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Analysis of Risk Factors of Early Mortality After Pericardiectomy For Constrictive Pericarditis

Jing-bin Huang, MD,[1] Zhao-ke Wen, MD,[1] Jian-rong Yang, MD,[1] Jun-jun Li, MD,[1] Min Li, MD,[1] Chang-chao Lu, MD,[1] Da-ying Liang, MD,[2] Cheng-xin Wei, MD[3]

[1]Department of Cardiothoracic Surgery, The People's Hospital of Guangxi Zhuang Autonomous Region, and Guangxi Academy of Medical Sciences, Nanning, Guangxi, China; [2]Department of Cardiothoracic Surgery, Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, Nanning, Guangxi, China; [3]Department of Cardiothoracic Surgery, The People's Hospital of Liuzhou City, Liuzhou, Guangxi, China

VISUAL ABSTRACT

Key question: Risk factors and etiology of early mortality following pericardiectomy remain unknown.

Key findings: In our study, incomplete pericardial dissection, fluid overload, and tuberculosis pericarditis are associated with operative deaths following pericardiectomy.

Take-home message: Early surgical intervention is advocated, complete pericardiectomy (phrenic to phrenic removal and removal of the postero-lateral and inferior wall pericardial thickening) on CPB for complete relief of the constriction of the heart should be the routine.

ABSTRACT

Background: We aimed to investigate risk factors of early mortality following pericardiectomy.

Methods: This was a retrospective study of patients undergoing pericardiectomy between January 1994 and May 2021 at The People's Hospital of Guangxi Zhuang Autonomous Region, Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, and The People's Hospital of Liuzhou City.

Results: This study included 826 patients, who were divided into two groups: group with operative deaths ($N = 66$) and group without operative deaths ($N = 760$). There were 66 operative deaths (66/826, 8.0%). The causes of operative deaths were multiorgan failure (86/826, 10.4%). Preoperative CVP ($P < 0.001$), chest drainage ($P < 0.001$), surgical duration ($P < 0.001$), fluid balance postoperative day D2 ($P < 0.001$), and tuberculosis pericarditis ($P = 0.001$) in group with operative deaths were significantly higher than those in group without operative deaths.

Univariate and multivariate analyses showed that factors associated with operative deaths include male ($P < 0.001$), age ($P < 0.001$), ICU retention time ($P < 0.001$), postoperative hospitalization time ($P < 0.001$), preoperative central venous pressure ($P = 0.018$), postoperative central venous pressure ($P < 0.001$), D0 fluid balance ($P < 0.001$), D2 fluid balance ($P < 0.001$), postoperative chest drainage ($P = 0.029$), surgical duration ($P = 0.003$), serum creatinine baseline ($P = 0.002$), serum creatinine 24h after surgery ($P < 0.001$), serum creatinine 48h after surgery ($P < 0.001$), blood lactate ($P < 0.001$), and tuberculosis pericarditis ($P = 0.033$).

Conclusion: In our study, incomplete pericardial dissection, fluid overload, and tuberculosis pericarditis are associated with operative deaths following pericardiectomy.

INTRODUCTION

Constrictive pericarditis is the result of chronic inflammation characterized by fibrous thickening and calcification of the pericardium that injuries diastolic filling, decreases cardiac output, and ultimately results in heart failure. The operative mortality risk of pericardiectomy still is high, ranging between 5% and 20%. Determining the risk factors of early mortality after pericardiectomy for constrictive pericarditis has clinical significance for the management of patients who undergo pericardiectomy [Vondran 2019; Rupprecht 2018]. The objective of this study was to determine the risk factors of early mortality following pericardiectomy.

PATIENTS AND METHODS

Design: This was a retrospective, observational cohort study of patients undergoing pericardiectomy between January 1994 and May 2021 at The People's Hospital of Guangxi Zhuang Autonomous Region, Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, and The People's Hospital of Liuzhou City. Medical records were reviewed.

Inclusion criteria: Patients undergoing pericardiectomy between January 1994 and May 2021 at The People's Hospital

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Correspondence: Jing-bin Huang, MD, Department of Cardiothoracic Surgery, The People's Hospital of Guangxi Zhuang Autonomous Region, and Guangxi Academy of Medical Sciences, 6 Taoyuan Road, Nanning, 530021, Guangxi, China, Telephone 86-771-2188205, Fax 86-771-2188214 (e-mail: hjb010222@163.com).

of Guangxi Zhuang Autonomous Region, Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, and The People's Hospital of Liuzhou City.

Exclusion criteria: Patients with missing medical records.

Variables to be analyzed: Gender (female/male), age, weight before diuresis, weight after diuresis, time between symptoms and surgery, thickness of pericardium, NYHA class, cachexia, pulmonary tuberculosis, rheumatic heart disease, infective endocarditis, valvular heart disease, coronary heart disease, pleural effusion, left ventricular end diastolic dimension, left ventricular ejection fractions, aortic insufficiency, mitral regurgitation, tricuspid regurgitation, thickened pericardium, pericardial effusion, pericardial calcification, serum creatinine, mean intubation time, ICU retention time, hospitalization time after surgery, central venous pressure, postoperative chest drainage, surgical duration, bleeding during operation, fresh-frozen plasma, packed red cells, fluid balance on operation day, the first day following operation and the second day following operation, low cardiac output syndrome, acute renal injury, multiorgan failure, long-term intubation, empyema, hepatic failure, respiratory failure, ventricular fibrillation, use of inotropic medication, blood lactate, extracorporeal membrane oxygenation (ECMO) requirement, and death.

Preoperative diuresis protocol: Hydrochlorothiazide tablet 25 mg bid, furosemide tablet 20 mg bid. Diuresis treatment lasted 7 to 30 days.

Low cardiac output syndrome: All patients were monitored with a pulmonary artery catheter in the operation room and intensive care unit. Cardiac output and venous oxygen saturation of hemoglobin continuously were measured. Low cardiac output syndrome is defined by a cardiac index of less than 2.0 L/min/m2 in the operation room and intensive care unit. LCOS is characterized by clinical signs or symptoms including elevated blood lactate or rapid increase in blood lactate, decreased central venous oxygen saturation, increased arterial to central venous oxygen saturation difference, decreased urine output, increased peripheral skin temperature to core body temperature difference, and low echocardiographic Doppler-derived cardiac index, high inotrope requirement [Welch 2018; Unai 2019].

Postoperative LVEDD was measured by transthoracic echocardiography postoperatively 1 to 7 days in the intensive care unit. Perioperative death was defined as death within 30 days of the operation or during the same hospital admission.

Serum creatinine was used as the diagnostic standard of acute renal injury.

According to Kidney Disease Improving Global Outcomes classification, if serum creatinine increases by ≥ 0.3 mg/dl (26.5 μmol/l) within 48 hours, serum creatinine is 50% higher than the baseline within first seven days, or urine output is below 0.5 ml/kg/hour for six hours, the patient is considered to have acute renal injury [Claure-Del Granado 2016; Parke 2015].

Multiorgan failure is regarded as a continuous process of varying levels of organ failure rather than an all-or-none event. To characterize multiorgan failure, six different organ systems are regarded as "key organs:" lungs, cardiovascular system, kidneys, liver, coagulation system, and central nervous system [Lee 2015].

Hepatic failure is defined as a severe liver injury, potentially reversible in nature and with onset of hepatic encephalopathy within 8 weeks of the first symptoms in the absence of pre-existing liver disease [Meersch 2017].

Respiratory failure is a condition in which the respiratory system fails in one or both of its gas exchange functions. It is defined by an arterial oxygen tension of ≤ 8.0 kPa (60 mmHg), an arterial carbon dioxide tension of ≥6.0 kPa (45 mmHg) or both [Gatti 2020].

Statistical analyses: Continuous variables are reported as means ± SE. Survival rates were estimated using the Kaplan-Meier method. The chi-square test, the Kruskal-Walls test or the Wilcoxon rank-sum test, as appropriate, were used to evaluate relationships between the preoperative variables and selected intraoperative and postoperative variables. The relationships with perioperative risk factors were assessed by means of contingency table methods and logistic regression analysis. *P* values less than 0.05 were considered to be statistically significant. All analyses were performed using IBM SPSS version 24.0 software (IBM SPSS Inc., USA).

Univariate logistic regressions with early mortality as an outcome were analyzed first. Then, the Variance Inflation Factor was calculated to explore the independence of the selected variables. The results are listed in Table 7, and there is no evidence to show dependence among the selected factors. (Table 7) Therefore, the significant variables were entered into multiple logistic regressions without an interaction term, and the stepwise variable selection method was used to identify the potential risk factors of early mortality.

Ethics approval: The experiment protocol for involving humans was in accordance with the Helsinki Statement and national guidelines and was approved by the Medical Ethics Committee of The People's Hospital of Guangxi Zhuang Autonomous Region, Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, and The People's Hospital of Liuzhou City. They gave the authors approval to waive the need for patient consent for publishing data in the study about the patients.

RESULTS

Characteristics of the population under study: During the study period, 829 patients underwent pericardiectomy; of them, three met the exclusion criteria, so a total of 826 patients were eligible and included in the study group.

Diagnosis of constrictive pericarditis: The diagnosis of constrictive pericarditis was made on the basis of clinical manifestation, echocardiography, chest computed tomography scan, cardiac catheterization, surgery, and pathological criteria. Typical symptoms and signs are a prominent change in the x and y descent in jugular venous pulse, dyspnea upon exertion, palpitations, abdominal distension, as well as edema in the ankles or legs. Echocardiography and chest computed tomography scan revealed a severely thickened or calcified pericardium and cardiac catheterization revealed elevated

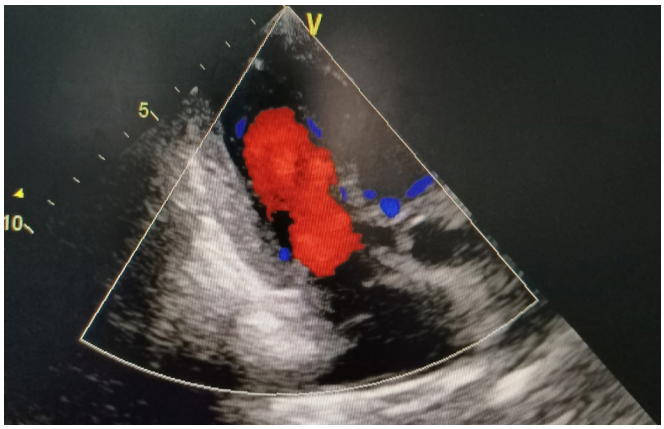

Figure 1A. Transthoracic echocardiography shows the thickened pericardium.

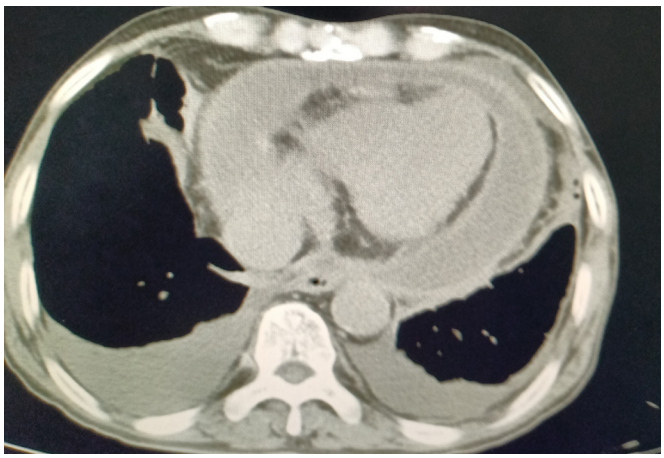

Figure 1B. Chest computed tomographic scan shows the significantly thickened and calcified ring of pericardium.

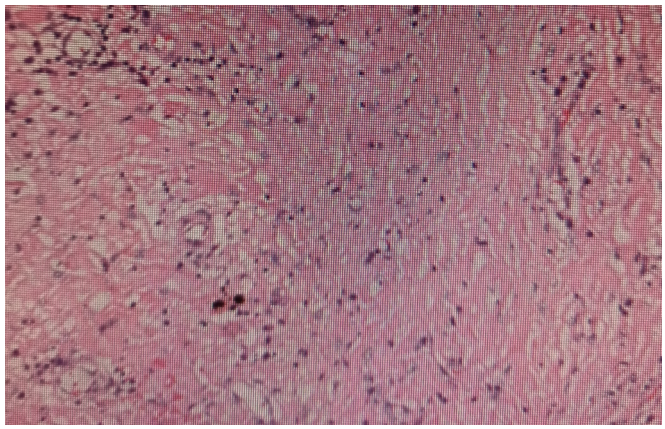

Figure 1C. Histopathologic studies of pericardium show tuberculosis changes including typical granuloma and caseous necrosis.

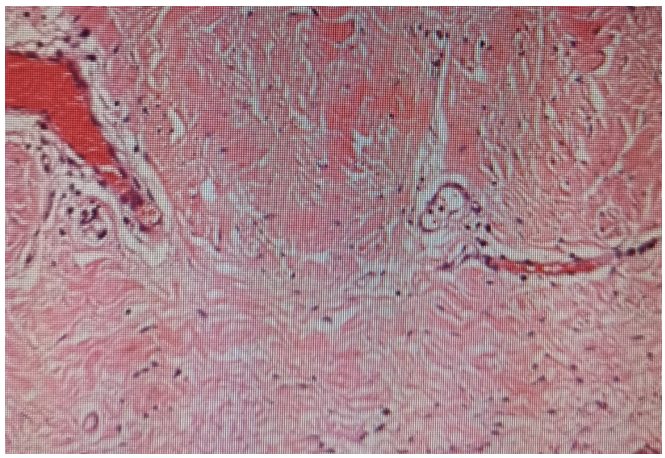

Figure 1D. Histopathologic studies of pericardium show chronic nonspecific inflammatory changes.

end-diastolic pressure and the "square root sign" of right ventricular pressure tracing. Surgical and pathological findings were reviewed to confirm the preoperative diagnosis [Prowle 2010]. (Figure 1A) (Figure 1B) (Figure 1C) (Figure 1D)

Surgical technique: Pericardiectomy was performed via sternotomy. The pericardium was removed between the two phrenic nerves and from the great vessels to the basal aspect of the heart. The pericardium was palpated to identify a relatively soft and uncalcified area after median sternotomy, and the thymus removed laterally. Dissection was started at the base of the aorta, extended downward to the lateral and posterior walls of the left ventricle, followed by the diaphragmatic pericardium. The pericardium over the right atrium and venae cava was resected last. If calcified plaques penetrating the epicardium were present, we left small "islands" of calcified pericardial tissue. Cardiopulmonary bypass was avoided during surgery except for concomitant valve replacement.

Follow up: All survivors discharged from hospital were monitored to the end date of the study. At the outpatient department, all patients were investigated with echocardiogram, electrocardiogram, and X-ray chest film, once every 3 to 12 months. At the last follow up, patients were contacted by telephone or micro-massage or interviewed directly at the outpatient department.

Preoperative and operative data: This study included 826 consecutive patients undergoing pericardiectomy for constrictive pericarditis. The patients were divided into two groups: group with operative deaths (N = 66) and group without operative deaths (N = 760). (Table 1) (Table 2)

Mortality: There were 66 operative deaths (66/826, 8.0%). The causes of operative deaths were multiorgan failure (86/826, 10.4%), including cardiogenic shock + AKI + ventricular fibrillation (15/86), cardiogenic shock + AKI (46/86), cardiogenic shock + AKI + hepatic failure + septicemia (10/86), cardiogenic shock + AKI + respiratory failure (15/86). (Table 6)

Resource utilization: Preoperative CVP (23.3±0.5 versus 19.9±0.2 mmHg, P < 0.001) in the group with operative deaths were significantly higher than that of the group without operative deaths (Table 2). One patient required extracorporeal membrane oxygenation.

Fluid balance on operation day (D0) of the group with operative deaths was significantly less negative than that of the group without operative deaths (-521.2±52.0 ml versus -1185.8±31.5 ml, $P < 0.001$). Fluid balance on postoperative day (D2) of the group with operative deaths was significantly more negative than that of the group without operative deaths (-1465.4±154.9 ml versus -506.2±23.0 ml, $P < 0.001$). Use of adrenaline in the group with operative deaths was significantly higher than that of the group without operative deaths (100% versus 25.9%, $P < 0.001$; 1.8±0.02 versus 0.02±0.01 μg/kg/min, $P < 0.001$, respectively). (Table 3)

Chest drainage (1483.6 ± 85.7 versus 793.8 ± 17.8 ml, $P < 0.001$) and surgical duration (215.1 ± 6.1 versus 179.7 ± 2.2 mins, $P < 0.001$) of the group with operative deaths were significantly more than those of the group without operative deaths.

Table 4 shows the use of inotropic medication ($N = 826$). (Table 4)

Postoperatively, CVP decreased statistically significantly ($P < 0.001$), and LVEDD and LVEF improved statistically significantly ($P < 0.001$ and $P < 0.001$, respectively. (Table 5)

Common early postoperative complications included acute renal injury (222/826, 26.9%), long-term intubation time >48h (393/826, 47.6%), and multiorgan failure (86/826, 10.4%) (Table 6).

Analysis of risk factors of early mortality after pericardiectomy: Univariate analysis of potential risk factors of LCOS showed that numerous factors are associated with operative deaths, including male ($P < 0.001$), age ($P < 0.001$), ICU retention time ($P = 0.009$), postoperative hospitalization time ($P < 0.001$), preoperative central venous pressure ($P < 0.001$), postoperative central venous pressure ($P < 0.001$), D0 fluid balance ($P < 0.001$), D2 fluid balance ($P < 0.001$), postoperative chest drainage ($P < 0.001$), surgical duration ($P < 0.001$), serum creatinine baseline ($P < 0.001$), serum creatinine 24h after surgery ($P < 0.001$), serum creatinine 48h after surgery ($P < 0.001$), fresh-frozen plasma ($P = 0.001$), blood lactate ($P < 0.001$), and tuberculosis pericarditis ($P < 0.001$).

When they were included in multivariate analysis models, multivariate analyses also showed that numerous factors are associated with operative deaths, including male ($P < 0.001$), age ($P < 0.001$), ICU retention time ($P < 0.001$), postoperative hospitalization time ($P < 0.001$), preoperative central venous pressure ($P = 0.018$), postoperative central venous pressure ($P < 0.001$), D0 fluid balance ($P < 0.001$), D2 fluid balance ($P < 0.001$), postoperative chest drainage ($P = 0.029$), surgical duration ($P = 0.003$), serum creatinine baseline ($P = 0.002$), serum creatinine 24h after surgery ($P < 0.001$), serum creatinine 48h after surgery ($P < 0.001$), blood lactate ($P < 0.001$), and tuberculosis pericarditis ($P = 0.033$).

Histopathologic study results: Histopathologic studies of pericardium tissue from every patient were done. The diagnosis of tuberculosis was confirmed on the basis of clinical findings and histopathologic features, including the presence of typical granuloma and caseous necrosis, acid-fast bacilli in Ziel-Nelson tissue staining, and bacteriologic studies using the polymerase chain reaction (PCR) test on the pericardial fluid or tissue for evidence of mycobacterium tuberculosis.

In this series from Guangxi, China, characteristic histopathologic features of tuberculosis (434/826, 52.5%) of pericardium were the most common histopathologic findings, and 260 patients (392/826, 47.5%) had the histopathologic findings of chronic nonspecific inflammatory changes. (Figure 3) (Figure 4)

Follow-up results: There were 760 survivors discharged from the hospital and 684 patients were monitored to the end date of the study. Follow up was 90.0% (684/760) completed. The mean duration of follow up was 126.4 ± 3.5 months (range 1 to 342), seven late deaths (7/684, 1.0%) occurred at 131, 193, 208, 210, 215, 240, and 300 months after being discharged from our hospital. Three died of heart failure,

Table 1. Preoperative characteristics of the patients ($N = 826$)

Variable	Value
Female/male, n	270/556
Age, years	53.9±0.6 (range, 17.0 to 73.0)
Weight before diuresis, kg	56.1±0.4 (range, 36.0 to 80.0)
Weight after diuresis, kg	53.8±0.4 (range, 34.0 to 75.0)
Time between symptoms and surgery, month	9.3±0.9 (range, 0.3 to 120.3)
BMI before diuresis, kg/m^2	21.9±0.1 (range, 15.4 to 31.3)
BMI after diuresis, kg/m^2	21.0±0.1 (range, 14.5 to 28.2)
NYHA class	
II, n	462 (55.9%)
III, n	347 (42.0%)
IV, n	17 (2.1%)
Cachexia, n	33 (4.0%)
Pulmonary tuberculosis, n	17 (2.1%)
Rheumatic heart disease, n	33 (4.0%)
Infective endocarditis, n	9 (1.1%)
Valvular heart disease, n	34 (4.1%)
Coronary heart disease, n	28 (3.4%)
Pleural effusion, n	74 (9.0%)
Preoperative LVEDD, mm	41.7±0.2 (range, 29.0 to 60.0)
Preoperative LVEF, %	62.5±0.3 (range, 51.0 to 77.0)
Aortic insufficiency, n	58 (7.0%)
Mitral regurgitation, n	70 (8.5%)
Preoperative tricuspid insufficiency, cm^2	1.8±0.1 (range, 0.0 to 13.5)
Thickened pericardium, n	825 (99.9%)
Thickness of pericardium, mm	20.2±0.3 (range, 3.0 to 30.0)
Tuberculosis pericarditis, n	434 (52.5%)
Pericardial effusion, n	406 (49.2%)
Pericardial calcification, n	196 (23.7%)
Patients with CPB, n	76 (9.2%)

BMI, weight/(height^2), (kg/m^2)

Table 2. Preoperative data

Variable	Group with operative deaths (*N* = 66)	Group without operative deaths (*N* = 760)	*P*-value
Male, n (%)	24 (36.4%)	532 (70.0%)	<0.001
Age, years	61.5±1.3	52.9±0.5	<0.001
Preoperative CVP, mmHg	23.3±0.5	19.9±0.2	<0.001
Preoperative LVEDD, mm	41.0±0.6	41.7±0.2	0.289
Preoperative LVEF, %	64.3±1.3	62.4±0.2	0.030
Baseline serum creatinine, μmol/l	94.0±3.1	78±1.1	<0.001
Height, cm	151.5±3.1	160.5±0.3	<0.001
BMI before diuresis, kg/m^2	21.5±0.4	21.0±0.1	0.315
BMI after diuresis, kg/m^2	21.4±0.4	21.0±0.1	0.287
Time between symptoms and surgery, months	11.8±2.5	9.0±2.1	0.312
Thickness of pericardium, mm	19.5±0.5	20.2±0.2	0.379

Table 3. Operative data

Variable	Group with operative deaths (*N* = 66)	Group without operative deaths (*N* = 760)	*P*-value
Intubation time, hours	79.1±7.2	69.6±2.7	0.319
ICU retention time, days	3.9±0.3	5.9±0.2	0.007
Postoperative hospitalization time, days	3.9±0.3	17.4±0.5	<0.001
Postoperative CVP, mmHg	14.2±0.3	11.6±0.1	<0.001
D0 fluid balance, ml	-521.2±52.0	-1185.8±31.5	<0.001
D1 fluid balance, ml	-439.4±186.3	-555.9±37.6	0.401
D2 fluid balance, ml	-1465.4±154.9	-506.2±23.0	<0.001
Chest drainage, ml	1483.6±85.7	793.8±17.8	<0.001
Serum creatinine 24h after surgery, μmol/l	108.5±5.0	80.1±0.8	<0.001
Serum creatinine 48h after surgery, μmol/l	201.7±3.6	92.8±1.2	<0.001
Fresh-frozen plasma, ml	1012.1±71.1	635.6±30.5	<0.001
Packed red cells, unit	0.7±0.1	0.5±0.1	0.063
Surgical duration, min	215.1±6.1	179.7±2.2	<0.001
Adrenaline, %	100% (66/66)	25.9% (197/760)	<0.001
Adrenaline	1.8±0.02	0.02±0.01	<0.001

Table 4. Use of inotropic medication (*N* = 826)

Inotropic medication	*N* (%)
Dopamine	477 (57.7%)
Milrinone	17 (2.1%)
Dopamine + milrinone	55 (6.7%)
Dopamine + adrenaline	131 (15.9%)
Dopamine + adrenaline + milrinone	112 (13.6%)
Dopamine + adrenaline + milrinone + norepinephrine	14 (1.7%)
Dopamine + norepinephrine + milrinone + levosimendan	12 (1.5%)
Dopamine + adrenaline + norepinephrine	8 (1.0%)

Table 5. Operative results (*N* = 826)

Variable	Preoperative	Postoperative	*P*-value
CVP, mmHg	19.9±0.2	11.7±0.1	<0.001
LVEDD, mm	41.8±0.2	43.7±0.2	<0.001
LVEF, %	62.4±0.3	64.4±0.3	<0.001
TI, cm^2	1.8±0.1	1.7±0.1	0.210

Table 6. Postoperative mortality and complications (*N* = 826)

Causes of postoperative mortality	*N*
Cardiogenic shock + AKI + ventricular fibrillation	12
Cardiogenic shock + AKI	36
Cardiogenic shock + AKI + hepatic failure + septicemia	8
Cardiogenic shock + AKI + respiratory failure	10
Complication	N (%)
Acute renal injury, n	222 (26.9%)
Multiorgan failure, n	86 (10.4%)
Long-term intubation >48h, n	393 (47.6%)
Empyema, n	9 (1.1%)
Hepatic failure, n	9 (1.1%)
Respiratory failure, n	14 (1.7%)
Ventricular fibrillation, n	16 (1.9%)
Reoperation, n	5 (0.6%)
Concomitant cardiac procedures underwent CPB	N
Constrictive pericarditis + rheumatic heart disease	33
Constrictive pericarditis + valvular heart disease	34
Constrictive pericarditis + infective endocarditis	9
Multiorgan failure	
Cardiogenic shock + AKI + ventricular fibrillation	15
Cardiogenic shock +AKI	46
Cardiogenic shock + AKI + hepatic failure + septicemia	10
Cardiogenic shock + AKI + respiratory failure	15

one of cerebral hemorrhage, and three of unknown reasons. The latest data of follow up showed that 656 survivors were in NYHA class I (656/684, 95.9%) and 21 were in class II (21/684, 3.1%). (Figure 5)

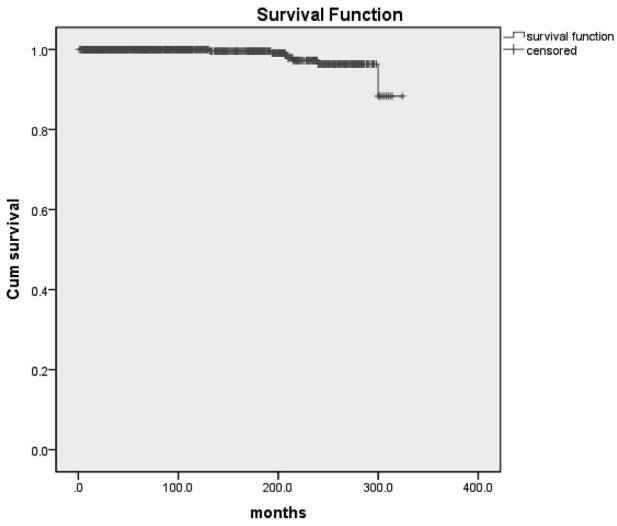

Figure 2. Kaplan-Meier curve for survival

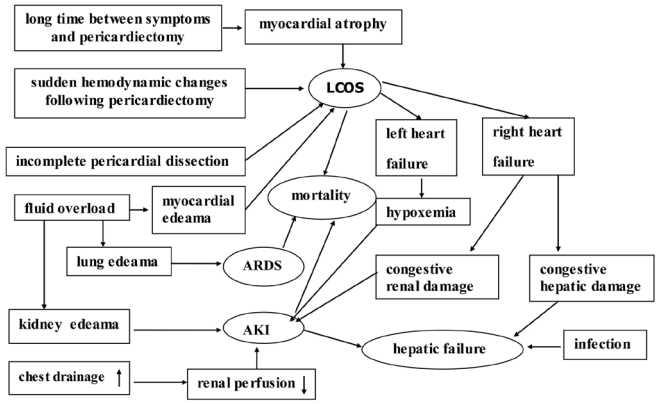

Figure 3. Etiology of early mortality following pericardiectomy

DISCUSSION

Constrictive pericarditis arises as a result of the fibrous thickening of the pericardium, due to chronic inflammatory changes from various injuries. Increased pulmonary and systemic venous pressures manifest clinical features of left and right heart failure. Right-sided heart failure symptoms predominate over left-sided heart failure symptoms, due to the equalization of pressures [van den Berg 2003; Dongaonkar 2010].

In our study, fluid balance on operation day of the group with operative deaths was significantly less than that of the group without operative deaths. Fluid balance on day 2 of the group with operative deaths was significantly more than that of the group without operative deaths. Both univariate and multivariate analyses showed that fluid balance on operation day and fluid balance on postoperative day 2 are associated with early mortality after pericardiectomy.

Fluid therapy is fundamental for the optimization of cardiac output as stroke volume depends on preload, according to the Frank-Starling principle. During fluid administration, cardiac function needs to be closely monitored either with echocardiography or with cardiac output monitoring. Fluid overload must be avoided during the postoperative period. A negative fluid balance is preferable after pericardiectomy to avoid severe complications. A positive fluid balance after cardiac surgery has been associated with increased mortality. Recent studies have shown the relationship of fluid overload with increased mortality and adverse outcomes like pulmonary edema, cardiac failure, delayed wound healing, tissue breakdown, and impaired bowel function, hence, management and optimization of fluid balance becomes a central component of the management of patients after pericardiectomy. Patients with fluid overload (FO) defined as an increase in body weight of over 10% had significantly more respiratory failure, need of mechanical ventilation, and had more sepsis [Bhattad 2020; Wilder 2016; Ahmad 2019]. Values of FO% ≥10% are strongly associated with higher morbidity,

Table 7. Analysis of risk factors of early mortality after pericardiectomy

Model	OR	95% CI	*P*-value
Univariate analysis of risk factors of early mortality after pericardiectomy			
Male	1.005	0.154-0.440	<0.001
Age	1.058	1.032-1.085	<0.001
Weight before diuresis	0.905	0.875-0.935	<0.001
Weight after diuresis	0.911	0.880-0.944	<0.001
Height	0.875	0.845-0.905	<0.001
BMI before diuresis	0.959	0.883-1.041	0.314
BMI after diuresis	1.047	0.962-1.140	0.287
Time between symptoms and surgery	1.005	0.995-1.015	0.315
Bleeding during operation	1.000	1.000-1.001	0.300
Thickness of pericardium	0.982	0.943-1.022	0.378
Intubation time	1.002	0.998-1.005	0.330
ICU retention time	0.898	0.829-0.973	0.009
Postoperative hospitalization time	0.402	0.325-0.497	<0.001
Preoperative CVP	1.119	1.070-1.171	<0.001
Postoperative CVP	1.273	1.177-1.377	<0.001
Preoperative LVEDD	0.974	0.926-1.023	0.288
D0 fluid balance	1.002	1.001-1.002	<0.001
D2 fluid balance	0.999	0.998-0.999	<0.001
D1 fluid balance	1.000	1.000-1.000	0.401
Serum creatinine baseline	1.009	1.004-1.015	<0.001
Serum creatinine 24h after surgery	1.032	1.023-1.040	<0.001
Serum creatinine 48h after surgery	1.074	1.067-1.091	<0.001
Fresh-frozen plasma	1.000	1.000-1.001	0.001
Packed red cells	1.195	0.988-1.445	0.066
Surgical duration	1.008	1.004-1.012	<0.001
Preoperative tricuspid regurgitation	0.869	0.744-1.015	0.076
Tuberculosis pericarditis	3.675	2.003-6.744	<0.001
Blood lactate	1.651	1.502-1.816	<0.001
Chest drainage	1.002	1.001-1.002	<0.001
Multivariate analysis of risk factors of early mortality after pericardiectomy			
Male	0.199	0.101-0.394	<0.001
Weight before diuresis	0.834	0.755-0.942	0.003
Weight after diuresis	1.120	0.993-1.264	0.065
ICU retention time	1.876	1.555-2.263	<0.001
Postoperative hospitalization time	0.361	0.275-0.472	<0.001
D0 fluid balance	1.002	1.001-1.002	<0.001
D2 fluid balance	0.998	0.998-0.999	<0.001
Serum creatinine baseline	1.013	1.005-1.021	0.002
Serum creatinine 24h after surgery	1.019	1.019-1.036	<0.001
Serum creatinine 48h after surgery	1.057	1.032-1.083	<0.001
Fresh-frozen plasma	1.000	1.000-1.000	0.920

Tuberculosis pericarditis	2.203	1.067-4.550	0.033
Surgical duration	1.258	1.079-1.467	0.003
Chest drainage	0.999	0.998-1.000	0.029
Preoperative CVP	0.807	0.676-0.963	0.018
Postoperative CVP	1.200	0.983-1.466	0.073
Tuberculosis pericarditis	50.68	2.01-1277.8	0.017
Blood lactate	9.026	4.166-19.55	<0.001

including worse oxygenation levels, longer MV time, longer ICU stay, greater need for RRT, and even higher mortality. Patients with high FO% had more frequent dysfunction of multiple organs and death. Volume management without adequate monitoring is a risk for volume overload.

Causes of operative deaths following pericardiectomy: In our study, there were 66 operative deaths (66/826, 8.0%). The causes of operative deaths were multiorgan failure (86/826, 10.4%), including cardiogenic shock + AKI + ventricular fibrillation (15/86), cardiogenic shock + AKI (46/86), cardiogenic shock + AKI + hepatic failure + septicemia (10/86), and cardiogenic shock + AKI + respiratory failure (15/86) (Table 6).

Incomplete pericardial dissection is associated with operative deaths following pericardiectomy. The causes of low cardiac output syndrome are related to the incomplete resection of thickened pericardium, unsatisfactory relief of left ventricular compression, excessive ventricular dilatation after pericardial dissection, myocardial weakness, and heart failure. The relief of left heart compression is very important for the recovery of cardiac function after operation. The apical adhesions should be free enough to restore the rotation function of normal ventricular contractions [Bouchard 2010; Peacock 2010].

We removed the pericardium from phrenic nerve to phrenic nerve without CPB as the procedure of choice. However, this often results in insufficient removal of pericardium to relieve the constriction, especially in cases of complete encirclement of the heart, most frequently around the base by a heavily thickened calcified ring (Figure 2). In these situations, the postero-lateral and inferior wall pericardial thickening that are sometimes associated with severe cardiac compression are left behind. Therefore, in severe constrictive pericarditis as these, the textbook approach of phrenic-to-phrenic removal often will be not nearly enough to relieve the constriction. Therefore, complete pericardiectomy (phrenic-to-phrenic removal and removal of the postero-lateral and inferior wall pericardial thickening) on CPB for complete relief of the constriction of the heart should be the routine.

Median sternotomy provides more radical removal of the pericardium over the right atrium and venae cava and allows extensive pericardial removal by using cardiopulmonary bypass. Cardiopulmonary bypass aids in surgical dissection by emptying the ventricular cavities to define clearly the appropriate plane of dissection and facilitates the management of inadvertent cardiac injury.

Chest drainage (1483.6±85.7 versus 793.8±17.8 ml, $P < 0.001$) and surgical duration (215.1±6.1 versus 179.7±2.2 mins, $P < 0.001$) of the group with operative deaths were significantly more than those of the group without operative deaths. Univariate and multivariate analyses showed that chest drainage ($P = 0.029$) and surgical duration ($P = 0.003$) are associated with operative deaths (Table 7). Improvement of surgical techniques can decrease chest drainage and surgical duration.

Fluid balance on operation day and fluid balance on postoperative day 2 are associated with operative deaths following pericardiectomy. Fluid balance on operation day (D0) of the group with operative deaths were significantly less negative than that of the group without operative deaths (-521.2±52.0 ml versus -1185.8±31.5 ml, $P < 0.001$). While fluid balance on postoperative day D2 of the group with operative deaths was significantly more negative than that of the group without operative deaths (-1465.4±154.9 ml versus -506.2±23.0 ml, $P < 0.001$). Univariate and multivariate analyses showed that fluid balance on operation day (D0) ($P < 0.001$) and fluid balance on postoperative day D2 ($P < 0.001$) are associated with operative deaths (Table 7). Patients following pericardiectomy for constrictive pericarditis hospitalized in ICUs are constantly subjected to volume overload. In addition to the fluids received during the resuscitation phase, these patients receive a volume related to medications and nutrition, which easily promotes overload. Therefore, in this maintenance phase, it is important to minimize, or even avoid, the administration of non-essential fluids. Once fluid overload is identified in patients with greater hemodynamic stability and reductions in vasopressors and mechanical ventilation parameters, the removal of excess volume should become a target, promoting a negative water balance as soon as possible within 48 hours postoperatively. The control and optimization of fluid balance is a key element of management of patients following pericardiectomy, since inadequate fluid removal is associated with peripheral edema and pulmonary edema. During fluid administration, cardiac function needs to be closely monitored either with echocardiography or with cardiac output monitoring [Lyon 2005; Perazella 2013].

Patient selection and timing of pericardiectomy: Pericardiectomy is indicated once the diagnosis of constrictive pericarditis is made. Systematic antituberculosis drugs should be given to patients with constrictive pericarditis caused by tuberculous bacteria. Surgery should be performed after body temperature, erythrocyte sedimentation rate, and general nutritional status are normal or relatively stable and before cardiogenic cachexia and severe live function injury occur. In our study, preoperative CVP (23.3±0.5 versus 19.9±0.2 mmHg, $P < 0.001$) in the group with operative deaths were significantly higher than that of the group without operative deaths (Table 2). Univariate and multivariate analyses showed

that preoperative CVP (P = 0.018) are associated with operative deaths (Table 7). Therefore, early diagnosis and treatment of constrictive pericarditis are important. Early surgical intervention is advocated, as constrictive pericarditis is a progressive disease, and patients with a poor preoperative functional class are at the highest risk for perioperative death [Bagshaw 2010].

Histopathologic study results: In this series from Guangxi, China, tuberculosis (434/826, 52.5%) is the major cause of constrictive pericarditis (Figure 3, Figure 4). At present, idiopathic or viral pericarditis is the predominant cause of constrictive pericarditis in the Western world, followed by post-cardiotomy irritation and mediastinal irradiation [Gatti 2020; Maisch 2004]. In our study, tuberculosis pericarditis of group with operative deaths were significantly more than that of the group without operative deaths (69.0% versus 49.9%, P < 0.001). Univariate and multivariate analyses showed that tuberculosis pericarditis is associated with operative deaths (P = 0.033) (Table 7).

In conclusion, etiology of operative deaths following pericardiectomy is showed in Figure 3. Low cardiac output syndrome is fundamental in etiology of operative deaths following pericardiectomy. Incomplete pericardial dissection is associated with low cardiac output syndrome. Low cardiac output syndrome, AKI, ARDS, and hepatic failure can affect each other.

Study limitations: Limitations of the present study include its retrospective design. There may be a selection bias because of the retrospective nature of the study.

CONCLUSION

In our study, incomplete pericardial dissection, fluid overload, and tuberculosis pericarditis are associated with operative deaths following pericardiectomy. Further studies should be conducted with a larger sample size to confirm our study results.

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