Pericardiectomy vs Medical Management in Patients With Relapsing Pericarditis

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Abstract

Objective: To determine whether surgical pericardiectomy is a safe and effective alternative to medical management for chronic relapsing pericarditis.

Patients and Methods: Retrospective review of 184 patients presenting to the Mayo Clinic in Rochester, Minnesota, from January 1, 1994, through December 31, 2005, with persistent relapsing pericarditis identified 58 patients who had a pericardiectomy after failed medical management and 126 patients who continued with medical treatment only. The primary outcome variables were in-hospital postoperative mortality or major morbidity, all-cause death, time to relapse, and medication use.

Results: Mean $\pm$ SD follow-up was 5.5 ± 3.5 years in the surgical group and 5.4 ± 4.4 years in the medical treatment group. At baseline, patients in the surgical group had higher mean relapses (6.9 vs 5.5 ; $P = .01$), were more likely to be taking colchicine (43.1% [$n = 25$] vs 18.3% [$n = 23$]; $P = .002$) and corticosteroids (70.7% [$n = 41$] vs 42.1% [$n = 53$]; $P < .001$), and were more likely to have undergone a prior pericardiotomy (27.6% [$n = 16$] vs 11.1% [$n = 14$]; $P = .003$) than the medical treatment group. Perioperative mortality (0%) and major morbidity (3% ; $n = 2$) were minimal. Kaplan-Meier analysis revealed no differences in all-cause death at follow-up ($P = .26$); however, the surgical group had a markedly decreased relapse rate compared with the medical treatment group ($P = .009$). Medication use was notably reduced after pericardiectomy.

Conclusion: In patients with chronic relapsing pericarditis in whom medical management has failed, surgical pericardiectomy is a safe and effective method of relieving symptoms.

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Management of relapsing pericarditis remains challenging because of the paucity of clinical data and the perceived benign nature of the disease. Approximately 1 of every 4 patients with acute pericarditis has at least 1 episode of relapse.¹⁻⁴ Many of these patients are adequately treated medically for their initial relapse and often are never symptomatic again. However, a subset of patients experience chronic relapsing pericarditis, and although the disease is not life-threatening, it can have a substantial effect on quality of life. Current recommendations on the management of relapsing pericarditis include treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine for the initial relapse,⁵ corticosteroids for patients in whom initial medical therapy has failed, and possibly immunosuppressive agents for patients in whom an autoimmune or inflammatory disease is the underlying cause.^{3,6} Although the use of corticosteroids for relapsing pericarditis can provide relatively rapid relief of symptoms, multiple studies have suggested that corticosteroid administration may favor relapses⁴⁻¹¹ and also predisposes the patient to multiple adverse events.

Surgical pericardiectomy has been proposed for the relief of symptoms due to persistent relapsing pericarditis. However, pericardiectomy remains controversial because of the paucity of data not only on perioperative morbidity and mortality in this group of patients but also on whether this procedure would improve the relapse rate vs medical treatment only. Our preliminary unpublished retrospective review of 41 patients who underwent pericardiectomy at Mayo Clinic in Rochester, Minnesota, from 1975 to 2000 for chronic relapsing pericarditis indicated that pericardiectomy in this setting may be beneficial. Twenty-five patients (61.0%) had follow-up at 1 year, with all patients reporting symptomatic improvement, and 23 of these patients (92.0%) were free of corticosteroids at follow-up.¹² However, the study had limitations in follow-up and no comparison to a medically treated group.

Thus, the aim of our present study was 2-fold. The first aim was to retrospectively examine perioperative mortality and morbidity in a nonrandomized group of patients undergoing pericardiectomy for chronic relapsing pericarditis at Mayo Clinic from January 1, 1994, through December 31, 2005, in

whom medical management had failed. The second aim was to compare relapse rate, all-cause death, and medication use in the follow-up period in patients undergoing pericardiectomy vs patients who received medical treatment only.

PATIENTS AND METHODS

Study Group

After approval by the Mayo Clinic Institutional Review Board, we retrospectively reviewed the medical records of 252 patients who presented to Mayo Clinic in Rochester, Minnesota, from January 1, 1994, through December 31, 2005, with a diagnosis of relapsing or recurrent pericarditis. The primary inclusion criterion was definite diagnosis of relapsing pericarditis. The clinical diagnosis of relapse was based on a prior diagnosis of acute pericarditis, subsequent recurrent chest pain, and one or more of the following signs: fever, pericardial friction rub, electrocardiographic changes, pericardial effusion on echocardiography, or pericardial inflammation on cardiac magnetic resonance imaging. Sixty-eight patients were excluded from study. Nine patients did not meet the inclusion criteria and were excluded. Additional exclusion criteria included age younger than 18 years ($n=13$), poor short-term prognosis (expected survival <6 months) ($n=2$), pericardiectomy performed elsewhere ($n=25$), or incomplete or missing baseline data ($n=19$). Of the remaining 184 patients, 57 had undergone a complete pericardiectomy, 1 patient had undergone a partial pericardiectomy (anterior phrenic to phrenic nerve and partial inferior pericardiectomy) at Mayo Clinic after failed medical management, and 126 patients continued with medical treatment only.

Pericardiectomy Procedure

Pericardiectomy performed for relapsing pericarditis was as complete as possible. Pericardectomy entailed removal of the whole pericardium overlying the heart and great vessels except for the pericardium posterior to the left atrium in the oblique sinus. In standard practice, a small strip of pericardium remains beneath the phrenic nerves. Complete pericardiectomy can be difficult through a left anterolateral thoracotomy, and if other, less invasive approaches are attempted, bilateral incisions may be necessary. We preferred a median sternotomy for most patients and began the operation with excision of the anterior portion of the pericardium from a point just anterior to the right phrenic nerve over the right ventricle and great vessels to a point just anterior to the left phrenic nerve. This portion of the procedure is facilitated by entering the pleural spaces early so that the phrenic nerve can be identified clearly and preserved. The heart is gently re-

tracted upward, and the diaphragmatic surface of the pericardium is removed. Finally, a portion of the pericardium is excised posterior to the left phrenic nerve and anterior to the left pulmonary veins. In contrast to pericardiectomy for chronic constrictive pericarditis, operation for relapsing pericarditis is usually simpler because of the absence of dense adhesions to the epicardium and because cardiac function is usually normal.

Outcome Variables

The primary follow-up outcome variables for both the surgically and medically treated groups were all-cause death, time to relapse, and medication use for relapsing pericarditis. Follow-up data were collected in accordance with Health Insurance Portability and Accountability Act regulations by mailed questionnaires sent to all patients, telephone surveys for patients who did not respond to mailed questionnaires, and review of clinical visits. Mortality status was obtained by first reviewing Mayo Clinic registration records to identify patients known to be deceased. Because many but not all deaths are recorded in these records, the Social Security Death Index was used in the remaining patients.

In addition, for the surgical group only, in-hospital postoperative mortality or major morbidity, defined by the Society of Thoracic Surgeons as a composite of all-cause death and 5 major complications, was analyzed. These 5 major complications are stroke (central neurologic deficit persisting >72 hours), renal failure (new requirement for dialysis or increase in serum creatinine level >2.0 mg/dL [to convert to $\mu\text{mol/L}$, multiply by 88.4] and >2 -fold the preoperative level), prolonged ventilation (>24 hours), deep sternal wound infection (requirement for operative intervention and antibiotic therapy, with positive culture), and need for a subsequent operation (for any reason). Patients were classified in a dichotomous fashion as having the outcome if they had one or more of these complications and/or death. These specific complications were chosen by the Society of Thoracic Surgeons to represent major morbidity for 2 reasons: first, they are either life-threatening or have the potential to cause permanent functional disability, and second, they tend to be uniformly reported and reliably extracted from medical records.¹³

To reduce observer bias, all data extraction was performed independently by 2 physicians (M.H.K. and N.S.A.) and then compared for accuracy. Unresolved discrepancies were adjudicated by a third physician (J.K.O.).

TABLE 1. Baseline Characteristics of the Study Population^{a,b,c}

Characteristic	Surgical (n=58)	Medical (n=126)	P value
Age (y), mean $\pm$ SD	46.0 $\pm$ 14.1	48.5 $\pm$ 16.1	.43
No. (%) female	31 (53.4)	69 (54.8)	.87
No. of relapses, mean $\pm$ SD	6.9 $\pm$ 4.2	5.5 $\pm$ 4.1	.01 ^d
No. (%) with chest pain	57 (98.3)	123 (97.6)	.78
No. (%) with dyspnea	19 (32.8)	25 (19.8)	.05 ^d
No. (%) with friction rub	3 (5.2)	14 (11.1)	.21
ESR (mm/h), mean $\pm$ SD	13.8 $\pm$ 15.2	25.2 $\pm$ 30.4	.09
CRP (mg/dL), mean $\pm$ SD	3.7 $\pm$ 6.6	3.9 $\pm$ 18.4	.53
WBC ($\times 10^9$ /L), mean $\pm$ SD	10.4 $\pm$ 3.9	8.5 $\pm$ 3.3	.007 ^d
No. (%) by cause			
Idiopathic	34 (58.6)	67 (53.2)	.59
Viral	8 (13.8)	14 (11.1)	.60
No. (%) undergoing cardiac surgery or intervention	13 (22.4)	20 (15.9)	.28
No. (%) with autoimmune disease	3 (5.2)	10 (7.9)	.15
No. of medications, ^e mean $\pm$ SD	1.9 $\pm$ 0.9	1.5 $\pm$ 0.7	.05 ^d
No. (%) taking medications			
NSAIDs	32 (55.2)	95 (75.4)	.01 ^d
Colchicine	25 (43.1)	23 (18.3)	.002 ^d
Corticosteroids	41 (70.7)	53 (42.1)	<.001 ^d
Immunosuppressive agents	10 (17.2)	15 (11.9)	.28

^aCRP = C-reactive protein; ESR = erythrocyte sedimentation rate; NSAIDs = nonsteroidal anti-inflammatory drugs; WBC = white blood cell.

^bSI conversion factor: To convert CRP to nmol/L, multiply by 9.524.

^cPatients were divided into 2 groups: surgical (patients who underwent a pericardiectomy at Mayo Clinic after their index visit) and medical (patients who received medical therapy only after their index visit).

^dSignificant P value ($P < .05$).

^eNumber of medications refers to use of NSAIDs, colchicine, corticosteroids, and immunosuppressive agents at baseline.

Statistical Analysis

Continuous variables were summarized as mean $\pm$ SD. Discrete variables were presented as frequencies and within-group percentages. Kaplan-Meier methods were used to estimate survival rates over time, and the log-rank test was used to assess differences between groups. Univariate comparisons were performed with the *t* test for continuous variables, χ^2 test for categorical variables, and Fisher exact test for categorical variables with fewer than 5 expected observations per cell. $P < .05$ was considered statistically significant.

RESULTS

A total of 184 patients were included in the study and were divided into a surgical group (pericardiectomy; n=58) and a medical group (isolated medical therapy; n=126). Mean follow-up was

5.5 $\pm$ 3.5 years in the surgical group and 5.4 $\pm$ 4.4 years in the medical treatment group. Follow-up at 30 days, 90 days, and 1 year was 95%, 93%, and 88%, respectively, for the surgical group and 97%, 95%, and 93%, respectively, for the medical treatment group.

Baseline characteristics are listed in Tables 1-3 and reveal no significant differences with regard to age, sex, symptoms at presentation, cause of relapsing pericarditis, and comorbid conditions, including coronary artery disease, diabetes mellitus, hypertension, hyperlipidemia, prior stroke, renal failure, neoplasm, or autoimmune disease. However, the surgical group had more mean relapses at the time of the initial index visit (6.9 $\pm$ 4.2 vs 5.5 $\pm$ 4.1; $P = .01$), was more likely to be taking colchicine (43.1% [n=25] vs 18.3% [n=23]; $P = .002$) and corticosteroids (70.7% [n=41] vs 42.1% [n=53]; $P < .001$), less likely to take NSAIDs (55.2% [n=32] vs 75.4% [n=95]; $P = .01$), and more likely to have undergone a prior pericardiectomy (27.6% [n=16] vs 11.1% [n=14]; $P = .003$) than the medical treatment group. Baseline echocardiographic data, including ejection fraction and the presence and size of pericardial effusions, were similar between the 2 groups; however, constrictive physiology was a more prominent feature in the surgical group (13.7% [n=7] vs 4.3% [n=5]; $P = .03$).

TABLE 2. Comorbid Conditions at Baseline for the Study Population^a

Characteristic	No. (%) of patients		P value
	Surgical (n=58)	Medical (n=126)	
Pericardiectomy	16 (27.6)	14 (11.1)	.003 ^b
Cardiac surgery	20 (34.5)	26 (20.6)	.04 ^b
CABG	2 (3.4)	5 (4.0)	.88
PCI	4 (6.9)	9 (7.1)	.97
CAD	11 (19.0)	14 (11.1)	.14
Diabetes mellitus	4 (6.9)	7 (5.6)	.71
Hypertension	18 (31.0)	30 (23.8)	.28
Hyperlipidemia	13 (22.4)	27 (21.4)	.87
History of smoking	8 (13.8)	24 (19.0)	.37
Stroke or TIA	2 (3.4)	1 (0.8)	.18
Renal failure	2 (3.4)	2 (1.6)	.56
Neoplasm	6 (10.3)	15 (11.9)	.78
Autoimmune disease	4 (6.9)	16 (12.7)	.26

^aCABG = coronary artery bypass graft; CAD = coronary artery disease; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

^bSignificant P value ($P < .05$).

TABLE 3. Echocardiographic Characteristics at Baseline for the Study Population^{a,b}

Characteristic	Surgical (n=51)	Medical (n=117)	P value
LVEF (%), mean $\pm$ SD	63 $\pm$ 6.0	63 $\pm$ 7.2	.96
No. (%) with LVEF <40%	0	2 (2)	.34
No. (%) with pericardial effusion	20 (39.2)	38 (32.5)	.40
None	31 (60.8)	80 (68.4)	
Mild	11 (21.6)	29 (24.8)	
Moderate	6 (11.8)	5 (4.3)	
Severe	4 (7.8)	4 (3.4)	
Constrictive physiology, No. (%)	7 (13.7)	5 (4.3)	.03 ^c

^aLVEF = left ventricular ejection fraction.^bEchocardiographic data were not available for 7 patients in the surgical group and 9 patients in the medical treatment only group.^cSignificant P value (P<.05).

In the perioperative period, the primary outcome variable for the surgical patients was in-hospital postoperative mortality or major morbidity. Of the 58 patients in the surgical group, 57 had a complete pericardiectomy and 1 patient had a partial pericardiectomy (anterior phrenic to phrenic nerve and partial inferior pericardiectomy). The mean hospital stay was 6.9 $\pm$ 2.8 days, with only one hospitalization longer than 14 days. There were no cases of in-hospital perioperative mortality (Table 4). Two patients (3.4%) had major complications postoperatively (Table 4). One patient had a stroke with residual long-term, left-sided weakness. The other patient had emergent surgery within 10 hours of his pericardiectomy for postoperative bleeding from an arterial vessel posterior to the heart and on the surface of the esophagus.

Pathologic examination of the excised pericardium in the 58 patients who underwent pericardiectomy revealed a total of 5 patients (8.6%) with features consistent with constrictive pericarditis and 53 patients (91.4%) with features consistent with chronic pericarditis. Of the 5 patients with constrictive pericarditis, 2 patients had definite constrictive physiologic features on preoperative echocardiographic examination, 2 other patients had some constrictive physiologic features, and 1 patient had no echocardiographic features of constriction.

In the follow-up period, the primary outcome variables were all-cause death, time to relapse, and medication use for both the surgical and medical groups. In the surgical group, 5 deaths (8.6%) occurred during the follow-up period, with 1 treat-

ment-related death (1.7%) occurring on day 68 after pericardiectomy due to methicillin-resistant *Staphylococcus aureus* sepsis and multiorgan failure. This patient was discharged from the hospital on day 11 in good condition, with no major morbidity postoperatively. Two patients (3.4%) died approximately 2 years after pericardiectomy: one patient of a newly diagnosed malignant mesothelioma and another patient of an acute myocardial infarction. Two other patients (3.4%) died of unknown causes at 5 and 8 years after pericardiectomy. Nine deaths (7.1%) occurred in the medical treatment group, with 7 patients (5.6%) dying of unknown causes, 1 patient (0.8%) dying of metastatic thyroid cancer 13 years after the index visit, and 1 patient (0.8%) dying of glioblastoma multiforme more than 4 years after the index visit. Overall, no significant difference was found in survival between the 2 groups (Figure 1).

However, a marked difference was found in the rate of relapse (Figure 2) between the 2 groups. The Kaplan-Meier curves for relapse separate early in the follow-up period, with the surgical group experiencing far fewer relapses than the medical treatment group (log rank P=.009). Five patients (8.6%) experienced relapse in the pericardiectomy group, and their characteristics are summarized in Table 5. Four patients had a history of prior pericardiotomy, and 1 patient had a perforated atrium after atrial fibrillation ablation. These 5 patients were all treated with multidrug therapy for relapsing pericarditis and had at least 9 relapses before proceeding with pericardiectomy. The mean time to relapse after pericardiectomy was 2.1 years,

TABLE 4. Perioperative Mortality and Morbidity of Patients Undergoing Pericardiectomy for Relapsing Pericarditis

Characteristic	No. (%) of patients (n=58)
Mortality	0
Morbidity	2 (3.4)
Permanent stroke	1 (1.7)
Renal failure	0
Prolonged ventilation	0
Deep sternal wound infection	0
Subsequent operation	1 (1.7)
Postoperative length of stay (d), mean $\pm$ SD	6.9 $\pm$ 2.8
Prolonged postoperative length of stay (>14 d)	1 (1.7)

Data are No. (percentage) of patients unless otherwise indicated.

FIGURE 1. Kaplan-Meier curves for death in patients who underwent pericardiectomy vs medical management for relapsing pericarditis ($P=.26$).

and 4 of 5 patients (80.0%) had notable improvement in symptoms after pericardiectomy.

When comparing medication use for relapsing pericarditis in follow-up (Table 6), although a trend was found toward less medication use in the surgical group compared with the medical group, this finding was not statistically significant (29.6% [$n=16$] vs 43.4% [$n=53$]; $P=.09$). Similarly, a statistically nonsignificant trend was found toward reduced corticosteroid use in the surgical group (7.4% [$n=4$] vs

18.0% [$n=22$]; $P=.07$). When comparing medication use before and after pericardiectomy for the surgical group, the use of NSAIDs, colchicine, and prednisone was notably reduced after pericardiectomy (Table 7).

In the medical treatment group, 36 patients (28.6%) had a relapse after their index visit. Interestingly, patients in the medical treatment group also used considerably fewer NSAIDs, colchicine, and prednisone in follow-up (Table 7). We had hypothesized that patients with a longer duration of corticosteroid taper would be less likely to experience a relapse; however, our data did not support this hypothesis (Figure 3). No significant differences were found in the time to relapse for patients who had a short duration of corticosteroid taper (≤ 3 months) vs patients with a longer duration of taper (> 3 months). Multiple other corticosteroid duration time points were analyzed, with no significant differences found (data not shown). Patients who were treated with any duration of corticosteroids were more likely to have a relapse compared with patients who were not treated with corticosteroids (Figure 3; $P=.007$). Treatments with NSAIDs, colchicine, and immunosuppressive agents were all analyzed independently for relapse rate, with no significant differences found (data not shown), suggesting that the main determinant for relapse in the medical treatment group was corticosteroid use.

DISCUSSION

To our knowledge, this is the first study to compare pericardiectomy and medical management in patients with refractory relapsing pericarditis. We studied 184 patients with refractory relapsing pericarditis treated at our institution between January 1, 1994, and December 31, 2005, 58 of whom underwent pericardiectomy and 126 who received only medical treatment after the index visit. Baseline data for the 2 groups were similar, with the exceptions that the surgical group had more relapses and were more likely to be treated with corticosteroids and colchicine, have constrictive physiologic features, and have undergone previous cardiac surgery when compared with the medical treatment group at the index visit.

Although most patients with relapsing pericarditis improve with medical therapy, a subset of patients continue to have persistent relapsing pericarditis that, although not life-threatening, is often intolerable and imposes a major barrier to their quality of life.⁴ First-line medical treatment for symptom relief has included NSAIDs⁴ and colchicine, which has also been effective in preventing recurrences.^{5,8,10} Corticosteroid use has been controversial and has been recommended only when first-line treatment has failed. However, 60% to

FIGURE 2. Kaplan-Meier curves for relapse in patients who underwent pericardiectomy vs medical management for relapsing pericarditis ($P=.009$).

TABLE 5. Characteristics of All Patients With Relapse After Pericardiectomy^a

Characteristic	Patient No.				
	1	2	3	4	5
History of prior cardiac surgery or intervention	Yes (pericardiectomy)	Yes (pericardiectomy)	Yes (pericardiectomy)	Yes (pericardiectomy)	Yes (atrial perforation during ablation)
History of autoimmune disease	No	Yes (SLE)	Yes (unknown CTD)	No	No
Medications before pericardiectomy	Colchicine, prednisone, and hydroxychloroquine	Prednisone, hydroxychloroquine, and methotrexate	Ibuprofen, prednisone, and hydroxychloroquine	Ibuprofen, colchicine, and prednisone	Celecoxib and prednisone
No. of relapses before pericardiectomy	>10	>10	>10	9	>10
Time to relapse after pericardiectomy (y) ^b	0.53	2.02	4.03	0.64	3.20
Medications to treat initial relapse after pericardiectomy	Prednisone	Prednisone and hydroxychloroquine	Ibuprofen, prednisone, hydroxychloroquine, and mycophenolate	Colchicine, prednisone, and hydroxychloroquine	Celecoxib, colchicine, and prednisone
No. of relapses after pericardiectomy	>10	1	1	1	3
Medications at last follow-up	Colchicine and prednisone	Hydroxychloroquine	Ibuprofen, prednisone, and hydroxychloroquine	None	Celecoxib
NYHA symptom class at last follow-up	IV	I	III	No symptoms	I
Symptom improvement after pericardiectomy	No	Yes	Yes	Yes	Yes

^aCTD = connective tissue disease; NYHA = New York Heart Association; SLE = systemic lupus erythematosus.

^bMean $\pm$ SD time to relapse for the 5 patients was 2.08 $\pm$ 1.54 years.

90% of patients with relapsing pericarditis have been treated with corticosteroids in most clinical series,¹⁴ and its use has been shown to be an independent risk factor for relapse.⁴⁻¹¹ Immunosuppressive therapy has generally been used when the underlying cause of pericarditis is autoimmune or rheumatologic in origin.⁶ The question that clinicians have in these cases of refractory relapsing pericarditis is what to do next when medical therapy has failed.

Although it has been suggested that pericardiectomy should be considered in patients with severe relapsing pericarditis in whom an adequate drug treatment has failed,⁶ the evidence-based data to support this are few. In 1990, Fowler¹⁵ described 9 patients who underwent pericardiectomy for recurrent pericarditis, only 2 of whom showed clear-cut early improvement in symptoms. However, the course of follow-up and extent of surgical resection were not described. Also in 1990, Tuna and Danielson¹⁶ reported that 95% of patients who underwent a complete pericardiectomy for recurrent pericarditis were symptom free after 1 year with no operative

or hospital deaths and argued that their favorable experience was attributable to the complete extent of the surgical resection of the pericardium. Both these studies are limited by small sample sizes, limited follow-up, and no comparisons with a medical treatment group. Since 1990, no other studies of adults undergoing pericardiectomy for relapsing pericarditis have been reported. Thus, many clinicians are hesitant to refer patients for pericardiectomy for relapsing pericarditis because of the lack of data and perceived risks of mortality and morbidity for this extensive surgery. In addition, it is unknown whether performing such a procedure will result in the end of the recurrences or a reduction in medical therapy, especially the use of corticosteroids.

Of the 58 patients who underwent pericardiectomy in our study, 53 (91.4%) were found to have pathologic features of chronic pericarditis and 5 (8.6%) were found to have pathologic features of constrictive pericarditis after examination of the excised pericardium. No perioperative deaths occurred, and only 2 patients (3%) had a major com-

TABLE 6. Comparison of Follow-up Medication Use in Patients Who Underwent Pericardiectomy vs Medical Management for Relapsing Pericarditis^{a,b}

Outcome	Surgical (n=54)	Medical (n=122)	P value
Follow-up (y), mean $\pm$ SD	5.5 $\pm$ 3.5	5.4 $\pm$ 4.4	.95
No. (%) using medications ^c	16 (29.6)	53 (43.4)	.09
No. of medications, mean $\pm$ SD	0.4 $\pm$ 0.7	0.6 $\pm$ 0.9	
No. (%) of medications			.58
0	37 (68.5)	70 (57.4)	
1	12 (22.2)	35 (28.7)	
2	3 (5.6)	12 (9.8)	
3	1 (1.9)	4 (3.3)	
No. (%) using NSAIDs	10 (18.5)	29 (23.8)	.45
No. (%) using colchicine	2 (3.7)	13 (10.7)	.13
No. (%) using corticosteroids	4 (7.4)	22 (18.0)	.07
No. (%) using immunosuppressive agents	5 (9.3)	14 (11.5)	.71

^aNSAIDs = nonsteroidal anti-inflammatory drugs.^bFollow-up medication refers to medication on last follow-up visit. Data were missing for 4 patients in the surgical group and 4 patients in the medical treatment group.^cRefers to use of at least 1 medication for treatment of relapsing pericarditis: NSAIDs, colchicine, prednisone, or immunosuppressive agents.

plication perioperatively. There was one treatment-related death (1.72%), which occurred on day 68 after pericardiectomy due to methicillin-resistant *S aureus* sepsis and multiorgan failure. The mean follow-up for both groups was approximately 5.5 years, and all-cause death was similar between the 2

groups. Interestingly, at the baseline index visit, the surgical group had more relapses and was treated with more medications than the medical group, suggesting that these patients were sicker. Despite this, during the follow-up period, the relapse rate was markedly lower after pericardiectomy compared with the medical treatment group. In addition, medication use for relapsing pericarditis was significantly decreased in both groups in the follow-up period. Although not significant, there was a trend toward decreased follow-up medication use and, in particular, decreased corticosteroid use in the surgical group compared with the medical treatment group. These data are especially important given our findings that in the medical group the most important variable that affected relapse was corticosteroid use, regardless of duration of therapy (Figure 3). Therefore, our data shed light on a possible alternative but safe and effective avenue for the treatment of refractory relapsing pericarditis.

It is important to speculate on the pathophysiologic mechanism of relapse after pericardiectomy as was found in 5 patients (8.6%) in our study. There are 2 potential explanations. The first is that these patients may have experienced pleuropericarditis because in the absence of pericardium the parietal pleura will lie adjacent to heart muscle. Cardiac magnetic resonance imaging could have potentially helped in differentiating pleural from pericardial inflammation but was not performed in these patients. Second, although a complete pericardiectomy was performed in all but one patient in

TABLE 7. Medical Management in Patients With Relapsing Pericarditis^{a,b}

Characteristic	Surgical			Medical		
	Before (n=58)	After (n=54)	P value	Before (n=126)	After (n=122)	P value
No. (%) using medication	56 (96.6)	16 (29.6)	<.001 ^c	120 (95.2)	53 (43.4)	<.001 ^c
No. of medications, mean $\pm$ SD	1.9 $\pm$ 0.9	0.4 $\pm$ 0.7		1.5 $\pm$ 0.7	0.6 $\pm$ 0.9	
No. (%) of medications			<.001 ^c			<.001 ^c
0	2 (3.4)	37 (68.5)		6 (4.8)	70 (57.4)	
1	22 (37.9)	12 (22.2)		60 (47.6)	35 (28.7)	
2	15 (25.9)	3 (5.6)		38 (30.2)	12 (9.8)	
3	15 (25.9)	1 (1.9)		13 (10.3)	4 (3.3)	
4	2 (3.4)	0		0	1 (0.8)	
No. (%) using NSAIDs	32 (55.2)	10 (18.5)	<.001 ^c	95 (75.4)	29 (23.8)	<.001 ^c
No. (%) using colchicine	25 (43.1)	2 (3.7)	<.001 ^c	23 (18.3)	13 (10.7)	.03 ^c
No. (%) using corticosteroids	41 (70.7)	4 (7.4)	<.001 ^c	53 (42.1)	22 (18.0)	<.001 ^c
No. (%) using immunosuppressive agents	10 (17.2)	5 (9.3)	.10	15 (11.9)	14 (11.5)	.80

^aNSAIDs = nonsteroidal anti-inflammatory drugs.^bFor the surgical patients, "before" refers to medications before pericardiectomy and "after" refers to medications on last follow-up. For the medical patients, "before" refers to medications at the index visit and "after" refers to medications on last follow-up.^cSignificant P value (P<.05).

our study, in standard practice, a small strip of pericardium remains beneath the phrenic nerves and posterior to the left atrium in the oblique sinus. This remnant of pericardium may have been a potential source for pericardial inflammation. However, it is encouraging that 4 of the 5 patients (80.0%) who experienced a relapse after pericardiectomy noted an improvement in symptoms and had far fewer relapses in the follow-up period compared with before pericardiectomy (Table 5).

Study Limitations

Several study limitations need to be discussed. Our study is retrospective, and all the limitations of a retrospective analysis apply. The selection of treatment modality was mainly based on clinician assessment of the severity of disease and patient preference. During the time of patient recruitment from 1994 to 2005, several important articles were published that changed the clinical management of relapsing pericarditis. The CORE (Colchicine for REcurrent pericarditis) study⁵ published in 2005 demonstrated that colchicine given during the first recurrence of pericarditis was effective in preventing future recurrences. In our study, only 25 surgical patients (43.1%) and 23 medical patients (18.2%) were treated with colchicine at the time of the index visit. In addition, numerous studies have linked corticosteroid treatment with a higher rate of relapse,⁴⁻¹¹ and the current literature recommends limited use of corticosteroids in relapsing pericarditis. Yet, 41 patients (70.7%) in the surgical group and 53 (42.1%) in the medical group were treated with corticosteroids at the index visit. It is evident from the follow-up data in our study that the most influential variable for relapse in the medical treatment group was the use of corticosteroids, regardless of the duration of use. Thus, it is certainly plausible that had all of the patients in our study been medically optimized during their initial relapse with NSAIDs and colchicine, with only limited use of corticosteroids, many may not have presented with subsequent relapses and thus may not have presented to a tertiary center for further management.

Recommendations

Despite the lower relapse rate in the surgical group, we must consider the fact that most patients in the medical treatment group did not have a relapse and were taking substantially fewer medications at follow-up. Although our data suggest that pericardiectomy is safe, the patients in the surgical group were relatively young and had few comorbid conditions. In addition, our surgeons were experienced at performing this procedure, and thus morbidity and mortality rates for pericardiectomy may differ at less expe-

FIGURE 3. Kaplan-Meier curves for relapse in the medical treatment group on the basis of duration of corticosteroid treatment ($P=.007$). The P value represents the statistical difference in relapse rate of the patients who did not receive corticosteroid ($n=79$; solid line) vs the patients who received corticosteroid ($n=47$; combination of short corticosteroid duration [$n=23$] and long corticosteroid duration [$n=24$] groups).

rienced centers. Hence, our recommendation remains that optimal medical management is the first-line treatment of relapsing pericarditis. However, if patients continue to have refractory recurrent symptoms and medical treatment has failed, especially when corticosteroids have been used for at least 6 months, we recommend that patients be considered for a pericardiectomy at an experienced surgical center.

CONCLUSION

With our current medical armamentarium for relapsing pericarditis, which includes NSAIDs, colchicine, corticosteroids, and immunosuppressive agents, most patients will be cured with appropriate medical therapy. However, there is still a group of patients who have refractory relapsing pericarditis, which notably compromises their quality of life. In this subset of patients, our study would suggest that pericardiectomy is safe and effective at reducing subsequent relapses when compared with continued medical treatment only.

ACKNOWLEDGMENTS

We gratefully acknowledge Dr Sharmi Shafi for her help with the preparation of the submitted manuscript.

Abbreviations and Acronyms: NSAIDs = nonsteroidal anti-inflammatory drugs

Grant Support: This study was supported by grant 1 ULI RR024150 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and the NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCRR or NIH. Information on NCRR is available at <http://www.ncrr.nih.gov/>. Information on Reengineering the Clinical Research Enterprise can be obtained from <http://nihroadmap.nih.gov>.

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