

Original article

# Constrictive Pericarditis: Etiologic Spectrum, Patterns of Clinical Presentation, Prognostic Factors, and Long-term Follow-up



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ABSTRACT

**Introduction and objectives:** Some reports have described a change in the etiologic spectrum of constrictive pericarditis. In addition, data on the relationship between its clinical presentation and etiology are lacking. We sought to describe the etiologies of the disease, their relationship with its clinical presentation and surgical findings, and to identify predictors of poor outcome.

**Methods:** We analyzed 140 consecutive patients who underwent surgery for constrictive pericarditis over a 34-year period in a single center.

**Results:** The etiology was idiopathic in 76 patients (54%), acute idiopathic pericarditis in 24 patients (17%), tuberculous pericarditis in 15 patients (11%), purulent pericarditis in 10 patients (7%), and cardiac surgery, radiation and uremia in 5, 3 and 2 patients respectively (4%, 2% and 1%). Mean duration of symptoms before pericardiectomy was 19 months (standard deviation, 44 months), the most acute presentation being for purulent pericarditis (26 days [range, 7-60 days]) and the most chronic for idiopathic cases (29 months [range, 4 days-360 months]). Perioperative mortality was 11%. There was no difference in mortality between etiologies. Median follow-up was 12 years (range, 0.1-33.0 years) in which 50 patients died. In a Cox-regression analysis, age at surgery, advanced New York Heart Association functional class (III to IV) and previous acute idiopathic pericarditis were associated with increased mortality during follow-up.

**Conclusions:** Most cases of constrictive pericarditis are idiopathic. Cardiac surgery and radiation accounted for a minority of cases. Etiologic investigations are warranted only in acute or subacute presentations. Age, advanced functional class, and previous acute idiopathic pericarditis are associated with increased mortality.

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## Pericarditis constrictiva: espectro etiológico, presentaciones clínicas, factores pronósticos y seguimiento a largo plazo

RESUMEN

**Introducción y objetivos:** Algunos estudios han descrito un cambio en el espectro etiológico de la pericarditis constrictiva. Además, no hay datos sobre la relación entre la forma de presentación clínica y la etiología. El objetivo de este estudio es describir las etiologías de la enfermedad, su relación con la forma de presentación clínica y los hallazgos quirúrgicos, así como identificar los factores predictivos de una mala evolución.

**Métodos:** Se analizó a un total de 140 pacientes consecutivos a los que se practicaron intervenciones quirúrgicas por pericarditis constrictiva en un mismo centro en un periodo de 34 años.

**Resultados:** La etiología fue idiopática en 76 pacientes (54%) y tras pericarditis aguda idiopática en 24 (17%), pericarditis tuberculosa en 15 (11%), pericarditis purulenta en 10 (7%) y cirugía cardíaca en 5 (4%), radioterapia en 3 (2%) y uremia en 2 (1%). La duración media de los síntomas antes de la pericardiectomía fue de 19 meses (desviación estándar: 44 meses); la forma de presentación clínica más aguda fue la de las pericarditis purulentas (26 [intervalo, 7-60] días) y la más crónica, la de los casos idiopáticos (29 meses [4 días-360 meses]). La mortalidad perioperatoria fue del 11%. No hubo diferencias en la mortalidad según etiologías. La mediana de seguimiento fue de 12 (0,1-33,0) años, durante los cuales fallecieron 50 pacientes. En un análisis de regresión de Cox, la edad en el momento de la operación, la clase funcional

Palabras clave:

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de la *New York Heart Association* avanzada (III–IV) y los antecedentes de pericarditis aguda idiopática se asociaron a una mayor mortalidad durante el seguimiento.

**Conclusiones:** La mayoría de los casos de pericarditis constrictiva son idiopáticas. La cirugía cardíaca y la radioterapia causan una minoría de los casos. Las presentaciones aguda y subaguda merecen un estudio etiológico. La edad, la clase funcional avanzada y la pericarditis aguda idiopática previa se asocian a mayor mortalidad.

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## Abbreviations

CP: constrictive pericarditis

CS: cardiac surgery

CT: computed tomography

PE: pericardial effusion

## INTRODUCTION

Since constrictive pericarditis (CP) was first described in 1669 by Lower,<sup>1</sup> some clinical aspects may have changed. Some studies<sup>2</sup> have recently suggested that the etiologic spectrum has changed in the last decades, basically due to an increase in the number of cases secondary to cardiac surgery (CS) or previous radiotherapy. However, this finding could be misleading. First, these studies were conducted in centers with a high cardiac surgical activity,<sup>3</sup> which could introduce some bias in the etiologic spectrum. In addition, the relationship between symptom duration before pericardiectomy and the etiology of CP was not described in detail. Finally, previous studies usually did not include accurate information on the different diagnostic procedures or imaging studies used to diagnose CP.

Our center, a referral center for pericardial diseases, has used a standardized protocol for diagnosis and management of pericardial disease<sup>4,5</sup> since 1975. In the present report we describe the etiologic spectrum, the relationship between the chronicity of clinical symptoms and the etiology of CP, the use of the different diagnostic procedures, and predictors of poor outcome, in a series of 140 consecutive patients with CP who underwent surgery in our institution in the last 34 years.

## METHODS

We conducted a retrospective study in a single tertiary center. The study was approved by the ethics committee of our institution. A total of 140 patients underwent pericardiectomy in our institution (*Hospital Universitari Vall d'Hebron, Barcelona, Spain*) for confirmed CP between January 1978 and May 2012. The clinical records were individually reviewed by a single investigator (Andreu Porta-Sánchez), devoting special attention to the presence of inflammatory systemic diseases, previous episodes of acute pericardial diseases, thoracic or mediastinal irradiation or previous CS, and the clinical and imaging studies performed. The time elapsed from the potential causative illness to the onset of symptoms of CP was quantified as well as the time to pericardiectomy. Surgical features were also recorded, with special attention to the involvement of the parietal and visceral layers. Mortality and follow-up data were obtained through outpatient clinic visits or by the electronic clinical records or by phone. Data from the Spanish National Institute of Statistics<sup>6</sup> were

obtained to generate an age and sex-matched population, and an estimated Kaplan Meier survival curve was generated to compare the long-term overall mortality in our patients with the general population.

## Definitions

Idiopathic CP was diagnosed when no apparent etiology was identified. Postacute idiopathic pericarditis was defined as CP occurring after a well-defined episode of acute idiopathic pericarditis (typical chest pain, pericardial friction rub, serial changes in the ST segment of the electrocardiogram). Tuberculous CP was defined when Koch bacillus was isolated from a pericardial specimen or when caseous granulomas were identified in a biopsy specimen. Purulent CP was diagnosed when pericardial fluid was macroscopically purulent or had a high polymorphonuclear content (> 90%). Postsurgical CP was diagnosed when CP was developed after an open-heart surgery. Radiotherapy CP was defined by the development of CP after a therapeutic chest radiation and after the exclusion of other causes of CP. In an arbitrary manner, the terms acute, subacute and chronic CP were applied, respectively, to patients who required pericardiectomy before 3 months, between 3 and 6 months, or after 6 months of the onset of clinical symptoms. Pericardial calcification was defined as the presence of calcification on a chest X-ray. Left ventricular systolic function was considered abnormal if left ventricular ejection fraction was estimated below 50%. The following echo-Doppler findings were considered diagnostic: the presence of pericardial thickening and notch of the interventricular septum, changes in E velocity superior to 25% related to respiratory movements, a rapid E wave deceleration, suprahepatic vein flow with “W” morphology or predominance of the diastolic component with diastolic inversion during expiration. The amount of pericardial effusion (PE) was classified as mild (< 10 mm of echo-free space in anterior and posterior pericardial spaces), moderate (10–20 mm) or severe (> 20 mm). Additional imaging studies were performed to confirm pericardial thickening or calcification (computed tomography [CT]) or to exclude an infiltrative cardiomyopathy (magnetic resonance imaging). If diagnosis of CP was still unclear after the imaging studies, a right and left heart catheterization was performed. Pericardiectomy was performed through median sternotomy in all cases. Although there have been several surgical advances in the last 30 years, the surgical approach for the treatment of CP has not substantially changed over this period. A wide pericardiectomy was attempted (phrenic-to-phrenic and diaphragmatic pericardium) and was successfully achieved in 95% of cases. Perioperative mortality was defined as death occurring during surgery or within the first 30 days of hospitalization.

## Statistical Analysis

The 1-way analysis of variance test was used for comparisons of continuous variables between etiologic groups. The chi-square

test was used to compare the frequencies of qualitative variables. A bivariate Cox regression model was used to identify potential prognostic factors and multivariate Cox regression analysis to identify the independent predictors of mortality. Variables with a *P* value < .2 in the bivariate Cox regression analyses were included in a stepwise Cox regression model. The discriminatory power of the final model was assessed by means of C-statistics, which were estimated by bootstrapping, taking 1000 sample bootstraps. Proportional hazards assumption was graphically checked for each variable. SPSS (IBM Corp., Released 2010, IBM SPSS Statistics for Windows, Version 19.0; Armonk, New York, United States) was used for the statistical analysis.

## RESULTS

### Clinical Findings

Table 1 summarizes the demographics and clinical findings of our 140 patients, as well as the etiologies of CP. The most common etiology was idiopathic (54% of cases). Inflammatory/infectious pericarditis (acute idiopathic/viral pericarditis, tuberculous and purulent pericarditis) accounted for 35% of cases. All patients presenting with acute or subacute pericarditis were treated with anti-inflammatory drugs, independently of the suspected etiology. Of 140 patients, 37 (26.4%) had had a previous episode of acute pericarditis. Previous acute pericarditis was more frequent in the idiopathic CP group (59.5%) than in the identifiable etiology CP group (40.5%). Remarkably, previous CS and radiotherapy accounted for only 4% and 2% of cases, respectively. The symptom duration for each etiology is summarized in Figure 1. Overall mean time of symptoms was 19.5 months (ranging from 8 days to 360 months). Figure 2 shows the distribution by groups (acute, subacute, or chronic) of the different etiologies of CP and their relationship to symptom duration before the pericardiectomy. Interestingly, almost all patients with purulent, tuberculous and neoplastic CP had an acute or subacute presentation, the most acute illness being observed in purulent CP, with a mean symptom duration of 0.9 months. In contrast, most cases of chronic illness were due to an idiopathic CP or postacute idiopathic pericarditis CP.

**Table 1**

Demographics and Clinical Manifestations and Frequencies of Etiologies

Demographics			
Sex, male	99 (70.7)		
Mean age at surgery, y	54.6 (17-80)		
Diabetes mellitus	16 (11.4)		
Hypertension	28 (20.0)		
Renal impairment	14 (10.0)		
Clinical findings			
Congestive heart failure	124 (87.3)		
Dyspnea	117 (82.4)		
Pre-surgery NYHA functional class			
I	26 (18.6)		
II	65 (46.4)		
III	34 (24.3)		
IV	15 (10.7)		
Chest pain	46 (32.6)		
Fever	33 (23.4)		
Syncope	2 (1.4)		
Etiology			
Idiopathic	32 (54.2) <sup>a</sup>	44 (54.3) <sup>b</sup>	76 (54.3) <sup>c</sup>
Acute idiopathic pericarditis	8 (13.6) <sup>a</sup>	16 (19.7) <sup>b</sup>	24 (17.1) <sup>c</sup>
Tuberculous	8 (13.6) <sup>a</sup>	7 (8.6) <sup>b</sup>	15 (10.7) <sup>c</sup>
Purulent	3 (5.1) <sup>a</sup>	7 (8.6) <sup>b</sup>	10 (7.1) <sup>c</sup>
Neoplastic	4 (6.8) <sup>a</sup>	1 (1.2) <sup>b</sup>	5 (3.6) <sup>c</sup>
Cardiac surgery	1 (1.7) <sup>a</sup>	4 (4.9) <sup>b</sup>	5 (3.6) <sup>c</sup>
Radiotherapy	3 (5.1) <sup>a</sup>	0 (0.0) <sup>b</sup>	3 (2.1) <sup>c</sup>
Uremia	0 (0.0) <sup>a</sup>	2 (2.5) <sup>b</sup>	2 (1.4) <sup>c</sup>
Total	59 (42.1) <sup>a</sup>	81 (57.9) <sup>b</sup>	140 (100.0) <sup>c</sup>

NYHA, New York Heart Association.

Data are expressed as No. (%) or median (range).

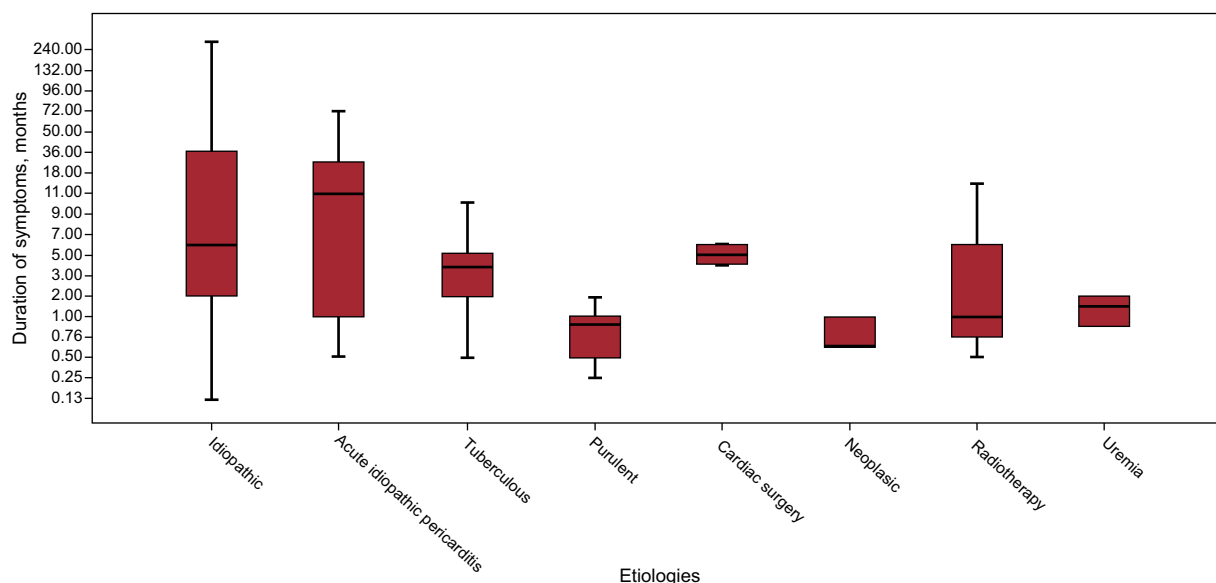
<sup>a</sup> Etiology (1978-1995).

<sup>b</sup> Etiology (1996-2012).

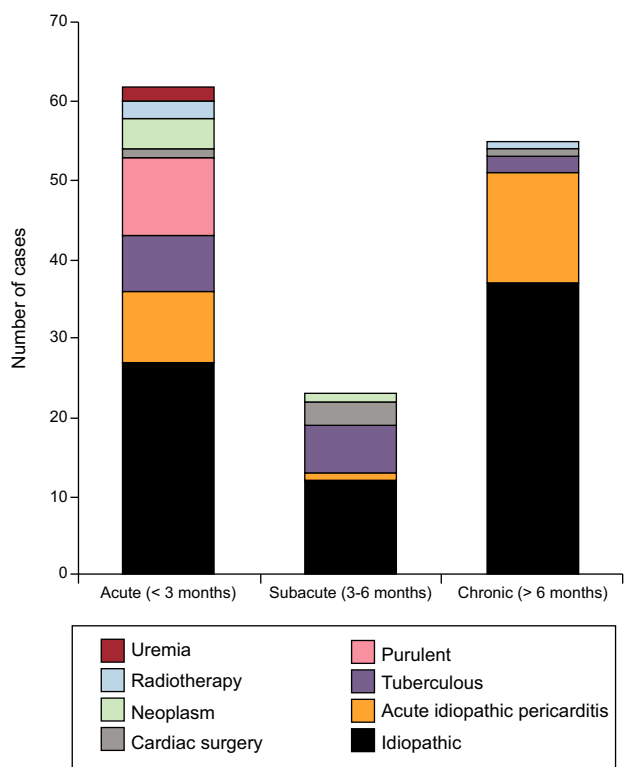
<sup>c</sup> Etiology (total).

### Diagnostic Tests

Table 2 shows the imaging and invasive tests performed and their diagnostic yield. Calcification in chest X-ray was seen in 26% of patients. Pericardial effusion was more often present in patients



**Figure 1.** Box-plot of symptom duration according with the etiology of constrictive pericarditis.



**Figure 2.** Number of cases of constrictive pericarditis for each etiology divided into acute (less than 3 months of symptoms), subacute (3-6 months) and chronic (more than 6 months).

with an acute or subacute presentation compared with those with chronic presentation (48 and 35% vs 9% respectively;  $P < .001$ ). Echocardiography showed diagnostic findings of constriction and/or pericardial thickening in 113 patients (83.7%). Moderate to severe PE was seen in 43 patients (30.7%) during their clinical course. The proportion of significant PE differed among etiologies: 3 etiologies had an important proportion of patients with significant PE—tuberculous (66.7%), radiotherapy (66%), neoplasm (60%), uremia (50%) and purulent (50%)—while the proportion of patients with significant PE was lower in those with postsurgery CP, postacute idiopathic pericarditis, and idiopathic CP (40.0%, 29.2% and 17.1%, respectively). Computed tomography, performed in 71 patients (50%), showed calcification or pericardial thickening (mean [standard deviation] pericardial thickness of 11.4 [6.8] mm) or PE in 93% of patients, and was normal in only 5 patients. The strength of CT in patients with suspected CP is its high positive predictive value for detecting calcification or thickening of the pericardium. Cardiac catheterization was performed in 53 patients (38%) and showed typical findings of constriction (equalization of end-diastolic pressures with dip-plateau morphology of diastolic ventricular curves and findings of ventricular interdependence) in 50 of them (95%), with a mean (standard deviation) right ventricular telediastolic pressure of 18.8, (5.1) mmHg and a mean (standard deviation) left ventricular telediastolic pressure of 20.8, (5.0) mmHg.

### Macroscopic Findings

Surgery showed involvement of both layers of the pericardium in most patients (61%) whereas an exclusive visceral involvement was only seen in 5 patients (7%).

**Table 2**  
Diagnostic Tests

<b>ECG</b>	138 (99)
Sinus rhythm	107 (76)
Atrial fibrillation	33 (25)
Low voltages	55 (39)
Diffuse ST-segment elevation	8 (6)
Negative T waves	88 (63)
Normal	28 (20)
<b>Chest X-ray</b>	140 (100)
Calcification	36 (26)
<b>Echocardiography</b>	135 (96)
Pericardial thickening	71 (53)
Pericardial effusion	
None	67 (49)
Mild (< 10 mm)	26 (19)
Moderate (10-20 mm)	16 (12)
Severe (> 20 mm)	26 (19)
Septal notch	89 (66)
Typical flows	97 (72)
Abnormal LVEF	28 (21)
<b>Computed tomography</b>	71 (51)
Pericardial thickening or calcification	53 (73)
Pericardial effusion	26 (35)
Normal	5 (7)
<b>Magnetic resonance</b>	13 (9)
Calcification	1 (10)
Pericardial thickening	4 (30)
Pericardial effusion	7 (53)
Normal	1 (10)
<b>Hemodynamic findings at cardiac catheterization</b>	53 (38)
Dip-plateau	50 (94)
Equalization of end-diastolic ventricular pressures	44 (87)
<b>Surgical findings</b>	104 (74)
Exclusive parietal involvement	34 (36)
Parietal and visceral involvement	63 (61)
Exclusive visceral involvement	7 (7)
<b>Total</b>	140 (100)

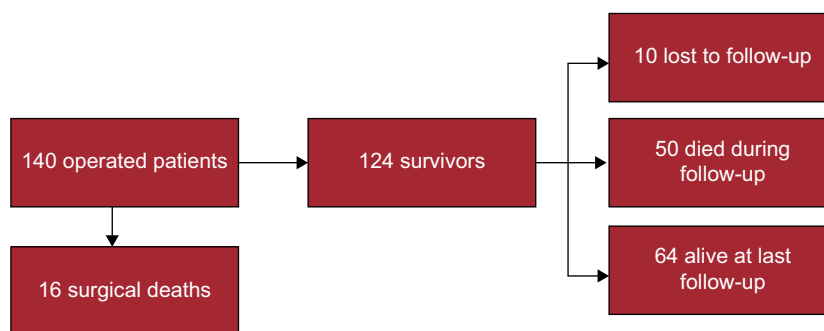
ECG, electrocardiogram; LVEF, left ventricular ejection fraction. Data are expressed as No. (%).

### Microscopic Pathology

Data on surgical pathology was available for 120 patients. Most of the patients had a fibrinous tissue (95 patients, 79%), while lymphoplasmacytic inflammation was identified in 5 patients (5.8%). Granulomatous inflammation was seen in 10 patients (8.3%) and in 4 of them *Mycobacterium tuberculosis* was identified in the biopsy. Four patients (3%) had adenocarcinoma identified in the biopsy. Three patients (2.5%) had an acute inflammation with neutrophils and lymphocytes. Only 1 patient had findings consistent with a purulent pericarditis.

### Perioperative Mortality

Figure 3 shows the flow-chart of patients. Perioperative mortality was 11.4% (16 out of 140 patients). Death was due to low-cardiac output syndrome in 6 patients, complications of a prolonged intensive care unit stay ending in sepsis in 5, mixed



**Figure 3.** Flow-chart of patients.

cardiogenic and septic shock in 2, advanced cancer in 1, and stroke in 1. In 1 patient the cause of death could not be determined. Regarding etiologies, 8 of the 16 patients who died in the first month had idiopathic CP, 2 patients had post-CS CP, 2 had neoplastic CP, 2 had purulent CP, 1 patient had a postacute idiopathic pericarditis CP, and 1 patient had radiation induced CP. **Table 3** shows the differences between patients who died and those who survived. Perioperative mortality was associated with older age (66.1 years vs 52.9 years;  $P < .002$ ), advanced New York Heart Association functional class (III or IV) at the time of surgery (odds ratio = 3.63; 95% confidence interval [95%CI], 1.23-10.70), and with the presence of moderate or severe PE during the course

of the disease (odds ratio = 3.40; 95%CI, 1.20-9.91]). There was a trend towards a higher mortality in the acute presentation (12.9% in acute patients vs 8.7% in subacute vs 10.9% in chronic). There were no differences in perioperative mortality between etiologies.

### Follow-up

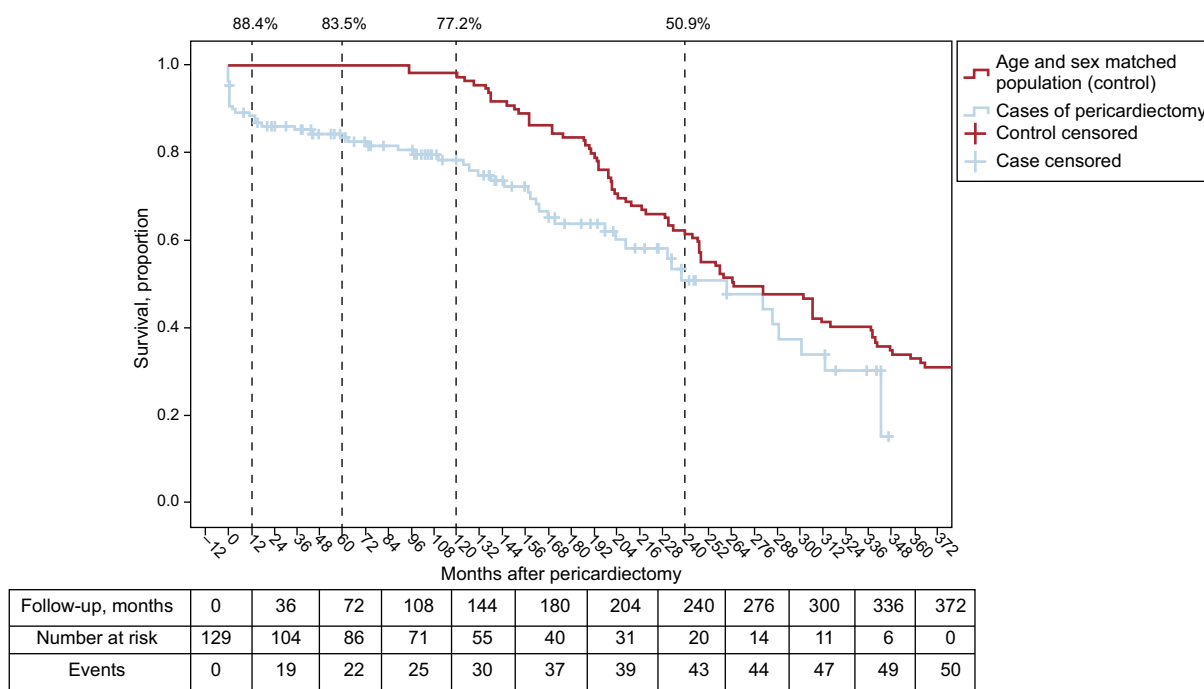
Ten patients were lost to follow-up after hospital discharge. Median follow-up among survivors was 12 years [range, 0.1-33.0 years]. **Figure 4** shows the Kaplan Meier curve of overall survival for our cohort of patients and an age and sex-matched Spanish population. Mean survival was 220 months (95%CI, 196-245).

**Table 3**  
Baseline Characteristics of Patients With Postoperative Mortality\*

Characteristics	Alive (n = 124)	Death (n = 16)	P
Age, mean (SD), y	52.95 (15.9)	66 (10.7)	.002
Sex, men	88 (71.0)	11 (68.8)	.854
<i>Clinical presentation</i>			
Dyspnea	14 (87.5)	103 (83.1)	.652
NYHA functional class III or IV during the disease	14 (87.5)	77 (62.1)	.045
NYHA functional class III or IV preoperatively	10 (62.5)	39 (31.5)	.014
Fever	4 (25.0)	29 (23.4)	1
Symptom duration, mean (SD), months	18.9 (41.0)	23.7 (59.3)	.684
Acute, < 3 months	8 (50.0)	54 (43.5)	.805
Subacute, 3-6 months	2 (12.5)	21 (16.9)	
Chronic, > 6 months	6 (37.5)	49 (39.5)	
Previous acute idiopathic pericarditis	34 (27.4)	3 (18.8)	1
Etiology (identifiable vs idiopathic)	9 (56.3)	91 (73.4)	.153
<i>ECG features</i>			
Rhythm (sinus vs other)	10 (62.5)	97 (78.2)	.163
Abnormal	12 (75.0)	100 (80.6)	.741
Low voltages	4 (25.0)	51 (41.8)	1
Negative T waves	8 (50.0)	80 (65.6)	.223
Chest X-ray (calcification)	3 (18.8)	33 (26.6)	1
<i>Echocardiographic features</i>			
Normal LVEF (> 50%)	13 (86.7)	94 (78.3)	.453
Pericardial effusion at diagnosis	7 (43.8)	29 (23.4)	.079
Moderate or severe pericardial effusion	9 (60.0)	33 (27.5)	.01
<i>Surgery (involved layers)</i>			
Exclusive parietal	5 (38.0)	29 (32.0)	.54
Parietal and visceral	7 (54.0)	56 (61.0)	.91
Exclusive visceral	1 (8.0)	6 (7.0)	1

ECG, electrocardiogram, LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD, standard deviation. Data are expressed as No. (%) or mean (standard deviation).

\* No hazard ratios are shown due to the low number of patients in each category.



**Figure 4.** Kaplan-Meier curve for overall survival of our patients (blue) and Kaplan-Meier curve for an age and sex-matched Spanish population (red). Survival at time intervals of 1 year, 5 years, 10 years, and 20 years.

At 20 years follow up, 50.9% of patients were still alive. Compared with the general age and sex-matched Spanish population, the survival rate of these patients was markedly inferior, although curves tended to overlap beyond 20 years of follow up. There were 50 deaths after the postoperative period (30 days). There were no differences in mortality between different etiologies. The bivariate-Cox model analysis of patients who survived the perioperative period and completed the follow-up (114 patients) identified age (hazard ratio [HR]= 1.05;  $P < .001$ ), the presence of dyspnea at clinical presentation (HR = 4.66;  $P = .013$ ), and New York Heart Association functional class (III-IV) during the disease or before surgery (HR = 2.76;  $P = .011$  and 2.97,  $P = .003$  respectively) as potential predictors of late mortality (Table 4). The multivariate analysis retained age at surgery (HR = 1.052; 95%CI, 1.017-1.088;  $P = .003$ ), advanced New York Heart Association functional class before surgery (HR = 4.028; 95%CI, 1.792-9.054;  $P = .001$ ), and having had a previous episode of acute pericarditis (HR = 2.931; 95%CI, 1.261-6.810;  $P = .012$ ) as long-term mortality predictors of death (Table 5). The C-statistic of our final model was 0.75, thus indicating an adequate discriminatory power.

## DISCUSSION

This is a contemporary series of a large group of patients with CP who underwent pericardiectomy in a single institution serving as referral center for pericardial diseases and using a standardized protocol for its diagnosis and management followed for more than 30 years. The analysis of this series provides new insights into the etiologic spectrum, clinical presentation, usefulness of diagnostic methods and prognostic factors in this disease. By contrast to prior contemporary reports, our study shows that most CP are idiopathic, with CS and radiation accounting for only a minority of cases. Long-term survival after pericardiectomy is not affected by the etiology, while age, advanced functional class, and previous acute idiopathic pericarditis are potential prognostic factors.

## Etiologic Spectrum

Based on series of patients who underwent surgery between 1970 and 2000, some authors<sup>2,3,7-9</sup> have suggested a change in the etiologic spectrum of CP with a trend toward a larger proportion of patients with postcardiac surgery (18% to 37% of cases) and postradiation CP (9% to 31% of cases). In particular, CS accounted for a proportion as high as 37% in one series.<sup>3</sup> By contrast, in our series, the most frequent etiologies were idiopathic (54% of cases) followed by inflammatory/infectious CP (35%), whereas postsurgical and postradiation CP accounted for only 4% and 2% of cases, respectively. No changes between the frequencies of etiologies were observed between the periods 1978-1995 and 1996-2012. Although this discrepancy may partially be explained by the different structure of hospitals, it seems quite improbable that a different volume in CS, oncology and radiotherapy procedures could lead to such large differences on estimates. According to the incidence of CP after CS (0.09%–0.30%) reported in different studies,<sup>2,3</sup> we should have seen a larger number of cases. Another plausible explanation may be that CP after CS is often transient.<sup>10,11</sup> Thus one can postulate that some pericardiectomies could have been avoided if a more conservative strategy had been adopted.<sup>12</sup> It is our practice to be specially vigilant for this possible outcome<sup>13</sup> and establish the indication of pericardiectomy only in cases with a severe and persistent constriction.

Remarkably, in our study an acute viral/idiopathic pericarditis was the cause of CP in 17% of cases. This is in accordance with prospective studies<sup>4,14</sup> that have estimated the probability of developing CP after an acute pericarditis to be as low as 1%.

## Relationship Between Etiology and Clinical Features. Considerations for Etiologic Studies

Constrictive pericarditis is the final manifestation of a very wide range of pericardial insults. The time elapsed between the causal

**Table 4**  
Univariate Cox Regression Estimates of Baseline Clinical Characteristics

Characteristics	Alive (n = 64)	Death (n =50)	HR (95%CI)	P
Age at surgery, mean (SD), y	51.51 (17.10)	58.80 (12.10)	1.053 (1.026-1.08)	<.001
Women	22 (28.6)	15 (31.3)	0.770 (0.410-1.448)	.419
Clinical presentation (dyspnea)	65 (81.3)	31 (91.2)	4.658 (1.386-15.661)	.013
<i>NYHA functional class</i>				
III or IV during the disease	49 (68.0)	23 (31.9)	2.758 (1.266-6.010)	.011
III or IV preoperatively	21 (26.3)	14 (40.0)	2.966 (1.433-6.138)	.003
Fever	21 (77.8)	6 (22.2)	0.439 (0.179-1.075)	.071
<i>ECG findings</i>				
Rhythm	16 (61.5)	10 (38.5)	1.300 (0.617-2.739)	.491
Abnormal ECG	64 (71.9)	25 (28.0)	1.220(0.543-2.742)	.631
Low voltages	15 (65.2)	8 (34.8)	1.220 (0.543-2.742)	.631
T wave inversion	59 (78.7)	16 (21.3)	0.570 (0.286-1.135)	.06
Symptom duration in months, mean (SD)	20 (46.00)	16 (31.01)	0.999 (0.989-1.007)	1
Acute (< 3 months)	36 (45)	22 (44)	0.916 (0.367-2.285)	.479*
Subacute (3-6 months)	14 (17.5)	6 (12.0)	1.122 (0.452-2.787)	
Chronic (> 6 months)	30 (37.5)	22 (44.0)		
Previous acute idiopathic pericarditis	19 (63.3)	11 (36.7)	0.485 (0.226-1.039)	.063
Etiology identifiable	68 (89.5)	8 (50.0)	0.824 (0.291-2.334)	.793
Chest X-ray (calcification)	22 (27.5)	8 (26.7)	0.695(0.313-1.540)	.37
<i>Echocardiography</i>				
Depressed LVEF (< 50%)	64 (71.1)	26 (28.9)	1.181 (0.511-2.730)	.697
Any PE	20 (71.4)	8 (28.6)	1.746 (0.759-4.017)	.190
Moderate to severe PE	23 (28.8)	9 (26.5)	0.947 (0.440-2.039)	.889
<i>Surgery (involved layers)</i>				
Exclusive parietal	21 (29.2)	6 (40.0)	1.629 (0.194-13.641)	.653
Parietal and visceral	47 (65.3)	8 (53.6)	0.605 (0.073-5.030)	.642
Exclusive visceral	4 (5.6)	1 (6.7)		

95%CI, 95% confidence interval; ECG, electrocardiogram, HR, hazard ratio; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PE, pericardial effusion; SD, standard deviation.

Baseline characteristics of patients who survived the first month after surgery and completed the long-term follow-up (114 patients).

Unless otherwise indicated, data are expressed as No. (%), mean (standard deviation).

\* Omnibus.

illness and the development of constriction can be variable. The relationship between the etiology and the clinical development of constriction has not been analyzed in previous studies. This information is important in 2 ways: on the one hand, in the attempt to predict the possible chronology of progression to constriction after the different kinds of aggression to the pericardium, and on the other hand, to establish the advisability of etiologic investigations in patients with constriction. For instance, nearly all cases of constriction due to specific and potentially treatable causes (mainly purulent or tuberculous pericarditis) require pericardiectomy in the first 6 months (acute

and subacute constriction), an observation that is in accordance with our previous experience with tuberculous and purulent pericarditis.<sup>15-17</sup> In particular, purulent pericarditis can show a hyperacute progression to constriction, the shortest interval being 8 days. Accordingly, patients with purulent pericarditis must be carefully monitored in the first weeks and patients with tuberculous pericarditis in the first months. If constriction does not develop in the first 6 months, it is unlikely to appear later on. In contrast to acute and subacute cases, no specific treatable etiologies were found in the group of patients with chronic CP (more than 6 months). These findings suggest that, in patients who present with CP, etiologic investigations are only warranted for acute and subacute cases.

**Table 5**  
Adjusted Independent Predictors of Adverse Outcome Adjusted for Potential Confounders

Variable	P	HR (95%CI)
Age at surgery	.002	1.054 (1.020-1.090)
NYHA functional class III or IV preoperatively	.006	3.139 (1.397-7.055)
Previous acute idiopathic pericarditis	.010	2.790 (1.274-6.113)
Negative T waves in ECG	.299	0.682 (0.331-1.404)

95%CI, 95% confidence interval; ECG, electrocardiogram; HR, hazard ratio; NYHA, New York Heart Association.

## Use and Diagnostic Yield of Imaging and Diagnostic Techniques

In our series, calcification of the pericardium in the chest X-ray was seen only in 26% of cases, in agreement with other recent series.<sup>18</sup> However, this finding should be carefully searched for, as its presence in a patient with clinical suspicion of CP is sufficient to establish a firm diagnosis. The global diagnostic yield of echocardiography-Doppler was approximately 84%. An unsuspected finding was the high percentage of patients with PE, which can be explained by the fact that 43% of patients underwent

surgery during the first 3 months of the disease when patients remained symptomatic despite medical treatment (anti-inflammatory drugs and/or diuretics when indicated). These patients could have had an effusive-CP.<sup>19</sup> The diagnostic yield of CT was as high as 93% and only 5 patients (7%) had a normal CT. Thus, although cases of CP with normal pericardial thickness have been described,<sup>20</sup> a strictly normal CT is evidence against a diagnosis of CP. However, this finding could be biased as the possibility that the diagnosis of CP could have been missed in some patients with normal CT cannot be excluded. Despite this high diagnostic yield, we believe that catheterization is not necessary in most patients. The diagnostic yield of magnetic resonance cannot be established from our data, as it was only performed in 9% (13 of 140 patients). In fact, CT may be superior to magnetic resonance due to its greater reliability in detecting calcium. Cardiac catheterization was done in 38% (53 of 140 patients) and showed typical diagnostic findings (dip-plateau with equalization of diastolic ventricular pressure curves in 94% and 87% respectively). Cardiac catheterization was also useful in excluding coronary artery disease in patients with risk factors or with anginal symptoms. During the time-span our series was collected, several advances have been made in imaging techniques and there is a tendency toward a more judicious use of the invasive diagnostic tests in our patients.<sup>21</sup> When there is clinical suspicion of CP, echocardiography-Doppler (showing a restrictive physiology) and CT (showing a thickened and/or calcified pericardium) should be enough to establish the diagnosis.

### Prognostic Factors

The perioperative mortality found in our series (11.4%) is in agreement with the experience of other authors.<sup>7,22,23</sup> Similar to other series, age and advanced New York Heart Association class were predictors of mortality. Unexpectedly, we also found the presence of PE to be more frequent in patients with a poor surgical outcome. Mortality was similar in acute, subacute and chronic presentations, although there seems to be a trend to higher mortality in the acute presentation. In contrast with the experience of other authors,<sup>18</sup> we did not find that the presence of pericardial calcification was as an independent predictor of perioperative mortality.

### Limitations

Our study has several limitations mainly related to its retrospective design and to the fact that we only analyzed patients who underwent surgery, thus excluding all patients who were not candidates for surgery because of comorbidities or poor clinical status. A small number of diagnosis of CP could have been missed, which could introduce some bias in the diagnostic yield of the different diagnostic procedures. However, the impact of these limitations is not expected to be sufficiently high to compromise the validity of the conclusions of the study.

### CONCLUSIONS

In our experience, idiopathic and postinflammatory/infectious pericarditis are still the most frequent causes of CP leading to pericardiectomy, while CS and radiotherapy-related pericarditis account for only a minority of cases. Purulent, tuberculous and neoplastic pericarditis show a characteristic pattern of acute or subacute progression to constriction. There are no differences in mortality between different etiologies. Echocardiography was the most common technique used to identify a physiologic

pattern of restriction/constriction and CT was the most reliable technique to document a thickened or calcified pericardium. Predictors of poor surgical or long-term prognosis are age, advanced clinical status, and the presence of moderate or severe PE.

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### CONFLICTS OF INTEREST

None declared.

### REFERENCES

- Lower R. *Tractatus de corde*. Londres: Allestry; 1669.
- Ling LH, Oh JK, Schaff HV, Danielson GK, Mahoney DW, Seward JB, et al. Constrictive pericarditis in the modern era: evolving clinical spectrum and impact on outcome after pericardiectomy. *Circulation*. 1999;100:1380–6.
- Bertog SC, Thambidorai SK, Parakh K, Schoenhagen P, Ozduran V, Houghtaling PL, et al. Constrictive pericarditis: etiology and cause-specific survival after pericardiectomy. *J Am Coll Cardiol*. 2004;43:1445–52.
- Permanyer-Miralda G, Sagristà-Sauleda J, Soler-Soler J. Primary acute pericardial disease: a prospective series of 231 consecutive patients. *Am J Cardiol*. 1985;56:623–30.
- Soler-Soler J, Permanyer-Miralda G, Sagristà-Sauleda J. A systematic diagnostic approach to primary acute pericardial disease. The Barcelona experience. *Cardiol Clin*. 1990;8:609–20.
- Instituto Nacional de Estadística. INEbase/demografía y población/fenómenos demográficos. Madrid: INE; 2014 [cited 2014 Dec 12]. Available at: [http://www.ine.es/inebmenu/mnu\\_dinamicapob.htm](http://www.ine.es/inebmenu/mnu_dinamicapob.htm).
- George TJ, Arnaoutakis GJ, Beaty CA, Kilic A, Baumgartner WA, Conte JV. Contemporary etiologies, risk factors, and outcomes after pericardiectomy. *Ann Thorac Surg*. 2012;94:445–51.
- Chowdhury UK, Subramaniam GK, Kumar AS, Airan B, Singh R, Talwar S, et al. Pericardiectomy for constrictive pericarditis: a clinical, echocardiographic, and hemodynamic evaluation of two surgical techniques. *Ann Thorac Surg*. 2006;81:522–9.
- Young PM, Glockner JF, Williamson EE, Morris MF, Araoz PA, Julsrud PR, et al. MR imaging findings in 76 consecutive surgically proven cases of pericardial disease with CT and pathologic correlation. *Int J Cardiovasc Imaging*. 2012;28:1099–109.
- Betrián Blasco P, Comas JG, Ferrer JC, Mendiña QF, García BM, Ipiña FG. Transient postoperative pericardial constriction in a child. *Int J Cardiol*. 2009; 131:e45–7.
- Haley JH, Tajik AJ, Danielson GK, Schaff HV, Mulvagh SL, Oh JK. Transient constrictive pericarditis: Causes and natural history. *J Am Coll Cardiol*. 2004;43:271–5.
- Marques AC, Calderaro D, Yu PC, Gualandro DM, Gonçalves LF, Mariani AW, et al. Acute pericarditis with transient constriction: Surgical impetus must be contained. *BMJ Case Rep*. 2009. <http://dx.doi.org/10.1136/bcr.07.2008.0571>.
- Sagristà-Sauleda J, Permanyer-Miralda G, Candell-Riera J, Angel J, Soler-Soler J. Transient cardiac constriction: An unrecognized pattern of evolution in effusive acute idiopathic pericarditis. *Am J Cardiol*. 1987;59:961–6.
- Imazio M, Brucato A, Maestroni S, Cumetti D, Belli R, Trincherio R, et al. Risk of constrictive pericarditis after acute pericarditis. *Circulation*. 2011;124:1270–5.
- Mesado D, Sarriá C, Bustamante J, Rodríguez JE, Domínguez L, Olivera MJ. Pericarditis constrictiva por *Propionibacterium acnes*. *Rev Esp Cardiol*. 2013; 66:407–9.
- Sagristà-Sauleda J, Permanyer-Miralda G, Soler-Soler J. Tuberculous pericarditis: Ten year experience with a prospective protocol for diagnosis and treatment. *J Am Coll Cardiol*. 1988;11:724–8.
- Sagristà-Sauleda J, Barrabés JA, Permanyer-Miralda G, Soler-Soler J. Purulent pericarditis: review of a 20-year experience in a general hospital. *J Am Coll Cardiol*. 1993;22:1661–5.
- Ling LH, Oh JK, Breen JF, Schaff HV, Danielson GK, Mahoney DW, et al. Calcific constrictive pericarditis: is it still with us? *Ann Intern Med*. 2000;132:444–50.
- Sánchez-Sauleda J, Angel J, Sanchez A, Permanyer-Miralda G, Soler-Soler J. Effusive-constrictive pericarditis. *N Engl J Med*. 2004;350:469–75.



20. Talreja DR, Edwards WD, Danielson GK, Schaff HV, Tajik AJ, Tazelaar HD, et al. Constrictive pericarditis in 26 patients with histologically normal pericardial thickness. *Circulation*. 2003;108:1852-7.
21. García-Orta R, Mahía-Casado P, Gómez de Diego JJ, Barba-Cosials J, Rodríguez-Palomares JF, Aguadé-Bruix S, et al. Novedades en imagen cardíaca 2013. *Rev Esp Cardiol*. 2014;67:127-34.
22. Ha JW, Oh JK, Schaff HV, Ling LH, Higano ST, Mahoney DW, et al. Impact of left ventricular function on immediate and long-term outcomes after pericardiectomy in constrictive pericarditis. *J Thorac Cardiovasc Surg*. 2008;136:1136-41.
23. Oreto L, Mayer A, Todaro MC, Mori N, Kress DC, Kleinman LH, et al. Contemporary clinical spectrum of constrictive pericarditis: A 10-year experience. *Int J Cardiol*. 2013;163:339-41.