

# Clinical features, management and outcome of patients with constrictive pericarditis – Experience from a third world country



Fateh Ali Tipoo Sultan <sup>a,\*</sup>, Muhammad Umer Tariq <sup>b</sup>

<sup>a</sup> Aga Khan University Hospital, Karachi

<sup>b</sup> Medstar Georgetown University

<sup>a</sup>Pakistan

<sup>b</sup>USA

**Objectives:** To study the clinical features, management and outcome of patients with constrictive pericarditis, at a tertiary care hospital of Pakistan.

**Design:** Descriptive study.

**Material & method:** All consecutive patients with the final diagnosis of constrictive pericarditis, admitted at Aga Khan University Hospital Karachi, during the year 2005 to 2015 were included in the study.

**Results:** A total of 21 patients were diagnosed and managed as constrictive pericarditis during the above mentioned period. Mean age was 39 + 19.9 years. There was a male preponderance with a male to female ratio of 2.5:1. The most common clinical features were those of right heart failure. Only 2 (9.5%) patients showed pericardial calcification on X-ray chest. Dilated atria and septal bounce were the most common echo features present in 15 (71.4%). MRI/CT was done in only 11 patients, of which eight showed increased pericardial thickness. Three had normal pericardial thickness on MRI/CT but were proved to have constriction surgically. Cardiac catheterization was done in nine patients only. Elevated filling pressures and square root sign were the most common findings, present in all (100%). Pericardiectomy was performed in 12 (57%) patients. Five more patients were advised surgery but two died before the surgery and three were taken to other hospitals as they wanted to explore other options beside surgery. Pericardial tissue histopathology was available in only 11 patients. It revealed tuberculosis in three cases, while in 8 cases it was nonspecific. Six patients died with an overall mortality of 28.6%. Five patients died during hospitalization, four without surgery and one after the surgery. One patient died during follow up (was considered unfit for the surgery). Mean follow up duration was 7.3 + 9.3 months. No death occurred on follow up in surgically treated patients.

**Conclusion:** Features of right heart failure is the most common mode of presentation of CP. The most probable etiology in this part of the world is tuberculosis, although difficult to prove on histopathology. Pericardiectomy is the usual recommended treatment due to advanced disease at the time of presentation.

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\* Corresponding author at: Cardiology section, Department of Medicine, Aga Khan University Hospital, Stadium Road, Karachi, Pakistan. E-mail addresses: [tipoo90@hotmail.com](mailto:tipoo90@hotmail.com) (F.A.T. Sultan), [ut2087@gmail.com](mailto:ut2087@gmail.com) (M.U. Tariq).



P.O. Box 2925 Riyadh – 11461KSA  
Tel: +966 1 2520088 ext 40151  
Fax: +966 1 2520718  
Email: [sha@sha.org.sa](mailto:sha@sha.org.sa)  
URL: [www.sha.org.sa](http://www.sha.org.sa)

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## Introduction

Constrictive pericarditis (CP) is defined as impedance to diastolic filling caused by a fibrotic pericardium [1]. In the past, tuberculosis (TB) was a very common etiology; however, due to control of this disease in the developed world, other causes such as prior cardiac surgery, radiation therapy, and idiopathic pericarditis have risen in importance [2-4].

The symptoms of the disease are a direct consequence of right sided heart failure. Diagnosis is usually difficult and multiple imaging modalities are used for making the diagnosis.

The treatment of CP can be divided in to medical and surgical treatments. Medical management applied generally is the administration of diuretics and supportive therapy for underlying conditions. In patients with transient CP, anti-inflammatory agents or steroids are indicated [5]. The surgical option is of pericardiectomy, which is the definitive treatment [6].

In countries such as Pakistan, the diagnosis of CP is usually delayed and results in poor outcomes. Literature from Pakistan does not exist on constrictive pericarditis. Considering that TB is still a great burden of disease in this part of the world, it is important to note the incidence of CP, its etiology, patterns of presentation and management options in Pakistan.

Therefore, we designed the study to analyze the clinical features, management and outcome of patients with constrictive pericarditis, at a tertiary care hospital of Pakistan.

## Materials and methods

Medical records of all the patients admitted with the diagnosis of constrictive pericarditis, at Aga Khan University Hospital, Karachi, from January 2005 to December 2015 were reviewed. Only patients with the final diagnosis of CP were included. Aga Khan University Hospital is a 650-bedded, tertiary care hospital in a big city of Pakistan, giving admissions to all kinds of patients. It has a high referral rate of cardiac patients from all over the country. A predesigned questionnaire was used for data collection. Follow-up data were collected from the medical records. Analysis was done with SPSS software (nineteen, SPSS Inc., Chicago, IL, USA).

## Results

A total of 21 patients were diagnosed and managed as CP during the 11-year period (2005-2015)

### Abbreviations

CP	Constrictive pericarditis
TB	Tuberculosis
ICU	Intensive care unit
JVP	Jugular venous pressure
TDI	Tissue Doppler imaging
NYHA	New York Heart Association

at Aga Khan University Hospital. Clinical characteristics are shown in Table 1. Mean age was 39 ± 19.9 years. There was a male preponderance with a male to female ratio of 2.5:1. Past history of TB was present in eight patients (38%) while history of cardiac surgery was present in four patients (19%). The most common clinical features were those of right heart failure. Pulsus paradoxus was present in only six patients (28.6%) and pericardial knock in four patients (19%).

The most common electrocardiography findings were nonspecific ST-T changes present in 13 patients (61.9%) and atrial fibrillation in six patients (28.6%). Chest radiography revealed pleural effusion in 17 patients (81%), while pericardial calcification was present in only two patients (9.5%).

Echocardiogram performed for all patients. Table 2 shows the findings on echocardiogram. Dilated atria and septal bounce were the most common echo features present in 15 patients (71.4%) followed by increased E to A ratio in 13 patients (61.9%).

Magnetic resonance imaging/computed tomography was performed in only 11 patients, of whom eight showed increased pericardial thickness. Three patients had normal pericardial thickness on magnetic resonance imaging/computed

Table 1. Clinical characteristics.

Clinical characteristics	Number of patients (21)	Percentage
Age (±standard deviation)	39 ± 19.9	—
Males	15	71.4%
History of tuberculosis	8	38%
Prior cardiac surgery	4	19%
History of pericarditis	3	14%
Shortness of breath	15	71.4%
Chest pain	6	28.6%
Pedal edema	13	61.9%
Ascites	14	66.7%
Raised jugular venous pressure	21	100%
Palpable liver	13	61.9%
Pulsus paradoxus	6	28.6%
Pericardial knock	4	19%

Table 2. Findings on echocardiogram.

Finding	Number of patients (21)	Percentage
Dilated atria	15	71.4%
Septal bounce	15	71.4%
Increased early/late ratio	13	61.9%
Respiratory variation	12	57%
Pulmonary artery pressure <50 mmHg	9	42.9%
Thickened pericardium on echocardiogram	9	42.9%
Trace to mild pericardial effusion	12	57%

Table 3. Findings on cardiac catheterization.

Findings	Number of patients (9)	Percentage
Elevated filling pressures	9	100%
LVEDP-RVEDP < 5	8	88.8%
Prominent Y descent	9	100%
Square root sign	9	100%
Ventricular interdependence	8	88.8%

LVEDP-RVEDP = left-right ventricular end-diastolic pressure.

tomography but were proved to have constriction surgically.

Cardiac catheterization was done in nine patients only. Elevated filling pressures and square root sign were present in all (100%), as shown in Table 3.

Pericardiectomy was considered in all patients except one, who had the milder form of disease and was managed conservatively. Three of the patients were declared unfit for the surgery due to severity of illness. Pericardiectomy was performed in 12 patients (57%). Pericardiectomy was performed via a median sternotomy incision. The whole pericardium was incised starting from left to right, removing the pericardium and releasing the left ventricle then left atrium then pulmonary artery followed by right atrium, right ventricle, and superior and inferior venae cava. Significant improvement in central venous pressure was the earliest sign observed in all patients immediately after pericardiectomy. However, the intensive care unit stay was relatively prolonged compared to other post-operative cardiac patients.

Five more patients were advised to avail of surgery but two died before the surgery could be undertaken and three were taken to other hospitals as they wanted to explore other options besides surgery.

Anti-tuberculous therapy was given in 10 cases (47.6%), considering TB as the underlying cause based on clinical features. Pericardial tissue histopathology was available for only 11 patients. It revealed TB in three cases, while in eight cases it was nonspecific.

Six patients died with an overall mortality of 28.6%. Five patients died during hospitalization, four without surgery and one after the surgery (perioperative mortality 8.3%). One patient died during follow-up (was considered unfit for the surgery). Mean follow-up duration was  $7.3 \pm 9.3$  months. Follow up was not available in three patients (taken to other hospital). No death occurred on follow-up in surgically treated patients. Functional class improved from III-IV to I-II in almost all patients who underwent pericardiectomy.

## Discussion

CP is an uncommon condition with difficult diagnosis. This is a small series but is important as these are the only data available from this country on this topic.

As opposed to the data from developed countries where cardiac surgery and mediastinal irradiation are common causes of CP [6], in this study only few patient had history of prior cardiac surgery and no patient had history of radiation exposure.

No post-radiation patient in this series could be due to the shorter survival of post-radiation patients in this part of the world, either due to advanced disease or fewer facilities for oncology patients. With improved cancer cure rates and greater longevity in future, cases of CP secondary to radiation would possibly be seen.

Clinical presentation of right heart failure in majority of patients in this study is similar to a large series from Mayo Clinic [6]. Clinical features such as peripheral edema, hepatomegaly, and ascites often lead to the misdiagnosis of chronic liver disease. However, jugular venous pressure is a clinical sign that helps in differentiation of CP from chronic liver disease and was elevated in all patients in this study.

Kussmaul's sign refers to an absence of an inspiratory abatement in jugular pressure. In CP, the stiff and inelastic pericardium cannot transmit intrathoracic pressure variations to the cardiac chambers and the increased inspiratory venous return leads to an enhanced central venous pressure because CP does not allow for right atrial expansion during inspiration. The presence of this

sign in a small number of patients in this study is similar to a large series from Stanford [7].

Pericardial knock is considered an important finding in CP. However, picking a pericardial knock depends upon the accuracy of clinical examination and auscultation and therefore its occurrence is variable in the literature [6,7].

Differentiation of CP from restrictive cardiomyopathy is important and usually difficult due to similar clinical presentation. Echocardiogram is the initial imaging modality, used for the diagnosis of CP. Hancock described three basic signs on echo in patients with CP [8]: septal bounce due to a sudden shift in position of the ventricular septum; ventricular septal shift with respiration; and moderate biatrial enlargement. Biatrial enlargement and septal bounce were the most common echo findings in this series. Pericardial thickness is another parameter on echo to differentiate between CP and restrictive cardiomyopathy, which was present in less than half of the patients.

Significant respiratory variation in mitral and tricuspid early diastolic filling velocity represents ventricular interdependence and is an important pathophysiologic feature in CP, which was present in over half of the patients in this study. This feature is absent in both normal individuals and in restrictive cardiomyopathy [9]. However, a considerable proportion of patients with CP do not demonstrate respiratory variation of mitral inflow velocity [9].

Tissue Doppler imaging (TDI) is a relatively new echocardiographic technique which is very helpful in differentiating CP from restrictive cardiomyopathy. Overall sensitivity and specificity for diagnosing CP using TDI incrementally with M-mode, 2D and transmitral flow Doppler is nearly 88.8% and 94.8% [10]. However, unfortunately, TDI was used in only few patients here and was diagnostic in all of these patients.

Hemodynamic evaluation on cardiac catheterization is important for the diagnosis of CP [1,10], but it is not always necessary due to good results obtained from noninvasive imaging modalities. Elevated filling pressures were observed in all patients who underwent cardiac catheterization in this study. One of the important information on invasive hemodynamic is discordance of ventricular pressures in patients with CP. During peak inspiration, there is a decrease in left ventricular pressure and a concomitant increase in right ventricular pressure. In patients with restrictive cardiomyopathy and in patients with normal pericardium there is concordance of left and right ven-

tricular pressures. In patients with constrictive pericarditis, the severity of the pericardial restraint is proportional to the degree of ventricular interaction seen on the peak inspiration [11]. Absence of discordance in one patient among those who underwent catheterization in this study, could be explained by the presence of less severe constriction in this patient.

Pericardiectomy is the accepted treatment of choice for CP; however, in the subacute form of CP, a trial of conservative therapy can be considered [5]. Most of the patients in this series had chronic (rigid) form of CP and pericardiectomy was considered in all patients except one who had the milder form of disease and was managed conservatively. This series represents a true picture of how the patients of CP are diagnosed in a very late stage in a third world country such as Pakistan. In view of unacceptably high perioperative mortality in cases with severe and end stage disease, three of the patients were declared unfit for the surgery. Pericardiectomy was performed in more than half of the patients with a perioperative mortality of 8.3%. Perioperative mortality of 8.3% is comparable to 7.6% reported in a large series of 395 patients published by Chowdhury et al. [12]. The perioperative mortality is highly dependent on the preoperative New York Heart Association (NYHA) status.

High mortality in those who did not undergo surgery indicated advanced disease at the time of diagnosis, attributed to poor health care facilities in the country and hence inability to diagnose CP at an early stage.

Long-term outcome of surgically treated patients was good with no deaths and significant improvement in functional class.

Near to half of the patients received anti-TB therapy, considering TB as the underlying cause based on clinical features. However, histopathology revealed TB in only three out of 11 patients for whom pericardial tissue histopathology was available. This number is much lower than what is expected, especially in the presence of prior history of TB in 38% of patients. This could be explained by the fact that tuberculous CP occurs at a much later stage after active tuberculosis, when it is difficult to demonstrate typical granulomas in the pericardial tissue.

## Conclusion

The most common mode of presentation of CP is shortness of breath, peripheral edema and ascites with raised jugular venous pressure. The most probable etiology in this part of the world is either

idiopathic or tuberculosis, although it is difficult to prove TB on histopathology due to advanced burnt out stage. Pericardiectomy is the usual recommended treatment due to advanced disease at the time of presentation. A significantly high mortality in the study group is most probably due to advanced disease at the time of diagnosis.

### Recommendations

We suggest that patients presenting with the aforementioned common symptoms must be seen with a high suspicion for CP to make an early diagnosis and to improve outcome.

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