

# Effect of Right Heart Systolic Function on Outcomes in Patients with Constrictive Pericarditis Undergoing Pericardiectomy

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## Abstract

**Background:** To determine the influence of right ventricular function in patients with constrictive pericarditis (CP) undergoing surgery and to compare the outcomes of patients who received surgery with those managed medically.

**Methods:** Patients with the diagnosis of CP and healthy volunteers were recruited from January 2006 to November 2011. Patients with CP chose to either receive pericardiectomy or medical management. Echocardiographic measurements were performed to evaluate heart function, and survival was recorded.

**Results:** A total of 58 patients with CP (36 received pericardiectomy, 22 managed medically), and 43 healthy volunteers were included. CP patients who received surgery had a higher survival rate than those managed medically ( $P = 0.003$ ), and higher survival was also seen in the subgroup of CP patients with severely impaired right systolic function. Albumin level, left ventricular end-diastolic dimension, and tricuspid regurgitation velocity were associated with survival in CP patients who received surgery.

**Conclusions:** Preoperative right heart function does not affect surgical outcomes. Patients with severely impaired preoperative right systolic function obtain a greater survival advantage with surgery than with medical treatment.

**Key words:** Constrictive Pericarditis; Right Heart Function; Pericardiectomy; Medical Management

## INTRODUCTION

Constrictive pericarditis (CP) is characterized by a thickened and fibrotic pericardium, and the rigid and nonpliable pericardium results in impaired diastolic heart function leading to heart failure. Causes of CP include tuberculosis (TB), cardiac surgery, and mediastinal irradiation; however, in most cases, the cause cannot be determined.<sup>[1-4]</sup> Untreated patients with CP exhibit a progression of symptoms typically leading to death.<sup>[1-4]</sup> Therefore, in those with CP, pericardiectomy is considered the only effective treatment.<sup>[5-7]</sup> Pericardiectomy has been shown to improve hemodynamics, symptoms, and quality of life in patients with CP.<sup>[5-7]</sup> However, a low output syndrome persists after pericardiectomy in many patients, and is considered an important cause of postoperative mortality.<sup>[8,9]</sup> In addition, it is generally believed that patients with poor right systolic function have a poor prognosis and are likely

to develop a postoperative low output syndrome, and are thus poor surgical candidates.<sup>[10]</sup> Ha *et al.*<sup>[11]</sup> reported that abnormal left ventricular contractility and relaxation were associated with higher operative mortality and poorer long-term outcomes in patients with CP undergoing pericardiectomy. However, few studies have been performed to examine the influence of right ventricular function in patients with CP undergoing surgery.

The purpose of this study was to determine the influence of right ventricular function in patients with CP undergoing

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surgery and to compare the outcomes of patients with CP, who received surgery with those who were managed medically.

## METHODS

### Patients

This study included patients with the diagnosis of CP seen at Peking Union Medical College Hospital from January 2006 to November 2011. The study was approved by the Institutional Review Board of our College and all patients provided written informed consents.

Diagnosis of CP was made according to the following criteria: (1) The presence of clinical manifestations of CP, which might include chronic heart failure, edema, ascites, pleural effusion, hepatomegaly, increased jugular venous pressure, and syncope.<sup>[3,4]</sup> (2) Echocardiographic evidence of CP including ventricular septal shift with respiration, moderate bilateral atrial enlargement, increased pericardial thickness, respiratory variation of mitral inflow > 25%, and increased diameter of the inferior vena cava (IVC).<sup>[12-15]</sup> (3) Magnetic resonance imaging or computed tomography showing thickening of the pericardial layers (> 4 mm in diameter).<sup>[16,17]</sup> (4) Right heart catheterization and pathological findings after pericardiectomy. In all cases, the diagnosis of CP was made independently by 2 experienced cardiologists. Because it was important to differentiate CP from restrictive cardiomyopathy, in addition to considering clinical manifestations, several imaging studies were performed for the differential diagnosis and, if necessary, right heart catheterization was done. Besides that, intra-operative findings and postoperative pathological examination in all operated patients supported our diagnosis of CP. Patients with CP caused by tumors were excluded. In addition, only patients with inactive TB were included; those with active TB were excluded.

After a diagnosis of CP, the risks and benefits of surgery versus medical therapy were thoroughly discussed with the patient and family members by a medical team, and the patient chose to receive surgery or be managed medically. Common reasons for a patient to choose medical therapy were other underlying diseases and the perception that surgery caused an increased risk. The therapeutic cost was another concern that caused patients to choose medical therapy. In addition, the choice may have been influenced by the perception by Chinese of surgery as inherently dangerous. Some patients refuse to receive surgery, and it requires enough time for the communication between patients and surgeons to allow patients to know the potential good and bad consequences of the surgery. In addition, negotiation between patients and their relatives is needed. Thus, the decision-making is dependent on the perception of patients and their relatives of the surgery.

For patients in the medical group, treatments included those targeting the causes and those targeting the symptoms. For example, patients with CP due to TB were treated with anti-TB drugs such as pyrazinamide, rifampicin, and isoniazid, and patients with CP due to immune disorders were treated with hormones or immunosuppressive drugs. The

aim of symptomatic treatment was to alleviate symptoms of heart failure and prevent damage to other organs, e.g., liver damage. Symptoms were treated with diuretics and other medications depending on the patient's individual condition.

For all patients, medical history and clinical findings were recorded. Follow-up was done with clinic visits and telephone calls to the patients, their relatives, and their physicians. In addition to the patients with CP, 43 healthy volunteers were included for comparison of right heart function, as it is not known if patients with CP have worse right heart function or how severely affected their right heart function may be. The normal volunteers were recruited from persons receiving routine health checkups which included a medical history, biochemical tests, and heart echocardiography. Volunteers were age-matched to the CP patients.

Blood testing, including a complete blood count and tests of liver and kidney function was performed in the morning of the day after patients were admitted. Renal function was calculated according to the 4-variable Modification of Diet in Renal Disease equation:<sup>[18]</sup> (Glomerular filtration rate [GFR] [ml/min/1.73 m<sup>2</sup> = 186 × (serum creatinine [μmol/L]/88.4)<sup>-1.154</sup> × age [years]<sup>-0.203</sup> × 0.742 [if female]). Cardiac-related death was defined as death due to cardiac causes such as progressive congestive heart failure or sudden death.

### Echocardiography

Guidelines for the Echocardiographic Assessment of the Right Heart in Adults published by the American Society of Echocardiography in 2010,<sup>[19]</sup> define impaired right systolic function as a fractional area of change (FAC) < 0.35, S' < 10 cm/s, tricuspid annular plane systolic excursion (TAPSE) < 16 mm, or tissue myocardial performance index (MPI) > 0.55. We further defined severely impaired systolic right heart function if 3 or more of the above criteria were met.

Echocardiography was performed within 1 week after patients were admitted with a Vivid 7 (in the early years of the study) or a Vivid E9 ultrasound system (General Electric Company, CT, USA) with a 1.7/3.3-MHz transducer. General electric indicated that the transformation formula was the same for both models. Thus the data between the 2 devices is consistent. Two-dimensional and Doppler echocardiographic examinations were performed in a standard manner, and all measurements were repeated during 3 consecutive heart beats and data were recorded for offline analysis.

Right heart function evaluations were performed according to guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography.<sup>[19]</sup> The indexes of right heart function included right ventricle (RV) FAC. FAC was obtained by tracing the RV endocardium in both systole and diastole from the annulus, along the free wall to the apex, and then back to the annulus, along the interventricular septum. The percentage RV FAC was defined as: (End-diastolic area – end-systolic area)/end-diastolic area × 100. TAPSE or tricuspid annular motion was the distance of systolic

excursion of the RV annular segment along its longitudinal plane, determined in a standard apical 4-chamber view. The tissue Doppler S' was measured in an apical 4-chamber view with the pulsed Doppler sample volume placed in the tricuspid annulus. The RV MPI was obtained by the pulsed tissue Doppler method, and defined as (TCO-ET)/ET where TCO is the tricuspid closure opening time and ET is the ejection time.

### Surgical protocol and medical management

Three of the 36 operated patients were placed on cardiac bypass. For the operation, a midline incision was made at the sternum. Then pericardial stripping was performed, first at the outflow tract and then at the inflow tract, and first at the left ventricle and then at the RV. Procedures were done from anterior region of left or RV, to the apex of the heart, to the right ventricular outflow tract, pulmonary artery and aortic root, to the right ventricular body, to the diaphragmatic surface of the heart, and to the entrance of the superior and IVC. Sometimes, it was necessary first to release the stenosis of the right ventricular outflow tract and then open the thickened pericardium of the anterior wall of the RV. The extent of pericardial stripping was as follows: Left: Anterior to the left phrenic nerve; right: Surpassing the atrioventricular groove to avoid producing pressure difference; upper: Basis of major vessels (the right ventricular outflow tract and the main pulmonary artery were freed until there was no increase in right ventricular pressure); lower: Diaphragmatic surface (the apex of heart could elevate and rotate during the contraction). The atrial wall was thin and susceptible to tearing, and proper stripping was required at the atrial wall. The fibrous constriction ring at the entrance of the superior and IVC needed to be released and was cut or partially cut. It has previously been reported that "total pericardiectomy is defined as the removal of all anterior pericardium between the phrenic nerves from the great vessels superiorly down to and including the diaphragmatic surface."<sup>[1,4,7,20]</sup> This is consistent with our definition and the procedures used in the surgery [Figure 1].

The primary surgical goal was total pericardiectomy, which was defined as a wide resection of the pericardium with the phrenic nerves defining the posterior extent, the great vessels including the intrapericardial portion of superior vena cava-right atrium junction defining the superior extent, and the diaphragmatic surface including the IVC-right atrium junction defining the inferior extent of the pericardial resection.<sup>[7]</sup> Constricting layers

of the epicardium were removed if possible. Any excision less than total was defined as partial.

### Statistical analysis

Continuous variables were presented as a mean and standard deviation (SD), and the independent *t*-test was performed for group comparisons. For the continuous variables without normal distribution, median and inter-quartile ranges were presented, with Mann–Whitney *U*-tests for group comparisons. Categorical variables were presented as counts and percentages, with the Chi-square or Fisher's exact test used for group comparisons, as appropriate. Logistic regression analysis with stepwise model selection was used to predict which factors were correlated with survival. Variables with clinical significance for predicting survival were input into the multivariate model. Statistical analyses were performed with SAS 9.2 statistics software (SAS Inc., Cary, NC, USA). A two-sided *P* < 0.05 was considered to indicate statistical significance.

## RESULTS

### Clinical characteristics of constrictive pericarditis patients and normal subjects

A total of 101 subjects (58 patients with CP and 43 healthy volunteers) were included in the study. The mean follow-up duration was 25.33 ± 19.15 months (range, 0–99 months). Baseline characteristics of the patients and healthy volunteers are summarized in Table 1. The mean age of the patients with CP was 46.30 ± 18.50 years old and of the volunteers was 46.80 ± 14.50 years old (*P* = 0.887). There were no significant differences between CP patients and normal subjects in gender, age, GFR, left ventricular ejection fraction (LVEF), RV FAC, or tricuspid regurgitation velocity (all *P* > 0.05). Hemoglobin, left ventricular end-diastolic dimension (LVEDD), S', TAPSE, and IVC collapse percentage were significantly lower in CP patients as compared with normal subjects (all, *P* < 0.001). The median concentration for albumin was significantly lower in CP patients compared with normal subjects (3.6 vs. 4.5 g/dl, *P* < 0.001). Total bilirubin, MPI and IVC were significantly higher in CP patients compared with normal subjects (total bilirubin, *P* = 0.037; MPI and IVC both *P* ≤ 0.001).

Of the 36 patients receiving surgery, 17 (47%) had concomitant diseases including TB, coronary heart disease, rheumatoid



**Figure 1:** Pericardiectomy in patients with constrictive pericarditis. (a) A patient with constrictive pericarditis undergoing pericardiectomy. \*Indicating thick pericardium. (b) Preoperation echocardiography shows enlarged atriums, thick pericardium (as indicated by \*) and pericardial effusion (indicated by red arrow). (c) Postoperation echocardiography shows normal atrium without pericardial effusion.

**Table 1: Characteristics of patients with constrictive pericarditis and normal subjects**

Characteristics	Constrictive pericarditis patients (n = 58)	Normal subjects (n = 43)	P
Male, n (%)	36 (62.07)	19 (44.19)	0.074
Age (years)	46.30 ± 18.50	46.80 ± 14.50	0.887
Hemoglobin (g/dl)	12.70 ± 2.02	14.19 ± 1.61	<0.001*
Albumin (g/dl)	3.6 (3.1–3.8)	4.5 (4.4–4.7)	<0.001*
Total bilirubin (g/dl)	1.93 (1.15–2.93)	1.5 (1.15–1.59)	0.037
GFR (ml/min)	112.46 ± 34.34	108.46 ± 21.95	0.478
Left heart function			
LVEDD (mm)	40.16 ± 5.55	45.28 ± 4.27	<0.001*
Ejection fraction (%)	67.40 ± 8.92	69.07 ± 5.88	0.260
Right heart function			
FAC (%)	0.48 ± 0.11	0.48 ± 0.10	0.795
S' (cm/s)	6.65 ± 2.39	11.89 ± 1.96	<0.001*
TAPSE (mm)	11.56 ± 3.32	20.78 ± 2.32	<0.001*
MPI	0.53 ± 0.23	0.42 ± 0.07	0.001*
IVC (mm)	21.02 ± 3.9	14.87 ± 3.01	<0.001*
IVC collapse percentage	22.66 ± 19.48	55.84 ± 16.64	<0.001*
Tricuspid regurgitation velocity (m/s)	2.13 ± 0.38	2.13 ± 0.3	0.957
CVP (mmH2O)			
Before surgery	19.06 ± 5.28	–	
After surgery	9.51 ± 3.10	–	

\* $P < 0.05$ . Data are presented as  $n$  (%) or mean ± SD or median (IQR). GFR: Glomerular filtration rate; LVEDD: Left ventricular end-diastolic dimension; FAC: Fractional area change; TAPSE: Tricuspid annular plane systolic excursion; MPI: Myocardial performance index; IVC: Inferior vena cava; CVP: Central venous pressure; SD: Standard deviation; IQR: Interquartile range. N for CVP before surgery: 36; N for CVP after surgery: 35.

arthritis, hepatitis, and epilepsy. Of the 22 patients receiving pharmacotherapy, 11 (50%) had concomitant diseases. There was no significant difference in the proportion of patients with concomitant diseases. Therefore, on the basis of concomitant diseases, we failed to confirm that patients receiving pharmacotherapy were sicker than those who received surgery. In addition, based on our analysis for patients with serious right heart dysfunction, there was no significant difference between the surgery and pharmacotherapy groups presurgically in general condition or classification of heart failure. In the surgery group, right heart function ( $7.05 \pm 2.56$  cm/s) slightly higher than that in nonsurgery group ( $6.00 \pm 1.98$  cm/s), but this difference was not significant, and, therefore, cannot be used to indicate that patients without surgery were sicker.

### Characteristics of patients with constrictive pericarditis who received surgery and those managed medically

Of the 58 patients with CP, 36 patients received surgery and 22 did not. A comparison of patients with CP who received surgery with those who received medical management is shown in Table 2. Approximately, 64% of the CP cases were TB-related, and other causes of CP included postcardiotomy CP, immune disorders, radiation, and non-TB-related inflammation. Twenty-four patients (41.3%) had ascites;

10 (17%) had abnormal liver function. No CP patient had associated valve disease.

Before surgery, the dose of diuretics was significantly higher than that after surgery. Of 36 patients receiving surgery, the dose of diuretics increased after surgery in 1 patient, and the dose and type of diuretics remained unchanged in 11 patients after surgery. In remaining 24 patients, the dose of diuretics showed a decreasing tendency, of whom 20 patients were treated with intravenous diuretics before surgery and with oral diuretics after surgery; and 4 patients were treated with potent loop diuretics before surgery and with other diuretics (such as hydrochlorothiazide) after surgery. Of the 36 patients receiving surgery, vasoactive drugs were not used after surgery in 8 patients, and dobutamine and/or norepinephrine were used in the remaining patients to maintain blood pressure and peripheral perfusion. When the disease condition was stable, the dose of vasoactive drugs was reduced until the drugs could be discontinued. In the patients treated with vasoactive drugs, mechanical ventilation was discontinued in 20 patients within 24 h after surgery, in 5 patients within 3 days after surgery and in 2 patients within 1 week after surgery. Mechanical ventilation was maintained in 1 patient who finally died. Vasoactive drugs were important for a majority of patients in order to progress smoothly through the postoperative period.

An intra-aortic balloon pump was used in 2 patients after surgery, and extracorporeal membrane oxygenation (ECMO) in 1 patient, all of whom had stable hemodynamics and were discharged smoothly. Three patients died in the hospital, and 5 died during the follow-up period. Clinical symptoms were significantly improved before discharge except for those who died in the hospital. Some patients had no clinical symptoms upon discharge, and some still had clinical manifestations, such as mild dropsy and palpitation, that resolved gradually during the follow-up period.

The survival of CP patients who received surgery was significantly higher than of those who did not receive surgery (35 [97.2%] vs. 15 [68.2%],  $P = 0.003$ ). There were no significant differences in gender, age, symptom duration, cause of CP, length of hospital stay, hemoglobin, albumin, total bilirubin, GRF, left and right heart function, right heart MPI, tricuspid regurgitation velocity, New York Heart Association (NYHA) class, E/A, E/e' and central venous pressure between patients that received surgery and those who did not (all,  $P > 0.05$ ) [Table 2]. Of note, there were 5 patients with postcardiotomy CP. All of them received surgery (1 subtotal and 4 total pericardiectomies), and all survived until the end of the 5-year follow-up.

### Multivariable logistic regression analysis of factors associated with survival of patients with constrictive pericarditis

The results of the multivariable logistic regression analysis of factors predictive of survival are shown in Table 3. Receiving surgery, albumin level, tricuspid regurgitation,

**Table 2: Characteristics of constrictive pericarditis patients who received surgery and those managed medically**

Characteristics	Surgery (n = 36)	No surgery (n = 22)	P
Male, n (%)	22 (61.1)	14 (63.6)	0.848
Age (years)	43.69 ± 17.23	50.64 ± 20.11	0.168
Symptom duration (months)	20.54 ± 28.98	16.12 ± 17.03	0.467
Cause, n (%)			
TB	26 (72.2)	11 (50)	0.088
Other <sup>†</sup>	10 (27.8)	11 (50)	
Hospital stay (d)	34.28 ± 19.03	41.86 ± 54.29	0.533
Hemoglobin (g/dl)	12.56 ± 2.26	12.94 ± 1.58	0.486
Albumin (g/dl)	3.46 ± 0.49	3.44 ± 0.76	0.924
Total bilirubin (g/dl)	2.34 ± 2.01	2.55 ± 1.72	0.688
GFR (ml/min)	110.88 ± 34.18	115.04 ± 35.25	0.659
Left heart function			
LVEDD (mm)	39.61 ± 5.37	41.05 ± 5.84	0.344
Ejection fraction (%)	68.75 ± 8.29	65.18 ± 9.66	0.141
Right heart function			
FAC (%)	0.46 ± 0.12	0.50 ± 0.08	0.153
S' (cm/s)	7.05 ± 2.56	6.00 ± 1.98	0.106
TAPSE (mm)	11.37 ± 2.77	11.86 ± 4.12	0.622
MPI	0.51 ± 0.24	0.57 ± 0.23	0.342
Tricuspid regurgitation (m/s)	2.06 ± 0.38	2.24 ± 0.36	0.089
Survival, n (%)	35 (97.2%)	15 (68.2%)	0.003*
NYHA class	2.42 ± 0.73	2.5 ± 0.91	0.703
E/A	1.68 ± 0.70	2.19 ± 1.55	0.157
E/e'	8.42 ± 3.85	9.53 ± 4.41	0.315
CVP (mmH2O)			
Before surgery	18.91 ± 5.47	20.67 ± 2.31	0.588
After surgery	9.56 ± 3.23	9.0 ± 1.00	0.769

Data are presented as n (%) or mean ± SD. \* $P < 0.05$ ; <sup>†</sup>Other causes of constrictive pericarditis included postcardiotomy CP, immune disorders, radiation, and non-TB-related inflammation. N for CVP before surgery in patients with surgery: 33; N for CVP after surgery in patients without surgery: 3; N for CVP after surgery in patients with surgery: 32; N for CVP after surgery in patients without surgery: 3. GFR: Glomerular filtration rate; LVEDD: Left ventricular end-diastolic dimension; FAC: Fractional area change; TAPSE: Tricuspid annular plane systolic excursion; MPI: Myocardial performance index; NYHA: New York Heart Association; CVP: Central venous pressure; SD: Standard deviation; TB: Tuberculosis.

**Table 3: Multivariable logistic regression for prediction of survival patients with constrictive pericarditis**

Index	OR (95% CI)	P
Surgery (reference: No surgery)	53.14 (2.16–>999)	0.015
Albumin (g/dl)	1.37 (1.02–1.82)	0.035
Tricuspid regurgitation (m/s)	0.01 (<0.001–0.55)	0.026
LVEDD (mm)	1.33 (1.02–1.73)	0.032

Factors included in multivariable logistic regression were as follows: Receiving surgery, albumin level, tricuspid regurgitation, GFR, FAC, S', MPI and TAPSE of right heart function, tricuspid regurgitation, LVEDD and ejection fraction of left heart function, IVC collapse percentage. OR: Odd ratio; CI: Confidence interval; LVEDD: Left ventricular end-diastolic dimension; GFR: Glomerular filtration rate; FAC: Fractional area change; TAPSE: Tricuspid annular plane systolic excursion; MPI: Myocardial performance index; IVC: Inferior vena cava.

and LVEDD were found to be significant factors influencing survival. The albumin range was between 2.1 and 3.8 g/dl in the 8 patients who died. In 4 of them, albumin was below 3.0 g/dl, 3 had albumin around 3.0 g/dl, and only 1 patient's albumin was 3.8 g/dl. After adjusting for albumin level, tricuspid regurgitation velocity, and LVEDD, the odds of survival of patients that received surgery were significantly higher than that of patients that did not receive surgery (odds ratio [OR] = 53.14,  $P = 0.015$ ). After adjustment for receiving surgery, tricuspid regurgitation velocity, and LVEDD, the odds of survival were increased with every g/L increase in albumin ( $OR = 1.37$ ,  $P = 0.035$ ). After adjustment for receiving surgery, albumin, and LVEDD, the odds of survival were decreased with every m/s increase in tricuspid regurgitation velocity ( $OR = 0.01$ ,  $P = 0.026$ ). After adjustment for receiving surgery, albumin, and tricuspid regurgitation velocity, the odds of survival were increased with every mm increase in LVEDD ( $OR = 1.33$ ,  $P = 0.032$ ) [Table 3].

### Characteristics of constrictive pericarditis patients with severely impaired right heart systolic function

The characteristics of patients with severely impaired right heart systolic function who received surgery and those who did not receive surgery are shown in Table 4. There were 26 patients with severely impaired right heart systolic function, 15 of whom received surgery and 11 who did not receive surgery. Left heart ejection fraction and S' were significantly higher in patients who received surgery than those who did not receive surgery (LVEF: 68.13 vs. 60.18%,  $P = 0.02$ ; S': 6.47 vs. 5.08 cm/s,  $P = 0.03$ ). The survival of patients who received surgery was significantly higher than for those who did not receive surgery (15 [100%] vs. 7 [63.5%],  $P = 0.022$ ). No significant differences were found between patients who received surgery and those who did not with respect to gender, age, symptom duration, length of hospital stay, hemoglobin, albumin, total bilirubin, GFR, LVEDD, RV FAC, TAPSE, MPI, tricuspid regurgitation, NYHA class, E/A, and E/e' (all,  $P > 0.05$ ) [Table 4]. Among the CP patients who received surgery, there was no difference of outcome in the level of right heart function impairment ( $P = 1.000$ ; Table 5).

### Transient right heart function change after operation

Nine of the 36 CP operation patients underwent systemic right heart evaluation 1 month after the operation. Representative images of a patient with CP undergoing pericardiectomy, preoperation and postoperation echocardiography are shown in Figure 1. Two of these patients had undergone incomplete pericardiectomy because of the tight adhesion between parietal and visceral pericardium, and some hemostatic materials were used on the surface of the wound. Therefore the postoperative echocardiography shows decreased right heart diastolic volume (mean 15 ml), and also unchanged or decreased LVEDD. The other 7 patients, all of whom underwent complete pericardiectomy, had increased right

**Table 4: Characteristics of constrictive pericarditis patients with severely impaired right heart systolic function who received surgery and those managed medically**

Characteristics	Surgery (n = 15)	No surgery (n = 11)	P
Male, n (%)	10 (66.7)	6 (54.5)	0.689
Age (years)	39.80 ± 16.33	45.18 ± 21.73	0.477
Symptom duration (months)	20.91 ± 32.79	15.10 ± 14.98	0.552
Hospital stay (d)	38.93 ± 18.52	51.55 ± 75.09	0.597
Hemoglobin (g/dl)	128.47 ± 25.40	124.73 ± 15.90	0.672
Albumin (g/dl)	34.27 ± 5.16	34.18 ± 7.24	0.972
Total bilirubin (g/dl)	24.17 ± 16.70	29.29 ± 23.08	0.517
GFR (ml/min)	116.25 ± 34.43	119.99 ± 35.46	0.790
Left heart function			
LVEDD (mm)	38.87 ± 5.77	39.45 ± 5.28	0.793
Ejection fraction (%)	68.13 ± 6.80	60.18 ± 9.57	0.020*
Right heart function			
FAC (%)	0.47 ± 0.13	0.48 ± 0.09	0.689
S' (cm/s)	6.47 ± 1.33	5.08 ± 1.73	0.030*
TAPSE (mm)	10.49 ± 2.43	9.27 ± 3.26	0.287
MPI	0.69 ± 0.19	0.76 ± 0.17	0.415
Tricuspid regurgitation (m/s)	1.95 ± 0.22	2.19 ± 0.47	0.152
Survival, n (%)	15 (100)	7 (63.6)	0.022*
NYHA class	2.6 ± 0.91	2.27 ± 0.79	0.348
E/A	1.67 ± 0.67	2.22 ± 0.92	0.093
E/e'	8.71 ± 4.19	8.05 ± 3.04	0.662

\*P<0.05. Data are presented as number (%) or mean ± SD. GFR: Glomerular filtration rate; LVEDD: Left ventricular end-diastolic dimension; FAC: Fractional area change; TAPSE: Tricuspid annular plane systolic excursion; MPI: Myocardial performance index; RV: Right ventricle; NYHA: New York Heart Association; SD: Standard deviation.

**Table 5: Comparison of right heart function and survival**

Index	No to mild impairment (n = 21, %)	Severe impairment (n = 15, %)	P
Survived	20 (95.24)	15 (100)	1.000
Died	1 (4.76)	0 (0)	

Severe impairment in systolic right heart function means 3 or more of the criteria were met. Others were considered no to mild impairment.

heart volume, TAPSE and right heart diameter, although the increases did not reach statistical significance [Figure 2a]. One patient was followed up for 3 years, and by then she had normal right heart function, although her right heart was still enlarged [Figure 2b]. These results indicate that right heart function in CP patients undergoing operation tends to be normal although there might still be changes in right heart anatomy.

## DISCUSSION

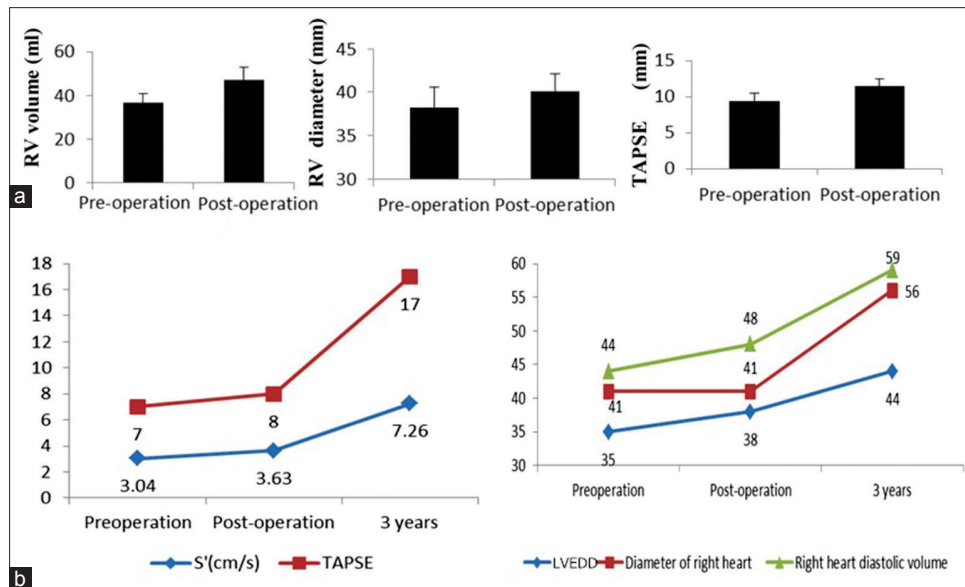
The results of the present study show the following: (1) right heart systolic function is significantly impaired in CP patients. (2) Preoperative right heart function may not influence the long-term outcome of CP patients, and surgery

should be the primary treatment for CP. (3) CP patients with worse right systolic heart function will benefit from surgery. (4) Transient right heart function changes after surgery may be compensated for over time, even in the presence of structural abnormalities, and result in normal apparent right heart function.

### Right heart function does not influence the long-term outcome of constrictive pericarditis patients, but surgery does

Even though it has long been established that surgery is the only definitive treatment for patients with CP,<sup>[2,5,7-9]</sup> pericardiectomy is a difficult operation with reported operative and late mortality ranging from 5–10% and 15–70%, respectively.<sup>[1,4,8]</sup> Early mortality associated with pericardiectomy is primarily a result of postoperative low cardiac output. Bashi *et al.*<sup>[10]</sup> assessed the outcome of 108 postoperative CP patients and found that 34 (31%) patients had low cardiac output, leading to 12 deaths and an in-hospital mortality rate of 11%. More recent reports have shown lower mortality rates. Lin *et al.*<sup>[21]</sup> reviewed the outcomes of 51 patients with CP of which 65% of the cases were TB-related and reported an in-hospital mortality rate of 3.9%. Cinar *et al.*<sup>[22]</sup> reported a perioperative mortality rate of 8.6% of CP patients who underwent surgery, and 5- and 10-year mortality rates of 1.6% and 9.7%, respectively. In the current study, there was only 1 postoperative death, and thus the in-hospital mortality rate was 3%. The patient who died had a diagnosis of radiation-induced CP, and the poor outcome of this patient is consistent with reports that radiation-induced CP has the poorest outcome compared to other causes of CP.<sup>[8]</sup>

Until date, there have been no reports indicating that preoperative right heart function is correlated with outcome in patients undergoing surgery for CP. There are probably a number of reasons that our results showed that right heart function did not influence the outcome of CP patients undergoing surgery. Firstly, because of advances in postoperative care during the past 20 years,<sup>[23,24]</sup> nearly all patients receive inotropic and ventilator support. At our hospital, the use of ECMO to provide hemodynamic support for patients with reduced right ventricular function after surgery is also common. Another reason is that the transient right ventricular dysfunction seen after pericardiectomy can be compensated for. Pericardiectomy releases the fixed right heart from the fibrotic pericardium, resulting in improved diastolic right heart function. More blood is returned to the right heart and volume overload develops, a phenomenon more commonly seen after total pericardiectomy.<sup>[25,26]</sup> The compensation for volume overload is more active tricuspid annulus displacement, as assessed by TAPSE. These phenomena suggest that more attention should be paid to patients who undergo total pericardiectomy as their right heart function changes may be greater than those seen in partial pericardiectomy, and current postoperative support might be sufficient to help patients through this clinically



**Figure 2:** Transient right heart function change before and after operation. (a) Shows increased right ventricle volume (ml), right ventricle diameter (mm) and Tricuspid annular plane systolic excursion (mm) 1 month after operation. (b) Increasing S' (cm/s), tricuspid annular plane systolic excursion (mm), left ventricular end-diastolic dimension (mm), diameter of right heart (mm) and diastolic right heart volume (ml) in a patient followed up for 3 years after operation.

critical period. These transient changes can normalize with time, and even though some CP patients might have right heart structural abnormalities such as an enlarged right heart, they do not exhibit manifestations of right heart failure, as we saw in some of our follow-up patients.

Patients with worse right heart systolic function will still benefit from surgery in terms of the late outcome. Surgical removal of the hypertrophied pericardium relieves symptoms associated with CP and restores systemic blood flow.<sup>[8,9]</sup> In this study, there were 8 patients who died; 1 with poor preoperative right heart systolic function in the surgery group due to low postoperative cardiac output and 7 in the medical management group. The causes of the 7 deaths in the medical management group included pulmonary infection leading respiratory failure, sudden death, renal failure due to hypotension, and heart failure, and are similar to the causes of death in CP patients in other reports.<sup>[8]</sup>

The incidence of severe right ventricular dysfunction in CP was approximately 45% (26/58), yet RV fractional area shortening (FAC) was no different in patients with CP than in healthy controls. The Guidelines for the Echocardiographic Assessment of the Right Heart in Adults<sup>[19]</sup> indicate that FAC, TAPSE, pulsed tissue Doppler S', and MPI are simple and reproducible methods of assessing right ventricular systolic function. CP may result in various types of change and constrictions at different positions of the pericardium. For example, some patients may have a severe constriction in the atrioventricular groove, but minimal constriction in other parts such as the right ventricular apex. The constriction may affect the total volume of the RV. However, RV fractional area measures the ratio of systolic and diastolic volumes, not the absolute volumes. Thus, it is possible that RV fractional

area shortening values are similar between CP patients and healthy controls.

### Risk factors for poor outcomes in patients with constrictive pericarditis

Our results showed that receiving surgery, albumin level, tricuspid regurgitation, and LVEDD were factors predictive of survival in patients with CP. Albumin is an indicator of nutritional status, and studies have confirmed that a low albumin level ( $\leq 3.3$  g/dl) is a poor prognostic factor in patients undergoing cardiac surgery.<sup>[27,28]</sup> Our results suggest this is also true for patients undergoing pericardiectomy for CP. The finding that LVEDD was associated with outcome has not been previously reported. The LVEDD is the internal diameter of left ventricle, and in CP patients, while only a minority demonstrate left systolic dysfunction, most have left diastolic dysfunction (in this study all patients exhibited left diastolic dysfunction). Due to constriction of the pericardium the heart cannot completely dilate, and a smaller LVEDD indicates more severe pericardial constriction. We also found that higher tricuspid regurgitation velocity was a risk factor for poor outcome. In echocardiography, pulmonary artery systolic pressure is calculated as  $4 \times (\text{tricuspid regurgitation velocity})^2 + \text{right atrial pressure}$  (if without right ventricular outflow tract). Therefore, tricuspid regurgitation velocity is a surrogate indicator of pulmonary artery systolic pressure.<sup>[19]</sup> Higher tricuspid regurgitation velocity indicates higher pulmonary artery systolic pressure, and our results showed that a greater degree of pulmonary hypertension may be a risk factor for poor outcomes after pericardiectomy for CP, which is in accord with a previous report.<sup>[1]</sup>

The sample size was small, but because CP is not a very prevalent disease, it is hard for a prospective study to obtain

a large sample size. To confirm that the effect of the small sample size was not severe, we retrospectively examined medical records from out hospital and found that of the 148 pericardiectomies performed for CP in the last 10 years, there were 5 perioperative deaths (3 due to right heart failure and 2 related to primary carcinoma), resulting in an overall death rate for pericardiectomy of 3%. This is similar to the finding in our current manuscript, and we are therefore confident that our data are reflective of survival status at our hospital, so that even if the sample size increased, the survival outcome would be similar.

There are some limitations to this study. First, the number of patients studied is relatively small, and the follow-up was short. TB is still the major cause of CP in China,<sup>[29]</sup> and the cause of CP in the majority of patients was TB. Thus, the results may not be applicable in other situations where the causes of CP are markedly different. It will be important to compare our results with future studies on non-TB-related CP patients, and patients with other causes of heart failure.

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### Conflicts of interest

There are no conflicts of interest.

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