiographic assessment of the RV functions, a TAPSE value of <16 mm has been defined as an abnormal RV function (13). Similarly, in a large study examining a series of 900 cases, a cut-off TAPSE value of >17 mm was defined to be a normal value (33). To be noted that, TAPSE is a one-dimensional, load and angle dependent measurement, which does not always reflect the global RV function. FAC has been validated with CMR (34), and a value <35% is considered to be abnormal by the guidelines (13). It has the advantage that it can be quickly and easily obtained as an alternative parameter to TAPSE. However, it is a two-dimensional measurement, which does not represent the global RV-function or the actual RV ejection fraction. RV S' has been validated and showed good correlations to radionuclide angiography and CMR determining RVEF (35,36). It is even better correlated than TAPSE and FAC when RVEF by CMR was normal to mildly normal (RVEF <50%) (37). A cut off value of RV S' <11.5 cm/s correlates with reduced RVEF (<45%) and RV S' value of <10 cm/s correlates with an impaired RV function, particularly in younger patients (13).

Generally, different factors and mechanisms could cause postoperative RV-dysfunction. Some factors are widely discussed and reported in earlier studies, which include the geometric changes in the RV chamber, intraoperative myocardial ischemia, pericardial disruption, influence of cardiopulmonary bypass, and postoperative adherence of the RV to the thoracic wall (30,38). Moreover, other factors such as LV function, may also influence RV function after MV repair (39). In the current study there was a statistically significant reduction in the LV systolic function as well, which has been reported by measuring the LV ejection fraction and MAPSE, notably, both values were not pathologically low. Similar to these results, Le Tourneau and colleagues reported biventricular function impairment as a strong negative predictor of both cardiovascular and overall survival (5).

Chronic MR causes persisting elevated pressure in the left atrium (LA) and consequent post-capillary PAH. A significant PAH with systolic pulmonary arterial pressure of >50 mmHg is reported in 20 to 30% patients presenting with severe MR (40,41) and increases up to 64% in patients presenting with class III–IV heart failure according to the New York Heart Association (NYHA) classification (21). In asymptomatic patients, in whom the prevalence of PAH is between 6 to 30% (42), the prevalence of PAH increases up to 58% under physical exercise (43). Early reports described that chronic elevated PAH is associated with poor outcome in patients with MR undergoing MV operation (44,45). PAH is then responsible for RV and RA enlargement resulting in RV-dysfunction (46). Similarly, we observed a significant correlation between the presence (P=0.021) and the severity (P=0.047) of PAH and the incidence of postoperative RV-dysfunction. Therefore, echocardiography and PAC were used to measure and prove the presence of PAH in those patients, correlation between the two measurement methods were reported recently (47). Concomitant tricuspid valve annuloplasty was performed when at least moderate TR and/or tricuspid annular dilatation >40 mm was present. Preoperatively 34.7% (n=32) of the patients had no PAH, 54.3% (n=50) of the patients had a moderate and 10.8% (n=10) a severe PAH. During follow-up, 46.9% (n= 15) of the patients initially presenting without PAH developed RV-dysfunction, 40% (n=20) of the patients initially presenting with moderate PAH and 60% (n=6) of the patients initially presenting with severe PAH developed a RV-dysfunction.

Furthermore, the adoption of minimally invasive mitral valve surgery (MIMVS) is increasing constantly due to reduced blood loss, wound infection, arrhythmias and hospital stay and is becoming the new gold standard access (48). In our institution, experienced surgeons tend to perform minimal invasive procedures especially in isolated MV-surgery. This however, did not play any role in patient selection and inclusion in this study as the main aim of the study is to evaluate the postoperative RV-function after MV-surgery and not the outcomes of the surgical access. A recent retrospective analysis showed that the RV deterioration is less pronounced following MIMVS in comparison to patients undergoing conventional surgery (6). Similarly, in the current study minimal invasive MV repair resulted in a reduced incidence of RV-dysfunction despite a longer bypass time. This could be attributed to the less manipulations of the heart during surgery as peripheral cannulation is performed and the small wound area of the heart.

Multivariate regression analysis of more than 15 cofounding variables reported presence of preoperative RV-dysfunction and prolonged ventilation times, as independent predictors of postoperative RV-dysfunction. Mechanical ventilation time are calculated from the time of intubation preoperatively till extubation within ICU-stay. This finding could be attributed to the potential association between the incidence of perioperative atelectasis and increased pressure overload on the right ventricle. Additionally, preoperative severe TR, preoperative severe PAH, and minimal invasive surgery are important factors which influence the incidence of postoperative RV-dysfunction. These three factors which report tend for significance (P value up to 0.1) would properly report significance correlation within the regression analysis when the cohort size would be larger (49).

Finally, the clinical implications drawn from our study findings emphasize the prevalence of RV-dysfunction following MV surgery. Ensuring adequate intraoperative support for both LV and RV function is pivotal in preserving postoperative RV functionality. As such, meticulous preoperative preparation for these patients become imperative. Enhancing their clinical status by optimizing heart failure medication before surgery is crucial. Additionally, a thorough postoperative assessment of the RV is vital to prevent any progression from dysfunction to outright RV failure. Long-term evaluations and prognosis regarding RV-dysfunction subsequent to MV surgery warrant further comprehensive studies that delve into the extended functionality of the RV.

Future studies with larger sample size and longer follow up are essential to investigate the geometrical changes of the RV after MV repair besides the functional alterations. Furthermore, it is necessary to investigates the RV function after MV surgery during exercise and not just during rest. So far, it is still not clear how good the RV capacity under stress would be if the RV-function could deteriorate rapidly. In the final stage of RV-dysfunction, ventriculo-arterial uncoupling ensues with reduced cardiac output and RV failure. The progression from RV-dysfunction to failure is a continuum marked by progressive RV dilation and increases in HR to maintain cardiac index.

Finally, the current study has several limitations as follow: this is a single center observational study with a relatively small number of patients. However, it represents our first results for this important postoperative drawback in patients with MR undergoing surgery. Multivariate regression analysis was performed to define protentional predictors of RV-dysfunction even though some potential cofounding variables were not able to be added to this analysis due to the small cohort. The lack of a reference standard for RV functional evaluation, like magnetic resonance imaging or three-dimensional echocardiography is another limitation of this study. To be noted that, RV strain analysis is easily to perform, more sensible and specific than FAC, RV S' and TAPSE, however the GE machines in our institution do not have the software to measure RV strain. Further studies with larger cohorts of patients and a longer follow-up are still warranted to evaluate the impact of RV-dysfunction on mid to long-term outcomes in patients undergoing MV surgery.

Conclusions

The current analysis reports a statistically significant reduction of RV-function after MV surgery which persists during early follow-up. So far, this finding has limited prognostic implications during an uneventful surgical course on those patients, hence, meticulous future screening to report mid- to long-term results is still warranted. Multivariate regression analysis reported preoperative RV-dysfunction, severe preoperative TR, severe PH, prolonged ventilation and minimal invasive surgery as potential confounding variables which may impact the incidence of postoperative RV-dysfunction. Further studies with larger cohort and longer follow-up are still under investigation to provide more clinical outcomes.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1727/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1727/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1727/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1727/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study obtained a review board approval according to the ethics committee of University Hospital Essen (Ref# 20-9403-BO), and informed consent was obtained from all individual participants.

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Cite this article as: Haddad A, Mohamed A, Arends S, Ishak B, Tsarenko O, Balaj I, Kamler M, Brenner T, Shehada SE. Echocardiographic right ventricular evaluation in cardiac surgery patients undergoing mitral valve reconstruction: a single center prospective observational study. J Thorac Dis 2024;16(4):2259-2273. doi: 10.21037/jtd-23-1727