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Personalised surgical treatment of functional mitral regurgitation

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Chapter 8

Vasoplegia after restrictive mitral annuloplasty for functional mitral regurgitation in patients with heart failure

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Abstract

Objectives: Patients undergoing heart failure surgery are at risk for developing postoperative vasoplegia. The aim of this study was to determine the incidence, survival, and predictors of vasoplegia in heart failure patients undergoing mitral valve repair for functional mitral regurgitation and to evaluate the effect of ischaemic versus non-ischaemic aetiology.

Design: Retrospective.

Setting: University medical centre, single institutional.

Participants: Heart failure patients with functional mitral regurgitation who underwent restrictive mitral annuloplasty (2006-2015).

Measurements and main results: One hundred twenty-two patients were included (48% ischaemic aetiology). The incidence of vasoplegia was 19% and was not influenced by mitral regurgitation aetiology. Ninety-day survival rate was decreased in vasoplegic compared with non-vasoplegic patients (65% v 93%, $p < 0.001$). After adjusting for age, gender, and heart failure aetiology, prior hypertension (odds ratio [OR] 0.28; 95% confidence interval [CI] 0.08 – 0.91; $p = 0.034$), higher creatinine clearance (OR 0.97; 95% CI 0.95 – 0.99; $p = 0.009$), and beta-blocker use (OR 0.25; 95% CI 0.09 – 0.73; $p = 0.011$) decreased the risk of vasoplegia. Anaemia (OR 3.00; 95% CI 1.10 – 8.20; $p = 0.032$) and longer cross clamp (OR 1.03; 95% CI 1.01 – 1.04; $p = 0.001$), cardiopulmonary bypass (OR 1.01; 95% CI 1.00 – 1.02; $p = 0.003$), and procedure times (OR 1.01; 95% CI 1.00 – 1.02, $p = 0.002$) increased the risk of vasoplegia.

Conclusions: Vasoplegia occurs in 19% of heart failure patients undergoing mitral valve repair for functional mitral regurgitation. It is associated with a poor early outcome. Prior hypertension, a higher creatinine clearance, and beta-blocker use were associated with a decreased risk of vasoplegia, whereas anaemia and longer procedure times were associated with an increased risk of vasoplegia, independent of heart failure aetiology.

Introduction

Functional mitral regurgitation (MR) is frequently observed in patients with ischaemic and non-ischaemic heart failure and results from a combination of increased systolic leaflet tethering and decreased closing forces secondary to left ventricular remodelling (Carpentier classification IIIb).^{1,2} Presence of functional MR is independently associated with poor prognosis.^{3,4} Surgical mitral valve repair — generally by implantation of a restrictive mitral annuloplasty (RMA) ring — may be considered in patients with moderate to severe MR and persisting symptoms of heart failure, despite optimal medical and device therapy.⁵⁻⁹ Mitral valve repair may result in durable correction of MR, left ventricular (LV) reverse remodelling, and beneficial clinical outcomes.¹⁰⁻¹³ However, each cardiac operation carries associated perioperative risks, which should be taken into account when considering a surgical intervention.

Vasoplegia is an important determinant for adverse postoperative outcome and is observed in 5% to 54% of patients undergoing cardiac surgery using cardiopulmonary bypass (CPB).¹⁴⁻¹⁷ Postoperative vasoplegia is defined as a state with low systemic vascular resistance despite a normal or high cardiac output, and the need for vasopressor therapy, owing to an imbalance of vasodilator and vasopressor mechanisms.¹⁴ Previous studies demonstrated that patients with heart failure with reduced ejection fraction and patients undergoing valvular procedures are at increased risk for developing vasoplegia after cardiac surgery, independent of surgical procedure times.¹⁸⁻²⁰ Therefore, the authors hypothesized that patients undergoing mitral valve repair for functional MR may be at substantial risk of postoperative vasoplegia, with potential deleterious outcomes.²¹

The aim of this study was to determine the incidence of postoperative vasoplegia in patients with functional MR because of ischaemic or non-ischaemic heart failure, to assess the prognostic impact of vasoplegia on early clinical outcome, and to identify its baseline predictors.

Methods

Study design and study population

For this retrospective cohort study, consecutive heart failure patients with reduced left ventricular ejection fraction (LVEF $\leq$ 35%) and functional MR, who underwent RMA (as a single procedure or with concomitant tricuspid valve annuloplasty, cardiac support device [CSD] implantation, or coronary artery bypass grafting) at the authors' institution between 2006 and

2015, were included. Patients were excluded if the diagnosis of vasoplegia could not be confirmed or ruled out because of the absence of continuous cardiac index recording during postoperative admission in the intensive care unit. This study was conducted in accordance with the declaration of Helsinki. The institutional ethical committee approved the study and waived the need for individual written informed consent.

Study outcomes and data collection

Haemodynamic, laboratory, clinical and survival data were collected prospectively in the patient information systems (EPD-Vision, Leiden, the Netherlands; Metavision, Itémedical B.V., Tiel, The Netherlands; CS-PDMS, Chipsoft, Amsterdam, The Netherlands) and analysed retrospectively. In line with the World Health Organization definition, anaemia was defined as a haemoglobin concentration <8.1 mmol/L for men and <7.4 mmol/L for women.²² Creatinine clearance was estimated with the Cockcroft-Gault formula.²³ For both variables, the last preoperative assessment was used. All patients underwent transthoracic echocardiographic evaluation before surgery. The images were digitally stored and analysed using commercially available software (GE Vingmed Ultrasound AS, Horten, Norway; EchoPAC version 112.0.1). The LVEF was determined from the apical 2- and 4-chamber views using Simpson's biplane method.²⁴ MR severity was graded qualitatively and semiquantitatively.⁶ Pulmonary hypertension was defined as an estimated peak tricuspid regurgitation velocity >2.9 m/s, measured with continuous wave Doppler.

Vasoplegia was defined as previously described: the continuous need for vasopressors (norepinephrine ≥ 0.2 mg/kg/min and any dose of terlipressin) combined with a cardiac index ≥ 2.2 L/min/m² for at least 12 consecutive hours, starting within the first 3 days postoperatively.¹⁶

Surgical Procedures

The indication for surgery was assessed by the multidisciplinary Heart Team, consisting of cardiologists, cardiothoracic surgeons, imaging specialists, heart failure specialists, and anesthesiologists.²⁵ All operations were performed through midline sternotomy using CPB, aortic cross-clamping, and intermittent antegrade warm blood cardioplegia. RMA was performed for moderate to severe functional MR in all patients. Ring size was determined by measuring the anterior leaflet height and then downsizing by 2 ring sizes using a semirigid annuloplasty ring (Physio ring, Edwards Life Sciences, Irvine, CA). RMA was considered successful in case no or mild MR and a leaflet coaptation height of ≥ 8 mm were observed on transoesophageal echocardiography. Tricuspid valve repair was performed with an

annuloplasty ring (Edwards Life Sciences MC3 ring or Edwards Physio Tricuspid) in patients with tricuspid regurgitation $\geq$ grade 3 or a tricuspid annular diameter ≥ 40 mm (or >21 mm/m² body surface area). Concomitant implantation of a CorCap CSD (Acorn Cardiovascular, St. Paul, MN) was performed in patients with non-ischaemic heart failure and a preoperative left ventricular end-diastolic diameter ≥ 65 mm or indexed left ventricular end-diastolic diameter ≥ 30 mm/m². The CSD is a passive external fabric mesh containment device that is implanted to reduce LV wall stress by providing circumferential diastolic support in order to prevent further LV remodelling. Concomitant myocardial revascularization was performed when indicated. Patients did not receive ACE inhibitors, ARBs, or diuretics on the day of surgery.

Anaesthetics and haemodynamic monitoring

Before induction all patients received an arterial catheter for invasive monitoring of blood pressure. A central venous catheter was inserted in the internal jugular vein and a flow-directed balloon-tipped pulmonary artery catheter (Edwards LifeSciences, Irvine, CA) was introduced after induction for continuous monitoring of cardiac output and pulmonary artery pressure. These data were used to calculate the cardiac index and systemic vascular resistance. Norepinephrine, 0.04 to 0.2 μ g/kg/min, was started when the mean arterial pressure was <65 mmHg and the cardiac index was normal (after adequate administration of intravascular fluids if necessary). The aim was for a mean arterial pressure >65 mmHg and adequate end-organ perfusion. When a norepinephrine dosage >1 μ g/kg/min was required, terlipressin was started. Both norepinephrine and terlipressin were reduced when the mean arterial pressure was >65 mmHg and end-organ perfusion was restored.

Statistical Analysis

Continuous variables are expressed as mean $\pm$ standard deviation (SD) when normally distributed or otherwise as median and interquartile range (IQR). The normality of data distribution was determined graphically using the Q-Q plot and tested with the Shapiro-Wilk Test of Normality. Categorical variables are presented as numbers and percentages. Missing values for cross clamp time ($n = 2$, 2%) were replaced using multiple imputations with predictive mean matching, which was repeated 100 times. Baseline age, gender, EuroSCORE, New York Health Association (NYHA) class, creatinine clearance, cross-clamp time, and procedure time were used as predictors in the model. The pooled data were used for analysis. Heart failure patients with ischaemic and non-ischaemic MR and vasoplegic and non-vasoplegic patients were compared. Comparison of continuous data was performed using 2-tailed unpaired Student's t-test for normally distributed variables or otherwise the Mann-Whitney U test. The

Kaplan-Meier method was used to assess 30-day and 90-day survival in vasoplegic and non-vasoplegic patients; the analysis was repeated for heart failure patients with ischaemic and non-ischaemic MR. The survival distributions were compared using the log-rank test.

To explore the association of variables with the occurrence of vasoplegia, univariable logistic regression analysis was performed. Odds ratios (OR) with 95% confidence intervals (CI) were reported. For each variable with a p-value <0.100 during univariable analysis, a multivariable logistic regression analysis was performed to assess their independent association with vasoplegia after adjusting for age, sex, and ischaemic heart failure.

Results

Study Population

A total of 127 patients with LVEF $\leq$ 35% and moderate to severe functional MR underwent RMA (as a single procedure or with concomitant tricuspid valve annuloplasty, CSD implantation, or coronary artery bypass grafting) at the authors' institution between 2006 and 2015. Because 5 patients in whom the presence of vasoplegia could not be assessed owing to absence of cardiac index measurements were excluded, the final population consisted of 122 patients. The baseline characteristics are described in **Table 1**. Mean age was 65 ± 9 years and the majority of patients were male (66%). Mean LVEF was $27 \pm 6\%$. Concomitant procedures were tricuspid valve annuloplasty (66%), CSD implantation (43%) and coronary artery bypass grafting (51%).

In total, 64 patients (52%) had functional MR owing to non-ischaemic heart failure and 58 patients (48%) because of ischaemic heart failure. As expected, baseline characteristics were different between these patient groups (**Table 1**). Patients with non-ischaemic MR were on average 7 years younger ($p < 0.001$), had a 5% lower mean LVEF ($p < 0.001$), and had more often NYHA class III and IV symptoms (73% vs. 50%, $p = 0.009$). In addition, patients with non-ischaemic MR had less often a history of previous cardiac surgery and more often used mineralocorticoid receptor antagonists and diuretics. Furthermore, patients with non-ischaemic MR more often received concomitant tricuspid valve annuloplasty and CSD implantation. Coronary artery bypass grafting was performed in 91% of patients with ischaemic MR. Fourteen percent of patients with non-ischaemic MR received concomitant coronary artery bypass grafting for single vessel coronary artery disease. Because coronary artery disease could not account for the degree of LV dysfunction on echocardiography in these patients, aetiology of MR was classified as non-ischaemic. A longer mean procedure time was observed in ischaemic compared with non-ischaemic MR patients (median 336 minutes [IQR 293 – 407] vs. 267 minutes [IQR 235 – 314], $p < 0.001$). The same was seen for cross-clamp time (median

127 minutes [IQR 110 – 164] vs. 80 [IQR 63 – 100], $p < 0.001$) and CPB time (median 186 minutes [IQR 154 – 227] v 135 [IQR 118 – 167], $p < 0.001$).

Table 1. Characteristics of the study population (n = 122).

	Overall n = 122	Non-ischaemic MR n = 64	Ischaemic MR n = 58	p-value¥
Age (years)	65 ± 9	62 ± 9	69 ± 9	<0.001
Male sex	66%	61%	72%	0.249
Body mass index (kg/m ²)	26 ± 4	26 ± 3	27 ± 4	0.093
Diabetes	28%	27%	29%	0.840
Prior CVA or TIA	10%	11%	9%	0.766
Prior hypertension	38%	30%	47%	0.063
LVEF (%)	27 ± 6	25 ± 5	30 ± 5	<0.001
NYHA class III or IV	62%	73%	50%	0.009
Pulmonary hypertension	57%	64%	50%	0.144
Previous cardiac surgery	7%	2%	12%	0.027
EuroSCORE II (%)	9(5-13)	9 (6-13)	8 (5-15)	0.693
Preoperative laboratory assessment				
Anemia	23%	19%	28%	0.285
Creatinine clearance (ml/min)	62(49-80)	62 (54-83)	60 (44-78)	0.222
Medication				
Beta-blocker	80%	78%	81%	0.823
ACE inhibitor/ARB	83%	86%	79%	0.349
MRA	56%	67%	43%	0.010
Diuretics	91%	98%	83%	0.003
Inotropes	4%	6%	2%	0.368
Concomitant procedures				
TVP	66%	81%	48%	<0.001
CSD	43%	81%	0%	<0.001
CABG	51%	14%	91%	<0.001
Cross clamp time (min)*	104(74-133)	80 (63-100)	127 (110-164)	<0.001
CPB time (min)	155(131-205)	135 (118-167)	186 (154-227)	<0.001
Procedure time (min)	296(255-360)	267 (235-314)	336 (293-407)	<0.001
ICU time (days)	3 (1-5)	3 (2-6)	3 (1-5)	0.654

* Data based on 120 patients. ¥ comparison of patients with ischaemic vs non-ischaemic MR. Continuous data are presented as mean±SD or median(IQR). Categorical data are presented as numbers (%). ACE = Angiotensin-converting enzyme, ARB = angiotensin receptor blocker, CABG = coronary artery bypass grafting, CPB = cardiopulmonary bypass, CSD = cardiac support device, CVA = cerebrovascular accident, ICU = intensive care unit, IQR = interquartile range, LVEF = left ventricular ejection fraction, MR = mitral regurgitation, MRA = mineralocorticoid receptor antagonist, NYHA = New York Heart Association, TIA = transient ischaemic attack, TVP = tricuspid valvuloplasty.

Incidence and clinical impact of vasoplegia

The incidence of vasoplegia in heart failure patients with functional MR was 19% (**Figure 1**). The incidence of vasoplegia was not significantly different between ischaemic and non-ischaemic MR patients (16% vs. 22%, $p = 0.488$). As shown in **Figure 2**, the duration of intensive care unit (ICU) admission was longer in patients with vasoplegia (median 8 days [IQR 5 – 26]) compared with patients without vasoplegia (2 days [IQR 1 – 4], $p < 0.001$). In addition, renal failure occurred more often in patients with vasoplegia (48% vs. 8%, $p < 0.001$). Accordingly, patients with vasoplegia received more continuous veno-venous hemofiltration (44% vs. 4%, $p < 0.001$). Furthermore, both 30-day (78% vs. 98%, $p < 0.001$) and 90-day survival rates (65% vs. 93%, $p < 0.001$) were lower in patients with vasoplegia compared with patients without vasoplegia (**Figure 3, A**). The same applies when the population is stratified for ischaemic (56% vs. 90%, $p = 0.002$) and non-ischaemic MR patients (71% vs. 96%, $p = 0.004$; **Figure 3, B**). There was no significant difference in survival when vasoplegic patients with ischaemic MR were compared with vasoplegic patients with non-ischaemic MR ($p = 0.458$). The same applies to non-vasoplegic patients ($p = 0.234$).

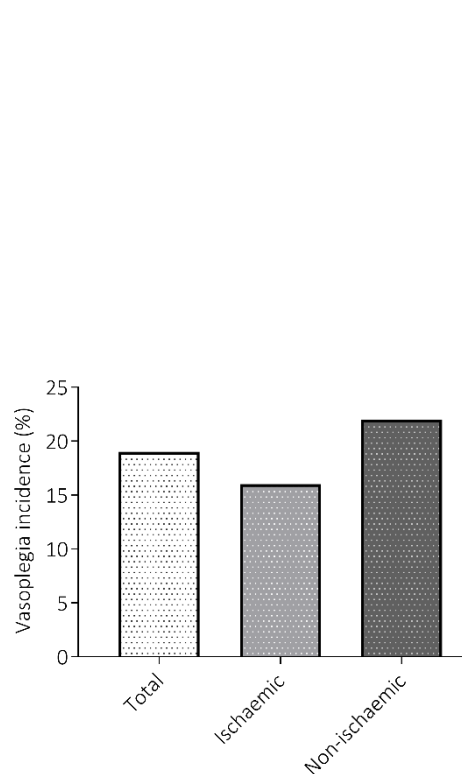


Figure 1. Incidence of vasoplegia in the total study population and in the subgroups (ischaemic and non-ischaemic heart failure patients).

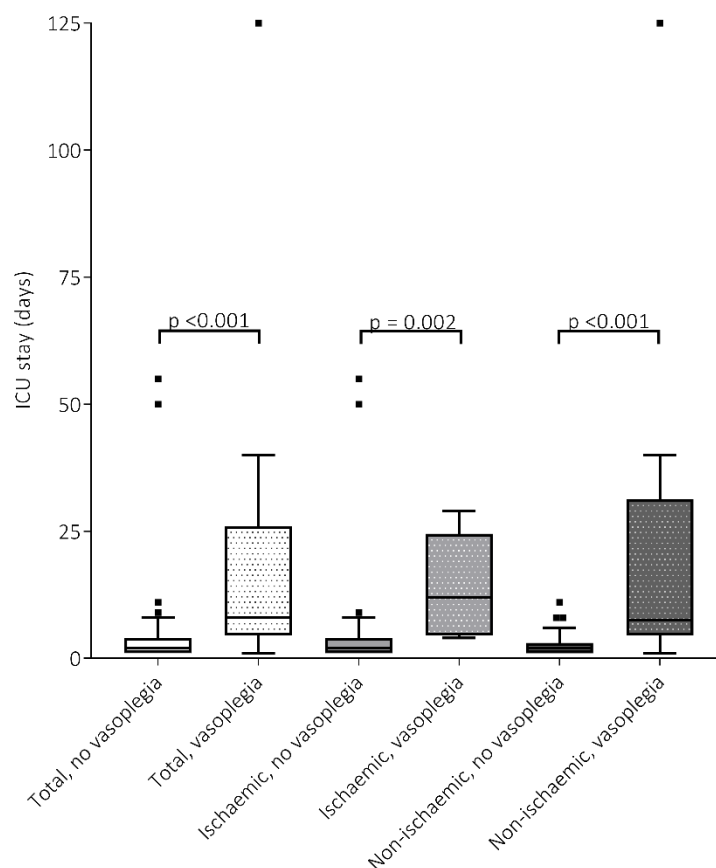


Figure 2. Duration of ICU stay in vasoplegic vs non-vasoplegic patients. Box plots of the IQR and median, with minimum and maximum indicated with whiskers. Outliers are plotted as individual

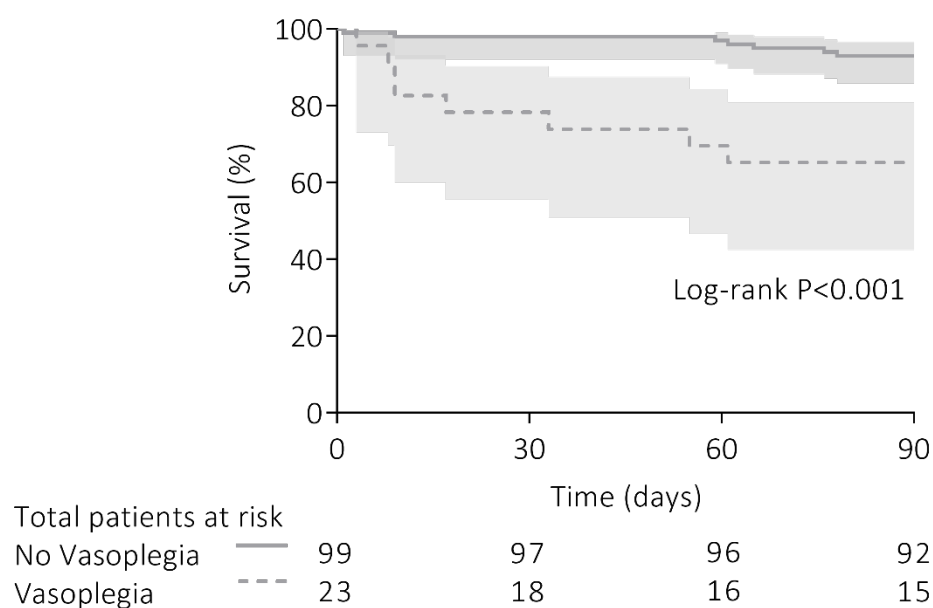


Figure 3 A. Kaplan-Meier survival curve of the total study population. Patients with (dotted line) and without (solid line) vasoplegia were compared. The shaded areas represent the 95% confidence intervals.

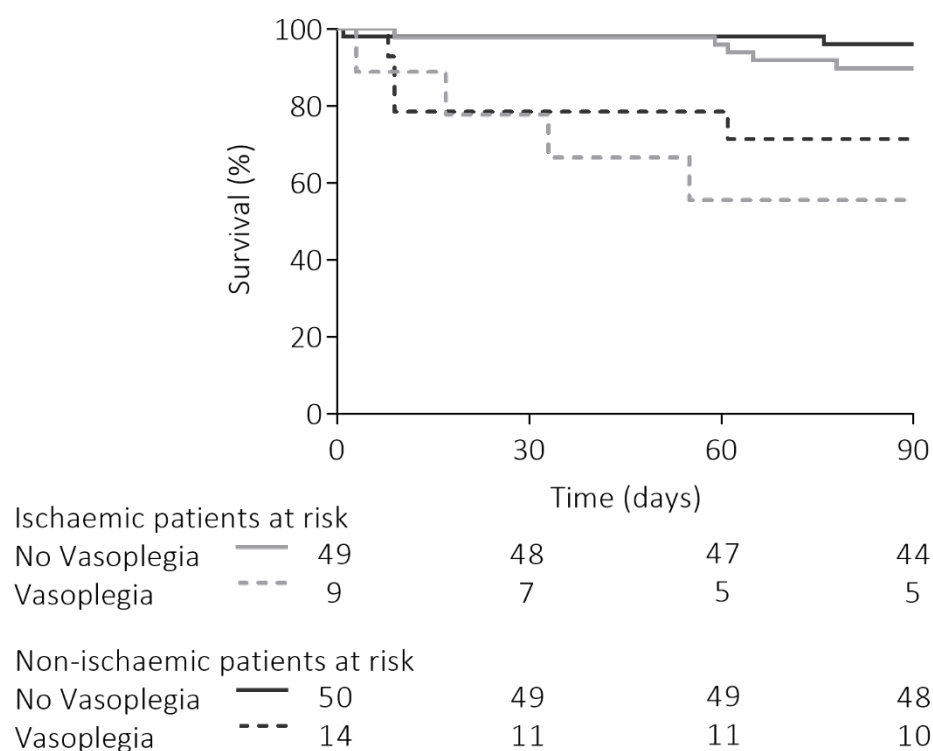


Figure 3B. Kaplan-Meier survival curve of ischaemic heart failure (black) and non-ischaemic heart failure patients (grey). Patients with (dotted line) and without (solid line) vasoplegia were compared. Survival rates were lower in vasoplegic patients for both ischaemic ($p = 0.002$) and non-ischaemic aetiology ($p = 0.004$).

Predictors of vasoplegia

Univariable analysis showed that prior hypertension and beta-blocker use were associated with a decreased risk of vasoplegia, whereas anaemia, longer cross-clamp time, CPB time, and total procedure time were associated with an increased risk of vasoplegia (Table 2).

Subsequent multivariable analysis showed that all characteristics mentioned earlier were associated with vasoplegia independent of age, gender, and ischaemic heart failure (Table 3). In addition, a higher creatinine clearance proved to be associated with a decreased risk of vasoplegia when corrected for age, gender, and ischaemic heart failure.

Table 2. Comparison of characteristics of vasoplegic and non vasoplegic patients, and univariable analysis for predictors of vasoplegia.

	Vasoplegia n = 23	No vasoplegia n = 99	Univariable OR (95% CI)	p-value
Age (years)	65 ± 8	65 ± 10	0.99 (0.95-1.04)	0.714
Male sex	74%	65%	1.55 (0.56-4.29)	0.399
Body mass index (kg/m ²)	25 ± 3	26 ± 4	0.90 (0.78-1.04)	0.146
Diabetes	26%	28%	0.90 (0.32-2.50)	0.832
Prior CVA or TIA	9%	10%	0.85 (0.17-4.16)	0.839
Prior hypertension	17%	42%	0.29 (0.09-0.90)	0.033
LVEF (%)	27 ± 6	27 ± 6	1.00 (0.92-1.09)	0.958
Ischaemic heart failure	39%	50%	0.66 (0.26-1.66)	0.372
NYHA class III or IV	70%	61%	1.49 (0.56-3.94)	0.426
Pulmonary hypertension	70%	55%	1.91 (0.72-5.04)	0.194
Previous cardiac surgery	4%	7%	0.60 (0.07-5.11)	0.638
EuroSCORE II (%)	12(7-14)	8(5-13)	1.02 (0.96-1.08)	0.479
Preoperative laboratory assessment				
Anaemia	39%	19%	2.71 (1.02-7.18)	0.045
Creatinine clearance (ml/min)	57(40-77)	62(52-81)	0.98 (0.96-1.00)	0.058
Medication				
Beta-blocker	61%	84%	0.30 (0.11-0.81)	0.018
ACE inhibitor/ARB	83%	83%	0.99 (0.30-3.26)	0.980
MRA	48%	58%	0.68 (0.27-1.68)	0.398
Diuretics	100%	89%		0.999
Inotropes	4%	4%	1.08 (0.12-10.14)	0.947
Procedure type				
TVP	65%	66%	0.98 (0.38-2.54)	0.968
CSD	52%	40%	1.61 (0.65-4.00)	0.306
CABG	61%	49%	1.65 (0.66-4.17)	0.287
Cross clamp time (min)	112(96-154)	98(72-123)	1.01 (1.00-1.02)	0.009
CPB time (min)	197(140-262)	150(128-195)	1.01 (1.00-1.02)	0.008
Procedure time (min)	334(296-465)	285(250-340)	1.01 (1.00-1.01)	0.003

ACE = Angiotensin-converting enzyme, ARB = angiotensin receptor blocker, CABG = coronary artery bypass grafting, CPB = cardiopulmonary bypass, CSD = cardiac support device, CVA = cerebrovascular accident, LVEF = left ventricular ejection fraction, MRA = mineralocorticoid receptor antagonist, NYHA = New York Heart Association, TIA = transient ischaemic attack, TVP = tricuspid valvuloplasty.

Table 3. Multivariable analysis assessing preoperative predictors for vasoplegia. Each variable is corrected for age, gender and ischaemic heart failure.

	Multivariable analysis OR (95% CI)	p-value
Prior hypertension	0.28 (0.08-0.91)	0.034
Anaemia	3.00 (1.10-8.20)	0.032
Creatinine clearance (ml/min)	0.97 (0.95-0.99)	0.009
Beta-blocker	0.25 (0.09-0.73)	0.011
Cross clamp time (min)	1.03 (1.01-1.04)	0.001
Cardiopulmonary bypass time (min)	1.01 (1.00-1.02)	0.003
Procedure time (min)	1.01 (1.00-1.02)	0.002

Discussion

The main findings of this study can be summarized as follows: 1) the incidence of vasoplegia in heart failure patients undergoing mitral valve repair for functional MR was 19%; 2) vasoplegia was associated with a prolonged ICU admission and an increased 30- and 90-day mortality rate; 3) prior hypertension, a higher creatinine clearance, and beta-blocker use were associated with a decreased risk of vasoplegia, whereas anaemia and longer procedure times were associated with an increased risk of vasoplegia; and 4) the results were independent of ischaemic or non-ischaemic functional MR aetiology.

Incidence of vasoplegia

In the present study, vasoplegia was observed in 19% of patients who underwent a mitral valve repair for functional MR. The incidence of vasoplegia in this study is higher compared with the incidence observed after isolated coronary artery bypass grafting (6.9%) in patients with and without heart failure.²⁶ However, the incidence of vasoplegia in this study is lower compared with the incidence observed after surgical left ventricular restoration (23%), CSD implantation (25%), LVAD implantation (33% – 61%), or orthotopic heart transplantation (11% – 54%) in patients with heart failure.^{15-17,27-29} The wide range of reported vasoplegia incidences may be explained by differences in definitions of vasoplegia,²⁸ although differences in patient and surgical characteristics play a role as well. In line with previous studies, the incidence of vasoplegia was not significantly different between patients with ischaemic and non-ischaemic MR.^{15-17,28}

Clinical impact of vasoplegia

In the literature, early postoperative (30-day and in-hospital) mortality after RMA for functional MR ranges from 2.6% to 8% in ischaemic^{11,12,30} and 5% to 5.8% in non-ischaemic patients.³¹⁻³³

The overall 30-day mortality rate after RMA in this study (6%; 5% in ischaemic and 6% in non-ischaemic MR patients) is comparable to these reports. However, 30-day mortality proved to be much higher in patients who developed postoperative vasoplegia (22%) compared with non-vasoplegic patients (2%, $p < 0.001$) independent of aetiology of functional MR.

Pathophysiology and predictors of vasoplegia

Several mechanisms have been proposed in the pathophysiology of vasoplegia. Landry and Oliver suggested 3 mechanisms: 1) activation of adenosine triphosphate dependent potassium channels on the vascular smooth muscle cell; 2) activation of inducible nitric oxide synthase; and 3) deficiency of arginine vasopressin (AVP).³⁴ The latter was confirmed by Colson et al., showing that vasoplegic patients have higher preoperative copeptin (a precursor of AVP) plasma concentrations, but lower AVP concentrations postoperatively.³⁵ Furthermore, Kortekaas et al. showed that pre-existing endothelial cell activation (reflected by higher baseline von Willebrand Factor propeptide and sP-selectin levels, both markers for heart failure) is associated with vasoplegia in patients undergoing mitral valve surgery.^{36,37} Further, the systemic inflammatory response caused by CPB and surgical trauma, plays a major role in vasoplegia.³⁸ Although the exact pathophysiology of vasoplegia has not yet been elucidated, its aetiology is multifactorial and results from activation of vasodilator mechanisms and inactivation of vasoconstrictor mechanisms.

In the present study, preoperative predictors of vasoplegia were assessed in heart failure patients undergoing mitral valve repair for functional MR. Heart failure patients proved to be at an increased risk of vasoplegia after cardiac surgery in several studies.¹⁸⁻²⁰ This might be explained by the fragile balance of the vascular system in patients with heart failure because all systems perform at maximal capacity to assure adequate perfusion pressure. This fragile balance can easily be disturbed by CPB and surgical trauma.

Several preoperative patient characteristics – no betablocker use, no hypertension, a lower creatinine clearance, and anaemia – proved to be associated with an increased risk of postoperative vasoplegia. Furthermore, prolonged CPB time was related to an increased risk of vasoplegia as well.

The authors hypothesize that these patient characteristics influence activation of vasodilation mechanisms and inactivation of vasoconstriction mechanisms (e.g., drug use, anaemia) and are a marker of the fragile balance of the vascular systems. Heart failure patients who tolerate a beta-blocker and are able to maintain an adequate haemoglobin level and renal function may simply represent a subgroup of patients better able to compensate for haemodynamic disturbances caused by surgical trauma and CPB. In contrast, studies in heart transplantation

patients did not find a difference in beta-blocker use between vasoplegic and non-vasoplegic patients.^{15,28,29} Interestingly, the overall use of beta-blockers in these studies was much lower (22% – 61%)^{15,28,29} compared with studies that found beta-blocker use to be protective (80% – 84%),¹⁶ indicating an important difference in study population.

In line with previous studies in heart failure patients,^{28,29} prolonged CPB time proved to be associated with an increased risk of vasoplegia (median 197 minutes in vasoplegic patients versus 150 in non-vasoplegic patients, $p = 0.008$). This might be explained by the systemic inflammatory response induced by CPB and surgical trauma, which disturbs the balance of the cardiovascular system. A longer CPB time and larger surgical trauma may induce a more severe systemic inflammatory response and consequently increase the risk of vasoplegia. However, a study with much longer CPB times (van Vessem et al., mean 193 ± 69 minutes¹⁶) did not observe an association between CPB time and vasoplegia after heart failure surgery. Therefore, the authors hypothesize that prolonged CPB time increases the risk of vasoplegia in heart failure patients until a certain duration threshold; when this threshold is reached, the risk of vasoplegia does not further increase. However, because a longer CPB time represents more extensive surgery, duration of CPB could simply be a marker of disease progression, although in this study left ventricular ejection fraction, NYHA class, and EuroSCORE II were not associated with an increased risk of vasoplegia.

Limitations

When interpreting the results of the current study, several study limitations should be taken into account. First, this was a retrospective observational study bearing associated biases. Second, this was a single centre study. Further research is necessary to verify if these results can be extrapolated to other centres.

Clinical Implications

Vasoplegia is a hazardous complication in heart failure patients undergoing mitral valve repair for functional MR and is related to a prolonged ICU admission and increased early mortality. Therefore, the likelihood of developing postoperative vasoplegia should be taken into account by the Heart Team when deciding on whether or not to perform surgery. Furthermore, preoperative optimization of haemodynamics and renal function could potentially reduce the risk of vasoplegia. Finally, vasopressin and methylene blue may be considered as treatment option in patients with vasoplegia resistant to fluid and vasopressor therapy.³⁹⁻⁴² However, further research is warranted to unravel the pathophysiologic mechanisms of vasoplegia after cardiac surgery in order to improve therapeutic and preventive treatment options.

Conclusion

Vasoplegia occurred in 19% of heart failure patients undergoing mitral valve repair for functional MR. It was associated with an impaired early outcome. Prior hypertension, a higher creatinine clearance, and beta-blocker use were associated with a decreased risk of vasoplegia, whereas anaemia and longer procedure times were associated with an increased risk of vasoplegia independent of MR aetiology.

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