Preoperative Pericardial Effusion is Associated with Low Cardiac Output Syndrome After Pericardiectomy for Constrictive Pericarditis

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ABSTRACT

Background: Low cardiac output syndrome is the main cause of death after pericardiectomy.

Methods: Patients who underwent pericardiectomy for constrictive pericarditis from January 2009 to October 2020 at our hospital were included in the study. Histopathologic studies of pericardium tissue from every patient were performed. All survivors were followed up.

Results: Ninety-two consecutive patients undergoing pericardiectomy were included in the study. The incidence of postoperative low cardiac output syndrome was 10.7% (10/92). There were five operative deaths. Mortality and incidence of LCOS in the group with pericardial effusion were significantly higher than those in the group without pericardial effusion. Tuberculosis of the pericardium (60/92, 65.2%) was the most common histopathologic finding in this study. Both univariate and multivariate analyses showed that preoperative pericardial effusion is associated with increased rate of low cardiac output syndrome. Eighty-five survivors were in NYHA class I (85/87, 97.7%), and two were in class II (2/87, 2.3%) at the latest follow up.

Conclusions: Preoperative pericardial effusion is associated with low cardiac output syndrome after pericardiectomy. Tuberculosis of the pericardium was the most common histopathologic finding in this study. For constrictive pericarditis caused by tuberculous bacteria, systematic antituberculosis drugs should be given. Preoperative pericardial effusion is associated with increased rate of low cardiac output syndrome. Perfect preoperative preparation is very important to reduce incidence of postoperative low cardiac output syndrome and mortality. It is very important to use a large dose of diuretics with cardiotonic or vasopressor in a short time after operation.

INTRODUCTION

Constrictive pericarditis is a disabling and progressive disease as a result of the fibrous thickening and calcification of the pericardium, due to chronic inflammatory changes from various injuries that impair diastolic filling, reduce cardiac output, and ultimately result in left and right heart failure. Data of pathological classification of constrictive pericarditis, and the association of preoperative pericardial effusion and postoperative low cardiac output syndrome are rare [Depboylu 2017; Melo 2019; Duncan 2020].

Low cardiac output syndrome is the main cause of death after pericardiectomy. We hypothesize that preoperative pericardial effusion is associated with low cardiac output syndrome and early mortality [Du 2020; Lomivorotov 2017; Ahmad 2019].

This prospective study aimed to investigate the pathological classification of constrictive pericarditis and the association of preoperative pericardial effusion and postoperative low cardiac output syndrome and early mortality.

PATIENTS AND METHODS

Study population

Patients undergoing pericardiectomy for constrictive pericarditis, from January 2009 to October 2020, at our hospital were included in the study. The diagnosis of constrictive pericarditis was determined by clinical presentation, echocardiographic study, chest computed tomographic (CT) scan, and cardiac catheterization, as needed. The most important diagnostic tool is the suspicion of constrictive pericarditis in a patient with signs and symptoms of right-sided heart failure that are disproportionate to pulmonary of left-sided heart disease. 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 revealed a severely thickened or calcified pericardium and cardiac catheterization revealed elevated end-diastolic pressure and the “square root sign” of right ventricular pressure tracing [Epting 2016; Mori 2019; Calderon-Rojas 2020]. Preoperative pericardial effusion was diagnosed by chest computed tomographic (CT) scan, transthoracic echocardiography, and intraoperative confirmation. Surgical and pathological findings were reviewed to confirm the preoperative diagnosis. Radical pericardiectomy was completed via sternotomy between the two phrenic nerves and from the great vessels to the basal aspect of the heart. All patients were monitored with a pulmonary artery catheter, cardiac output (CO) and venous oxygen saturation of
hemoglobin were continuously measured. Low cardiac output syndrome was defined by a cardiac index (CI) of less than 2.2 L/min/m². Perioperative death was defined as death within 30 days of the operation or during the same hospital admission [Calderon-Rojas 2020; Guerrero Orriach 2019; Gatti 2020].

**Histopathologic investigation**

Histopathologic investigation of pericardium tissue from every patient was completed. The diagnosis of tuberculosis pericardium 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.

**Follow up**

All survivors discharged from hospital were monitored. Patients were investigated with X-ray chest film, electrocardiogram, and echocardiogram at the outpatient department, once every 1 to 3 months. All survivors were contacted by micromassage or telephone or interviewed directly at the outpatient department at the last follow up.

**Statistical analysis**

All analyses were completed using IBM SPSS version 24.0 software (IBM SPSS Inc., USA). Continuous variables are reported as mean/median based on kurtosis/skewness tests. The Fisher’s and Chi-square tests, Kruskal-Walls test or Wilcoxon rank-sum test, as appropriate, were used to evaluate relationships between the preoperative, selected intraoperative, and postoperative variables. The relationships with perioperative risk factors were assessed by means of contingency table methods and logistic regression analysis. To explore the simultaneous effects of perioperative characteristics on early death, variables that were significant at the 0.1 level in univariate analysis were included in a multivariate logistic regression model. *P* values less than 0.05 were considered statistically significant.

**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, which gave the authors approval to waive the need for patient consent for publishing patient data in the study.

### RESULTS

#### Preoperative and operative data

Ninety-two consecutive patients undergoing pericardectomy were included in the study. The patients were divided into two groups: the group with preoperative pericardial effusion (N = 44) and the group without preoperative pericardial effusion (N = 48) (Table 1).

#### Mortality and low cardiac output syndrome

The incidence of postoperative LCOS in the study was 10.7% (10/92). There were five operative deaths. Mortality in the group with pericardial effusion was significantly higher than that in the group without pericardial effusion (11.4% versus 0, *P* = .016). Incidence of LCOS in the group with pericardial effusion was significantly higher than that in the group without pericardial effusion (18.3% versus 4.2%, *P* = .031).

#### Pathological classification of constrictive pericarditis

Tuberculosis of the pericardium (60/92, 65.2%) was the most common histopathologic finding in this study (Figure 1).

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**Table 1. Preoperative data**

| Variable                  | Group with pericardial effusion (N = 44) | Group without pericardial effusion (N = 48) | *P*  |
|---------------------------|-----------------------------------------|---------------------------------------------|------|
| Male, n (%)               | (%)                                     | (%)                                         |      |
| Age, years                | 57.2 ± 1.9                              | 48.9 ± 2.3                                  | .007 |
| Weight 1, kg              | 53.7 ± 1.2                              | 58.0 ± 1.4                                  | .023 |
| Weight 2, kg              | 51.1 ± 0.9                              | 54.8 ± 1.1                                  | .010 |
| Preoperative CVP, mmHg    | 20.64 ± 0.72                            | 20.23 ± 0.70                                | .685 |
| Preoperative LVEDD, mm    | 41.46 ± 0.58                            | 40.27 ± 0.45                                | .103 |
| Preoperative LVEF, %      | 60 ± 1.0                                | 63 ± 1.0                                    | .039 |

**Table 2. Operative data**

| Variable                  | Group with pericardial effusion (N = 44) | Group without pericardial effusion (N = 48) | *P*  |
|---------------------------|-----------------------------------------|---------------------------------------------|------|
| Operative death, n (%)    | 5(5/44, 11.4%)                          | 0                                          | .016 |
| Multiple organ failure, n (%) | 6(6/44, 13.6%)                      | 2(2/48, 4.2%)                              | .107 |
| LCOS, n (%)               | 8(8/44, 18.3%)                          | 2(2/48, 4.2%)                              | .031 |
| Incubation time, hours    | 89.3 ± 11.7                             | 63.6 ± 12.6                                | .140 |
| ICU retention time, days  | 5.6 ± 0.6                               | 5.1 ± 0.8                                  | .604 |
| Hospitalized time         |                                         |                                             |      |
| postoperative, days       | 14.96 ± 1.11                            | 13.73 ± 1.98                               | .367 |
| Postoperative CVP, mmHg   | 11.39 ± 0.49                            | 11.83 ± 0.38                               | .469 |
| D0 fluid balance, ml      | -1098.9 ± 119.9                         | -1425.8 ± 123.5                            | .061 |
| D1 fluid balance, ml      | -253.0 ± 156.8                          | -1258.3 ± 164.0                            | .001 |
| D2 fluid balance, ml      | -663.3 ± 111.9                          | -872.5 ± 94.6                              | .154 |
| Chest drainage, ml        | 826.1 ± 74.8                            | 1090.8 ± 84.2                              | .074 |
| Postoperative LVEDD, mm   | 42.13 ± 0.47                            | 42.23 ± 0.49                               | .109 |
| Postoperative LVEF, %     | 69 ± 1.0                                | 67 ± 1.0                                    | .410 |

MOF, multiple organ failure; D0, fluid balance on operation day; D1, fluid balance postoperative day 1; D2, fluid balance postoperative day 2
Also, 34.8% of patients (32/92) had the histopathologic finding of chronic nonspecific inflammatory changes (Figures 2 through 6).

The most common cause of constrictive pericarditis in China is tuberculosis. Early pericardiectomy can avoid the development of cardiogenic cachexia, severe hepatic insufficiency, and myocardial atrophy.

Analysis of risk factors of low cardiac output syndrome: Both univariate and multivariate analyses showed that preoperative pericardial effusion was statistically associated with increased rate of LCOS (OR = 5.11, \( P = .047 \) and OR = 9.002, \( P = .037 \), respectively) (Table 3).

**RESULTS OF FOLLOW UP**

All 87 survivors discharged from the hospital were monitored to the end date of the study, and follow up was 100% completed (N = 87). The mean duration of follow up was 52.4±4.5 months (range, 2 to 138), and no late death or reoperation occurred. Eighty-five survivors were in NYHA class I (85/87, 97.7%) and two were in class II (2/87, 2.3%) at latest follow up.

**DISCUSSION**

Preoperative pericardial effusion is associated with low cardiac output syndrome after pericardiectomy.

In this study, the incidence of postoperative LCOS was 10.7% (10/92). There were five operative deaths. Mortality in the group with pericardial effusion was significantly higher than that in the group without pericardial effusion (11.4%...
versus 0, \( P = .016 \). Incidence of LCOS in the group with pericardial effusion was significantly higher than that in the group without pericardial effusion (18.3\% versus 4.2\%, \( P = .031 \)).

Both univariate and multivariate analyses showed that preoperative pericardial effusion was a statistically significant independent predictor of increased rate of LCOS (OR = 5.11, \( P = .047 \) and OR = 9.002, \( P = .037 \), respectively) (Table 3).

Thickening of the pericardium oppresses the heart, making the heart diastolic restricted, right atrial pressure and left and right ventricular end diastolic pressure increased, vena cava blood flow blocked, venous pressure increased, cardiac output decreased, so that patients are in a state of high blood volume and tissue edema.

Due to the long-term compression of the thickened pericardium and myocardial ischemia, the heart denaturates and atrophies, and the heart has poor adaptability to the changes of hemodynamics [Fang 2020; Vlasov 2020; Acharya 2018]. After the heart is released, a large amount of blood flows back and the preload of the heart increases, which leads to the occurrence of heart failure or malignant arrhythmia, and even leads to cardiac arrest. The patients with low cardiac output had a long history, a large amount of ascites and peripheral edema before operation, and the cardiac function was mostly in grade III and IV. In order to reduce the incidence of postoperative low cardiac output syndrome, the patients with constrictive pericarditis should be operated as soon as possible after diagnosis. Low cardiac output syndrome is the main cause of death after pericardiectomy. Because of the serious myocardial damage, myocardial contractility and general condition of constrictive pericarditis are serious, perfect preoperative preparation is very important to reduce incidence of postoperative low cardiac output syndrome and mortality.

Before operation, a diet rich in protein and vitamin were given, and aggressive diuretics and appropriate cardiotonics were used to decrease preoperative pericardial effusion, tissue edema, and the amount of postoperative return heart blood. The amount of crystal input was strictly controlled. Fresh frozen plasma and albumin were properly imported. Regular antituberculosis treatment was given to patients with tuberculosis [Fang 2020; Vlasov 2020]. The patients with abnormal liver function should be treated with liver protective drugs and vitamin K1 should be used before operation.

During and after the operation, continuous invasive monitoring of arterial and venous pressure, control of fluid volume, a large amount of colloidal solution, active diuresis, cardiotonic drugs, and vasoactive drugs should be applied in order to avoid further aggravating the burden on the heart and causing heart failure.
Dissection and resection of thickened and conglutinated pericardium is the only effective treatment to relieve the mechanical restraint of the heart. Pericardial resection leads to a large increase in venous return blood volume in a short period of time, while the long-term bound heart has weakened contractility due to myocardial “disuse” atrophy, fibrosis, decreased compliance, myocardial ischemia and malnutrition, and cannot adapt to it. The volume and speed of fluid infusion should be reduced as much as possible, so that the heart is temporarily in the state of low volume load and gradually adapt to the change following pericardiectomy. In addition, monitoring CVP has guiding significance for postoperative treatment. After pericardiectomy, the heart is in a high-volume load state in a short period of time, and there is no concern of low blood volume [Vlasov 2020; Fang 2020]. At this time, large amount of diuresis becomes a feasible and necessary measure, which also is one of the key points for further improvement of cardiac function after operation.

After the mechanical restraint of the heart is released, the systolic force of the heart cannot bear a large amount of venous return blood volume in a short period of time. At this time, the problems of renal congestion and low renal vascular perfusion still exist. Proper use of diuretics can reduce blood volume and cardiac volume load and indirectly reduce renal congestion, increase renal vascular perfusion pressure and promote urination. Even some patients have a short-term decline in CVP after the narrowing is relieved, and then rise sharply. Therefore, after the pericardial constriction is relieved, a large amount of diuresis and cardiotonic drugs should be immediately supplemented. It is very important to use a large dose of diuretics with cardiotonic or vasopressor in a short time after operation.

Pathological discussion

Tuberculosis of pericardium (60/92, 65.2%) was the most common histopathologic finding in this study (Figure 1), and 34.8% of patients (32/92) had the histopathologic findings of chronic nonspecific inflammatory changes (Figures 2 through 6).

Constrictive pericarditis exhibits a heterogeneous pattern and arises from different causes, depending on the geographic area from where it is reported. Thirty-eight percent to 83% of the cases of constrictive pericarditis still are caused by tuberculosis in developing countries. Table 4 shows the prevalence of causal factors for constrictive pericarditis in treatment centers in the United States, China, Iran, and Spain [Wei 2019; Chandler 2016; Bautista-Hernandez 2016] (Table 4).

For constrictive pericarditis caused by tuberculous bacteria, systematic antituberculosis drugs should be given. Surgery should be performed after body temperature, erythrocyte sedimentation rate, and general nutritional status are close to normal or relatively stable [Thomas 2020; Cavigelli-Brunner 2018; Rupprecht 2018; Mehta 2017]. Antituberculosis treatment should be continued for 6 to 12 months to avoid recurrence.

Table 3. Analysis of risk factors of low cardiac output syndrome (N = 92)

| Model | OR   | 95% CI      | P     |
|-------|------|-------------|-------|
| Univariate analysis of risk factors for low cardiac output syndrome pericardial effusion | 5.11 | 1.022-25.562 | .047  |
| Multivariate analysis of risk factors for low cardiac output syndrome pericardial effusion | 9.002 | 1.146-70.74 | .037  |
| ICU retention time | 1.221 | 1.073-1.389 | .002  |

Table 4. Prevalence of causal factors for constrictive pericarditis in different area

| Cause                          | Cleveland Clinic (%) | Guangxi, China (%) | Iran (%) | Barcelona (%) |
|--------------------------------|----------------------|--------------------|----------|---------------|
| Idiopathic disease             | 46                   | 34.8               | 60       | 46.7          |
| Tuberculosis                   | 3.7                  | 65.2               | 22.2     | 6.7           |
| Post-cardiotomy                | 37                   | 0                  | 4.4      | 6.7           |
| Radiation therapy              | 9                    | 0                  | 0        | 13.3          |
| Malignancy                     | 0                    | 4.4                | 26.7     | 0             |
| End-stage renal disease        | 0                    | 8.9                | 0        |               |
| Miscellaneous                  | 4.3                  | 2.2                | 0        |               |

CONCLUSIONS

Preoperative pericardial effusion is associated with low cardiac output syndrome after pericardiectomy. Tuberculosis of pericardium was the most common histopathologic finding in this study. For constrictive pericarditis caused by tuberculous bacteria, systematic antituberculosis drugs should be given. Preoperative pericardial effusion was an independent predictor of increased rate of low cardiac output syndrome. Perfect preoperative preparation is important to reduce incidence of postoperative low cardiac output syndrome and mortality. It is very important to use a large dose of diuretics with cardiotonic or vasopressor in a short time after operation.

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