Meta-Analysis of Population Characteristics and Outcomes of Patients Undergoing Pericardiectomy for Constrictive Pericarditis

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We sought to systematically describe the epidemiology, etiology, clinical and operative characteristics as well as outcomes of patients who underwent pericardiectomy for constrictive pericarditis in the contemporary era. We conducted a systematic search of the MEDLINE, Embase, and Cochrane databases from their inception to April 1, 2020 for studies assessing the outcomes of pericardiectomy in patients with constrictive pericarditis. Studies with patients enrolled before 1985, pediatric patients or studies including >10% tuberculous pericarditis were excluded. The impact of pericarditis etiology on outcomes was evaluated with a meta-analysis. We analyzed 27 eligible studies and 2,114 patients. Etiology was most commonly idiopathic (50.2%), followed by after-cardiac surgery (26.2%) and radiation (6.9%). Patients were mostly men (76%), mean age 58 and with advanced symptoms (NYHA III/IV 70.1%). Total pericardiectomy was preferred (85.8%) and concomitant cardiac surgery was relatively common (23.8%). Operative mortality was 6.9% and 5-year mortality was 32.7%. Radiation and after-cardiac surgery patients had 3 and 2 times higher long-term risk for mortality respectively compared with idiopathic. A sensitivity analysis did not result in changes in the results. Thirty percent of included studies had more than low bias primarily originating from follow up and selection. Pericardiectomy is therefore performed mostly in middle-aged men with advanced symptoms and low co-morbidity burden and still caries significant operative mortality. Radiation and after-cardiac surgery patients have a significantly higher mortality risk compared with idiopathic. Several methodological issues and significant heterogeneity limit the generalization of these data and randomized controlled trials may have to be considered. **(Am J Cardiol 2021;146:120−127)**

Constrictive pericarditis presents clinically as heart failure and results from inflammation and fibrosis of the pericardium leading to impaired diastolic filling of both ventricles.[1,2] Pericardiectomy has been performed for the treatment of constrictive pericarditis for over 80 years[3−8] with significant improvement in symptoms[5]. Despite being considered curative, it has been associated with substantial late mortality, particularly for radiation and after-surgical constrictive pericarditis although some debate still exists on the issue. There are a significant number of studies on pericardiectomy in the contemporary era.[9,11−13] However, most of them represent single-center experiences with variation in outcomes and no systematic review has been performed to date.[14,15] We therefore performed a systematic review of patients with constrictive pericarditis who underwent pericardiectomy to better define this population's characteristics and outcomes in the current era, and to assess for bias and heterogeneity in published studies. We additionally evaluated the mortality risk after pericardiectomy based on the etiology of constrictive pericarditis in a meta-analysis.

Methods

This study was designed and performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[16] (**eTable 1**). The study protocol was registered in the international prospective register of systematic reviews with the unique identifier 18,4447 (under evaluation).

Studies were deemed eligible if they were prospective or retrospective cohort studies reporting outcomes of patients that underwent pericardiectomy for constrictive pericarditis. The studies needed to report the etiology of the disease and mortality. Studies including pediatric patients or patients enrolled before 1985 were excluded. We also

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excluded studies where tuberculous pericarditis comprised more than 10% of the cohort and studies including less than 5 patients. Studies were screened for overlapping cohorts and only the study with the largest cohort size and longest duration of follow-up was included.

The MEDLINE, Embase and Cochrane databases were searched for eligible studies from inception to April 1, 2020. A combination of free textwords and MeSH subheadings were used including the terms *pericarditis, constrictive, pericardiectomy, surgical removal,* and *pericardium*, appropriately linked with “AND” or “OR”.

After retrieval of all identified studies, two independent reviewers (AIT [Aspasia Tzani] and IPD) screened the studies first based on their title and abstract of citations, and secondly on their full manuscript. Disagreements were resolved by a third investigator (PNK). The reference list of selected publications was also manually searched to identify eligible studies.

The Newcastle-Ottawa Scale for non-randomized studies (S1) was used to evaluate the methodological quality and assess for bias of the included studies. Each study scored 1 or 0 for each of the items of the scale. Evaluation and scoring was performed by two individual investigators (AIT and IPD) and a third investigator (PNK) was used to reach consensus when necessary. The non-exposure group was defined as the group of patients with idiopathic constrictive pericarditis for the purposes of the meta-analysis only.

Categorical variables were reported as proportions, whereas continuous variables were reported as mean and standard deviation (SD). Comparisons between pooled categorical data from studies enrolling patients before and after 2,000 were performed using the Pearson’s chi-square 2-sided test.

A meta-analysis of all-cause mortality according to the etiology of constrictive pericarditis was performed using hazard ratios (HRs) that were extracted from each study or pooled from the Kaplan-Meier curves (S2). Pooled HRs and corresponding 95% confidence intervals (CI) were calculated with a random-effects model according to DerSimonian-Laird. Statistical heterogeneity between studies was assessed with Cochran Q statistic and the I^2 statistic; $p < 0.10$ for the chi-square test or I^2 greater than 50% indicated significant heterogeneity. Publication bias evaluation using Egger’s test for small study effect was performed for all-cause mortality. Meta-regression was used to assess the effect of patients’ clinical characteristics as moderators for all-cause mortality. A predefined sensitivity analysis was performed removing one trial at a time (leave-one-out analysis). A 2-tailed p value < 0.05 was considered statistically significant. Statistical analysis was performed using STATA/SE version 16 (Stata Corp, College Station, Texas).

Results

Initial screening identified 171 potentially eligible studies out of 1842 that resulted from our search strategy (**eFigure 1**). Forty-two studies had >10% tuberculosis patients and were excluded (**eFigure 2**). Twenty-seven studies finally met all inclusion criteria and were included in the analysis (**Table 1**). Most studies were retrospective cohort studies (n=25) and 2 were prospective. All studies were published between 1991 and 2019 while the majority of the studies (67%) enrolled patients between the years 2000 and 2010. Pooled mean follow-up time was 4 years (range 1.2 to 6.9 years).

A total of 2,114 patients were analyzed. Two hundred and thirty-six patients across 4 studies were enrolled before the year 2000 and 176 across 6 studies after. Pooled patient characteristics are summarized in **Table 2**. The majority of patients were men (76%), and pooled mean age was 58 years. Constrictive pericarditis was most commonly idiopathic (50.2%). The second most common etiology was after-cardiac surgery (26.2%), whereas radiation comprised less than 10% of the cases (8.9%)(**Figure 1**). Fewer cases were reported as after-cardiac surgery in etiology after the year 2000 (15% vs. 33%, p<.001), however the etiology of constrictive pericarditis was also more frequently unknown (20% vs 8%, p <0.001). Pericardial calcification was present in less than half of the patients (41.1%) (n=17 studies) and pericardial effusion in less than a third (29.3%) (n=11 studies) (**eTable 2**).

More than two thirds (70.1%) of patients with constrictive pericarditis had advanced heart failure (NYHA class III-IV), whereas a third (33.1%) had ascites (**Table 2**). Peripheral edema and hepatomegaly were frequent physical exam findings (64.7% and 35.6% respectively), however not consistently reported in studies (**eTable 2**). Left ventricular ejection fraction (LVEF) was preserved (mean LVEF=58%). There were no notable differences in major co-morbidities before and after 2000 with the exception of less frequent coronary artery disease (25% vs 29%, p = 0.005). Pre-operative laboratory and hemodynamic parameters are reported in **eTable 2** and **eTable 3**.

Almost 86% of patients underwent complete pericardiectomy. Notably this was true for only 69% in patients enrolled before 2000 (**Table 2**, **eTable 4**). The percent of pericardiectomies on bypass and with concomitant cardiac surgeries increased significantly after 2000 (37% from 18% and 40% from 16%, p <0.01 for both).

Table 3 summarizes short- and long-term outcomes after pericardiectomy for constrictive pericarditis. Inpatient/30-day all-cause mortality in the pooled cohort was 6.9% (range 0 to 29%) without significant differences before and after 2000. The most commonly reported complications after pericardiectomy were low cardiac output syndrome in 12.8% of cases (n=13/27 studies). Other inpatient characteristics such as length of stay and rates of transfusion were reported by only a minority of the studies (**eTable 5**). Pooled all-cause 1-year and 5-year mortality were 17.4% and 32.7% respectively. The rates of re-operation and re-hospitalization for heart failure were 8% (n=12/27 studies) and 11% (n=14/27 studies) respectively (**Table 3**, **eTable 6**). Patients enrolled after 2000 had higher 1-year and 5-year all-cause mortality rate compared with before 2000 (19.8% vs. 10%, p = 0.01 and 49.4% versus 20%, p <0.001 respectively).

Patients who underwent pericardiectomy for after-cardiac surgery constrictive pericarditis had significant higher risk of all-cause mortality when compared with patients with idiopathic etiology (HR: 2.15; 95% CI: 1.21 to 3.61, p = 0.01) (**Figure 2**) (n=9 studies). Patients with constrictive

Table 1
Study characteristics

Study	Study Origin	Type	NoS	Years of Enrollment	No of pts	Etiology					Complete Pericardi-ectomy	Follow up period,y Mean(SD)
						Idiopathic	Radiation	After-cardiac surgery	TB	Other		
Armstrong 2019	USA	Prospective cohort	6/7	2005-2018	8	8 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (87.5%)	4.7 (9.5)
Gatti 2019	France Italy	Retrospective observational	6/7	1986-2018	81	32 (39.5%)	6 (7.4%)	14 (17.8%)	13 (16.1%)	16 (19.7%)	59 (72.8%)	5.4 (1.3)
Vondran 2019	Germany	Retrospective observational	7/7	2011-2016	12	6 (50%)	0 (0%)	2 (16.7%)	NA	NA	9 (75%)	3 (3.5)
Radakovic 2018	Germany	Retrospective observational	7/8	2009-2016	79	44 (55.7%)	8 (10.1%)	13 (16.5%)	10 (12.7%)	4 (5.1%)	60 (75.9%)	NA
Nachum 2018	Israel	Retrospective observational	7/7	2005-2017	55	27 (49.1%)	3 (5.4%)	5 (9.1%)	0 (0%)	20 (36.4%)	53 (96.4%)	4.3 (3.2)
Nozohoor2018	Sweden	Retrospective observational	8/8	1991-2016	41	28 (68.3%)	1 (2.44%)	12 (29.3%)	0 (0%)	0 (0%)	24 (58.5%)	6.3 (6.2)
Lee 2017	Japan	Retrospective observational	6/7	1986-2017	22	8 (36.4%)	1 (4.5%)	16 (72.7%)	0 (0%)	1 (4.5%)	NA	6.6 (3.3)
Rupprect 2017	Germany	Retrospective observational	6/7	1995-2016	39	29 (74.4%)	1 (2.6%)	1 (2.6%)	1 (2.6%)	7 (17.9%)	39 (100%)	NA
Murashita 2017	USA	Retrospective observational	7/8	1990-2013	807	447 (55.4%)	92 (11.4%)	261 (32.3%)	0 (0%)	7 (86.7%)	807 (100%)	3.23(5.1)
Nishimura 2016	Japan	Retrospective observational	6/8	1985-2014	45	16 (35.6%)	1 (2.2%)	21 (46.7%)	4 (8.9%)	3 (6.8%)	36 (80%)	5.7 (1.5)
Ismail 2016	Germany	Retrospective observational	5/7	1997-2011	69	36 (52.1%)	3 (4.35%)	8 (11.6%)	6 (8.7%)	16 (23.2%)	19 (27.5%)	NA
Busch 2015	Germany	Retrospective observational	8/8	1995-2012	97	46 (47.4%)	9 (9.3%)	19 (19.6%)	NA	24 (24.7%)	53 (54.6%)	1.2 (3.96)
Choudhry 2015	USA	Retrospective observational	5/7	1999-2010	35	19 (54.3%)	3 (8.6%)	4 (11.4%)	NA	9 (25.7%)	0 (0%)	NA
Vistarini 2015	Canada	Retrospective observational	7/7	1994-2014	99	60(60.6%)	2 (2%)	13 (13.1%)	15 (15.1%)	9 (9.1%)	60 (60.6%)	4.5
Landex 2015	Denmark	Retrospective observational	5/7	1998-2012	47	17 (36.2%)	4 (8.51%)	13 (27.7%)	1 (2.13%)	12 (25.5%)	21 (44.7%)	3.5 (2.4)
Avgerinos 2015	USA	Retrospective observational	8/8	1997-2012	36	20 (55.6%)	3 (8.3%)	11 (30.6%)	2 (5.6%)	0 (0%)	35 (97.2%)	5.7
Shiraishi 2014	Japan	Retrospective observational	7/7	1992-2012	25	17 (68%)	NA	6 (24%)	1 (4%)	1 (4%)	25 (100%)	5.3
Buyukbayrak 2013	Turkey	Retrospective observational	5/7	-	8	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (100%)	6 (75%)	0.74
Komoda 2013	Germany	Retrospective observational	5/7	1996-2011	64	NA	NA	NA	NA	64 (100%)	64 (100%)	NA
Szabo 2013	Germany	Retrospective observational	7/8	1988-2012	89	49 (55.1%)	5 (5.6%)	21 (23.6%)	5 (5.6%)	9 (10.1%)	89 (100%)	NA
Ariyoshi 2012	Japan	Retrospective observational	4/7	2000-2011	16	0 (0%)	1 (6.2%)	6 (37.5%)	1 (6.2%)	8 (50%)	16 (100%)	NA
George 2012	USA	Retrospective observational	7/8	1995-2010	98	44 (44.9%)	17 (17.3%)	30 (30.6%)	0 (0%)	7 (7.14%)	94 (95.9%)	4.23 (4.5)
Barbetakis 2010	Greece	Retrospective observational	4/7	2000-2008	6	0 (0%)	6 (100%)	0 (0%)	0 (0%)	0 (0%)	2 (33.3%)	NA
Bertog 2004	USA	Retrospective observational	8/8	1977-2000	163	75 (46%)	15 (9.2%)	60 (36.8%)	NA	13 (8%)	119 (73%)	6.9 (3.9)
Sagristà-Sauleda J 2004	Spain	Prospective cohort	4/7	1986-2001	7	4 (57%)	1 (14.3%)	1 (14.3%)	1 (14.3%)	0 (0%)	7 (100%)	NA
Sun 2001	USA	Retrospective observational	6/7	1989-1996	30	15 (50%)	4 (13.3%)	10 (33.3%)	1 (3.3%)	0 (0%)	0 (0%)	3 (0.2)
DeValeria 1991	USA	Retrospective observational	6/7	1980-1989	36	17 (47.2%)	4 (11.1%)	8 (22.2%)	2 (5.6%)	7 (19.4%)	36 (100%)	4.7
Total		**6/7**	**2114**	**1063 (50.2%)**	**190 (8.9%)**	**555 (26.2%)**	**63 (3%)**	**245 (11.6%)**	**1740 (85.8%)**	**4.03**		

Abbreviations: Nos = New-Castle Ottawa scale; TB = tuberculosis; NA = not available.

Table 2
Clinical and operative characteristics

	All (n=2,114)	Before 2000 (n=236)	After 2000 (n=176)	p-value[a]
Demographics				
Age, years	58.4	55.1	60.1	-
Male gender	1593 (75.3%)	187 (79%)	140 (79.5%)	ns
Etiology of CP				
Idiopathic	1063 (50.2%)	111 (47%)	85 (48%)	ns
Radiation	190 (8.9%)	24 (10%)	18 (10%)	ns
After-cardiac surgery	555 (26.2%)	79 (33%)	26 (15%)	**<0.001**
TB	63 (3%)	4 (2%)	11 (7%)	ns
Other	245 (11.6%)	20 (8%)	32 (20%)	**<0.001**
Clinical characteristics				
Ascites	272 (33.1%)	80 (40%)	42 (37%)	ns
LVEF	58	50	57	-
NYHA III-IV	1322 (70.1%)	98 (57%)	63 (61%)	ns
DM	395 (20.2%)	28 (17%)	34 (22%)	ns
HTN	418 (44%)	52 (32%)	61 (40%)	ns
CAD	321(32.60%)	75 (39%)	38 (25%)	**0.005**
Operative data				
Total pericardiectomy	1740 (85.8%)	162 (69%)	147 (84%)	**<0.001**
Median sternotomy	1575 (88.9%)	146 (90%)	93 (96%)	ns
On pump	895 (45.8%)	30 (18%)	36 (37%)	**<0.001**
Concomitant surgery	489 (23.8%)	36 (16%)	74 (40%)	**0.002**

Abbreviations: CP = constrictive pericarditis; TB = tuberculosis; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; DM= Diabetes mellitus; HTN = Hypertension; CAD = Coronary artery disease; ns = not significant

[a] Calculated for studies before 2000 versus After 2000.

pericarditis caused by radiation had even higher risk of all-cause mortality using idiopathic constrictive pericarditis as the reference group (HR: 3.21; 95% CI: 1.56 to 6.50, p <0.01) (**Figure 2**) (n=7 studies) (**Figure 3**).

Eight of the 27 studies (30%) had more than low risk of bias (score less than 6/7 or 7/8 on the Newcastle-Ottawa Scale, **eTable 7**). We found moderate or high heterogeneity (I^2 >70%) of the studies evaluating the impact of constrictive pericarditis etiology on pericardiectomy outcomes. Egger's test for small study effect showed the absence of significant publication bias (**eFigure 3**). Meta-regression showed only pulmonary artery systolic pressure and male gender to be significant moderators of mortality when comparing after-cardiac to idiopathic and radiation to idiopathic constrictive pericarditis (both p <0.01) (**eTable 8**). Sensitivity analysis (leave-one-out approach) showed no difference in the meta-analyses results (**eFigure 4**).

Discussion

We present the first systematic review of pericardiectomy for constrictive pericarditis in the contemporary era. Our analysis of more than 2,100 patients provides clear insight into the epidemiology, etiology and clinical presentation of constrictive pericarditis in patients who underwent surgical treatment, and reports operative characteristics and outcomes of this population. On the other hand, we identify that 30% of included studies have more than low bias in regards to outcomes. Our meta-analysis shows higher mortality rates after pericardiectomy in patients with radiation or after-cardiac surgery constrictive pericarditis, however also identifies significant heterogeneity in existing studies. A secondary analysis also points out significant differences after the year 2000.

Excluding studies reporting on tuberculosis, our analysis shows that idiopathic, after-cardiac surgery and radiation are the most common causes of constrictive pericarditis being treated with surgery, at a ratio of 10:5:1. An increase in the percentage of after-cardiac surgery constrictive pericarditis in the modern era has been reported in large, single center studies and is attributed to the increase in cardiac surgeries;[9,12] over 200,000 cardiac surgeries occur yearly in the United States and constrictive pericarditis appears to complicate between 0.2% to 2% of them.[17-19]

Based on pooled clinical characteristics, we show that the most common profile of the patient who underwent pericardiectomy is that of a middle-aged male with advanced symptoms and without significant co-morbidities.[9,12,20] The results of our analysis highlight several important points regarding the operative characteristics of pericardiectomy in the modern era. First, the vast majority of surgeries involve total pericardiectomy, i.e. from phrenic nerve to phrenic nerve laterally and from the diaphragm to the great vessels[10,21] via a median sternotomy. This finding is in accordance with results of studies suggesting higher mortality when partial pericardiectomy is performed and repeat pericardiectomy is required.[22,23] In addition, we found that cardiopulmonary bypass is used in less than half of pericardiectomies. Despite the fact that cardiopulmonary bypass may allow for more extensive stripping of the pericardium, particularly in cases with extensive calcification, it is not always necessary and could increase intra-operative bleeding and after-operative vasoplegia[24] (S3). On the other hand, our pooled results show that almost a quarter of pericardiectomies are performed with another concomitant

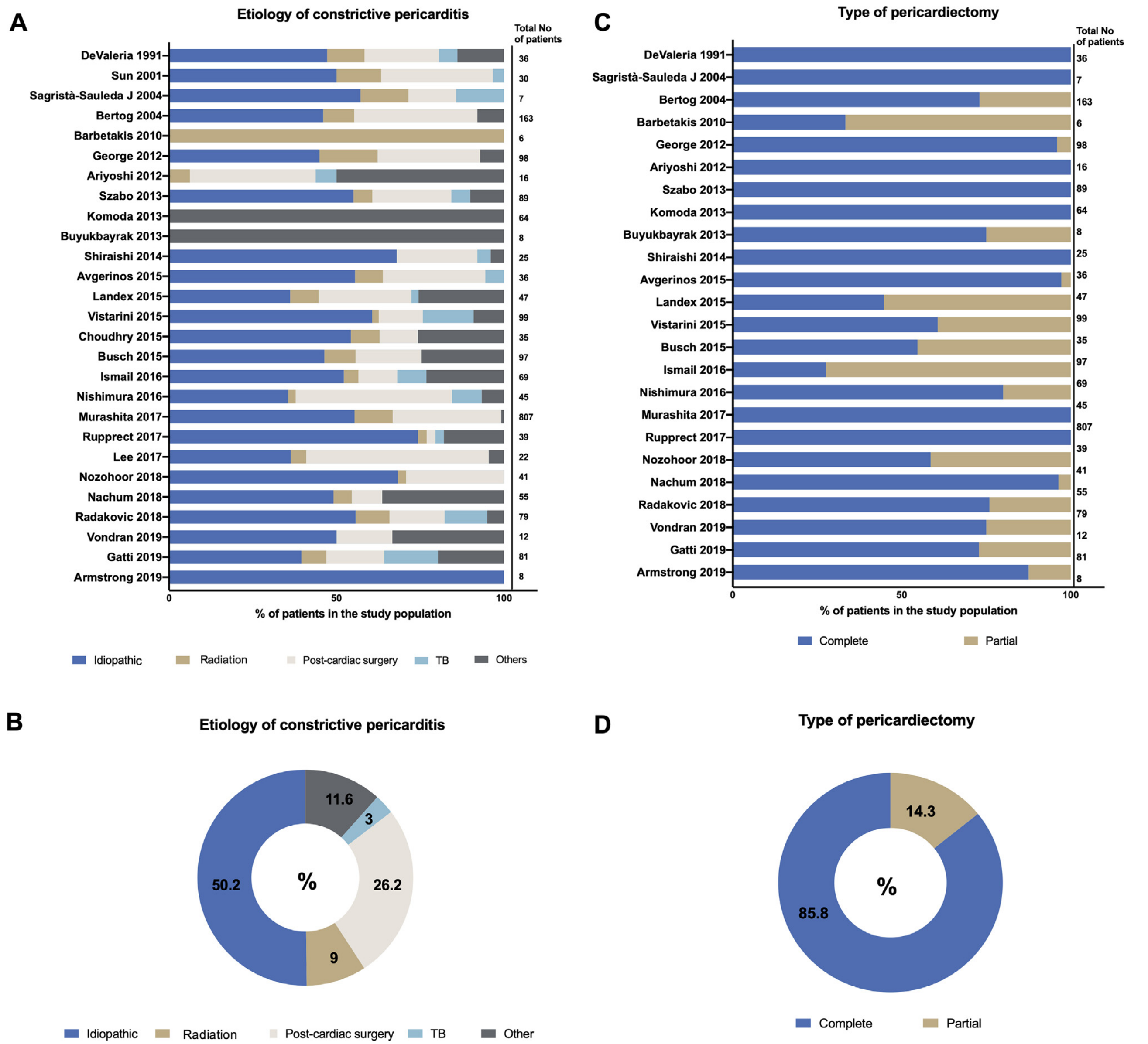

Figure 1. Etiology of constrictive pericarditis and type of pericardiectomy Stacked bars and donut charts summarizing the etiology of constrictive pericarditis and the type of pericardiectomy in each study (**A,C**) and in the overall population of the patients included in the systematic review (**B,D**).

Table 3
Outcomes

	All (n=2114)	Before 2000 (n=236)	After 2000 (n=176)	p-value[a]
Inpatient complications				
Acute kidney injury	795 (10%)	3 (1.5%)	4 (9.6%)	**0.005**
Sepsis	648 (4%)	3 (1.5%)	0 (0%)	0.299
Low cardiac output syndrome	423 (12.7%)	1 (2.7%)	4 (5.6%)	0.492
Inpatient/ 30-day mortality	146 (6.9%)	14 (5.9%)	5 (2.8%)	0.139
Long term complications				
Re-operation	44 (8%)	0 (0%)	6 (9%)	0.064
Heart failure	64 (11%)	8 (2%)	0 (0%)	**0.015**
All cause mortality				
1-year mortality	340 (17.4%)	23 (10%)	24 (19.8%)	**0.010**
5-year mortality	646 (32.7%)	40 (20%)	87 (49.4%)	**<0.001**
10-year mortality	696 (45%)	7 (19.4%)	17 (40.4%)	**0.045**
Cardiac-specific mortality	66 (9.6%)[b]	2 (3%)	4 (4.4%)	0.647
Follow-up				
Mean, years	4.02	6	4.1	-
Patients at last follow-up	1031 (98%)	228 (100%)	176 (100%)	-

[a] Calculated for studies before 2000 vs After 2000.
[b] Only 16 studies reported on cardiac-specific mortality with an average follow-up 3.6 years.

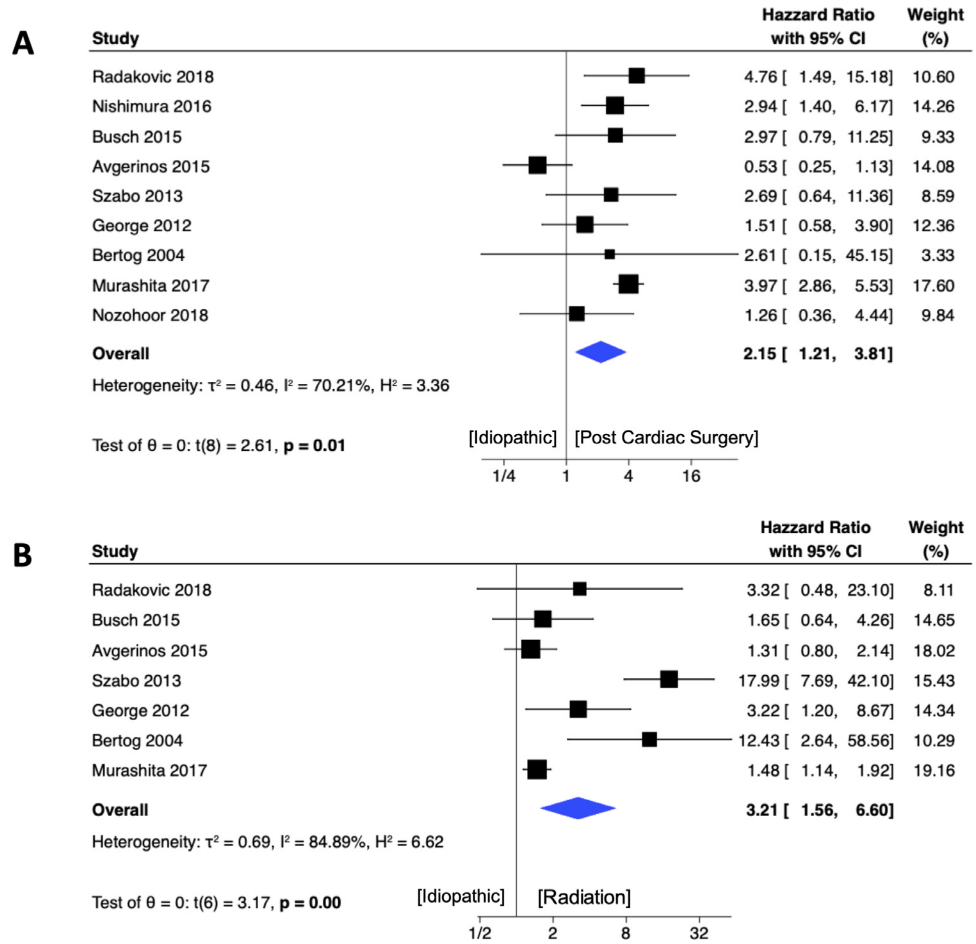

Figure 2. Mortality following pericardiectomy according to etiology of constrictive pericarditis. Forest plots comparing after-operative mortality following pericardiectomy for constrictive pericarditis due to previous cardiac surgery (**A**) or previous radiation (**B**) compared with idiopathic causes. The mean follow-up period was 9.5 and 8.5 years respectively. Individual study adjusted (when applicable) hazard ratios (HRs) and pooled HRs are also presented separately. The pooled HRs with 95% Confidence Intervals (Cis) were calculated using random-effects model.

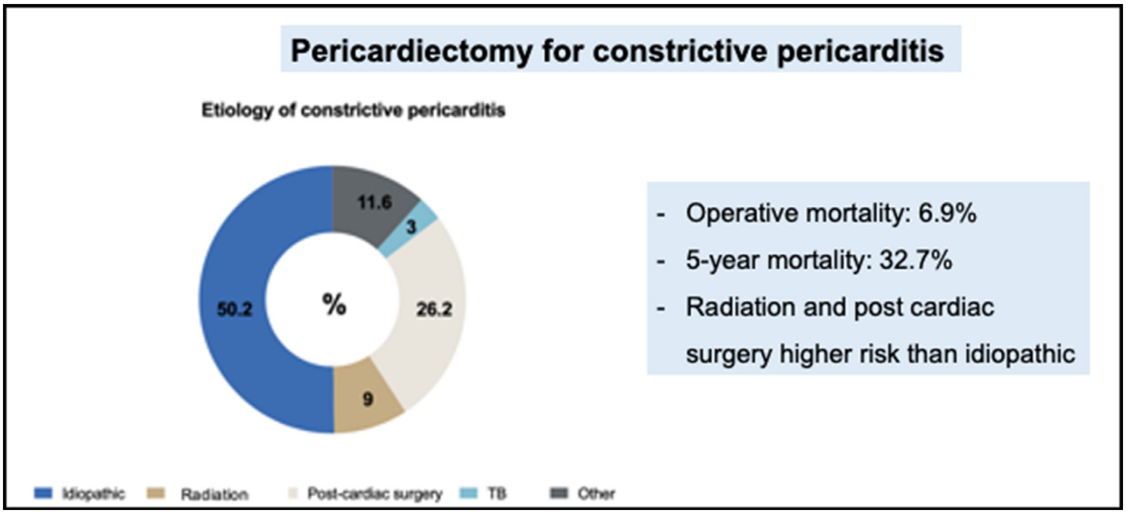

Figure 3. Overview of pericardiectomy for constrictive pericarditis.

cardiac surgery. In fact, after 2000, forty percent of pericardiectomies occurred with concurrent cardiac surgery. Significant tricuspid regurgitation complicates 20% of cases[25] and although repair of the tricuspid valve may be required, concomitant coronary artery bypass has been reported to be as common.

The pooled after-operative / 30-day mortality of 6.9% among over 2100 patients confirms that pericardiectomy still constitutes a surgery with significant risk.[26] We found significant variation in operative mortality among included studies, which could be potentially explained by statistical error in small cohorts. However, in large series and expert centers, operative mortality is close to our weighted average.[9,27] On the other hand, significant operative risk may explain why the typical clinical profile of these patients is one with advanced symptoms but a relatively low burden of co-morbidities. Chronic constriction has been associated with myocardial atrophy and subsequent myocardial dysfunction after pericardiectomy[28] with prior studies advocating for earlier surgery in the course of the disease (S4). Despite the fact that only a small percentage of patients require re-operation or have no improvement in heart failure after pericardiectomy, survival is not similar to the general population with 33% of patients not alive at 5-years. There appears to be no improvement in outcomes after 2000, and in fact we found worse survival. These results are unadjusted, and the increased frequency of concomitant cardiac surgery after 2000 could be a potential confounder.

Regarding the impact of etiology on outcomes, we found that radiation constrictive pericarditis carries three times this risk compared with the idiopathic type. The increased risk of radiation constrictive pericarditis is well known[6,27] and in fact, the futility of pericardiectomy in these patients has been proposed[7]. When meta-analyzed, after-cardiac surgery patients also have twice the mortality risk of those with idiopathic. It is worth noting however, that we found significant heterogeneity among studies reporting outcomes based on etiology of constrictive pericarditis.

Finally, we found that almost a third of included studies have significant bias, with major issues being follow up and selection bias. A moderate or higher degree of heterogeneity was also found in the studies reporting outcomes based on constrictive pericarditis etiology. Meta-regression pointed out to male gender and pulmonary artery systolic pressure as sources of heterogeneity. These findings advocate for caution when interpreting and generalizing the results of existing, observational studies on outcomes of pericardiectomy.

Pericardiectomy for constrictive pericarditis has been performed prior to the establishment of coronary artery bypass and modern cardiothoracic surgery care. We performed a systematic review to better define the characteristics of this patient population and its surgical outcomes in the contemporary era. The typical patient is a middle-aged male with advanced symptoms and relatively low burden of co-morbidities. Half of the cases are still of idiopathic etiology despite an increase in after-cardiac surgery patients. Despite the advances in surgical techniques and critical case, pericardiectomy still carries an operative mortality of almost 7% in expert centers. Radiation or after-cardiac surgery patients have 3 or 2 times higher long-term risk compared with idiopathic pericarditis. Finally, available evidence originates from a significant number of studies that suffer from significant heterogeneity and bias.

Credit Author Statement

Aspasia Tzani: Study Design, Protocol Writing, Literature Search, Data Extraction and Analysis, Manuscript Writing; Ilias P. Doulamis: Study Design, Protocol Writing, Literature Search, Data Extraction and Analysis, Manuscript Writing; Andreas Tzoumas: Literature Search, Data Extraction; Dimitrios V. Avgerinos: Supervision, Writing - Review & Editing; Dimitrios Koudoumas: Writing-Review & Editing; Gerasimos Siasos: Writing - Review & Editing; Manolis Vavuranakis: Writing - Review & Editing; Allan Klein: Supervision,Writing - Review & Editing; Polydoros N. Kampaktsis: Writing - Original Draft, Project administration, Writing - Review & Editing, Conceptualization.

Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2021.01.033.

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