



Evaluation of etiology of pericardial effusion in 81 patients who underwent pericardiostomy or pericardial window

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ABSTRACT

Introduction: A wide variety of diseases lead to pericardial effusion including systemic inflammatory diseases, pericarditis, reduced pericardial fluid reabsorption due to increased systemic venous pressure, pneumonia, pulmonary embolism, endocrine diseases, post-cardiotomy syndrome, trauma, hypothyroidism, renal-hepatic failure, collagen-vascular diseases, infectious, and malignancy. In this study, we aimed to evaluate the underlying etiology of pericardial effusions in patients underwent surgical pericardial drainage or pericardial window and contemporary management.

Materials and methods: Between January 2006 and January 2018, a total of 81 patients (49 males, 32 females; mean 52.9±10.6 years; range 5 to 84 years) who underwent subxiphoid pericardiostomy, pericardial window procedure with left anterior thoracotomy or subxiphoid approach, due to moderate or severe pericardial effusion and cardiac tamponade, were retrospectively analyzed.

Results: Malignancy was diagnosed either with histopathological examination of the pericardial biopsy and/or fluid in 17 (80.9%) of 21 patients had a previous history of malignancy. Of the 21 patients diagnosed with malignancy, six patients (7.5%) had leukemia/lymphoma, and six patients (7.5%) had thyroid papillary cancer. Mycobacterium tuberculosis was identified in only one (1.2%) patient's culture of the pericardial fluid. No etiology was found in the remaining 38 patients (46.9%); thus, they were considered as idiopathic pericarditis.

Conclusion: Tuberculosis is no longer the leading cause of pericarditis. Idiopathic pericarditis is the leading cause of pericardial effusion and malignancy is the next most common cause of pericardial effusion in our region.

Keywords: etiology, pericardial effusion, sub-xiphoidal pericardiostomy, pericardial tamponade

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INTRODUCTION

Pericardial effusion is a common disease which can be asymptomatic or presented with dyspnea, orthopnea, chest pain, hypotension, arrhythmias, and fever which depends on the underlying disease, accumulation rate and size of the fluid [1-3]. The prevalence rate of pericardial effusion with a known etiology is about 50-60% which depends on the geographic area [4]. The incidence of excessive pericardial effusion among the patients who underwent echocardiography examination ranges from 3% to 9% [5]. A wide variety of diseases lead to pericardial effusion including systemic inflammatory diseases, pericarditis, reduced

pericardial fluid reabsorption due to increased systemic venous pressure, pneumonia, pulmonary embolism, endocrine diseases, post-cardiotomy syndrome, trauma, hypothyroidism, renal-hepatic failure, collagen-vascular diseases, infectious and malignancy [1, 4, 5]. The incidence of idiopathic pericarditis ranges 40-86% [6]. In addition, viruses such as Coxiella burnetti, bacteria such as Mycoplasma pneumonia, and parasites such as Toxoplasma are thought to be responsible for most of the idiopathic pericarditis. Physiologically 10 to 50 mL fluid exists in the pericardial space [2, 4, 5]. Pericardial effusions can be classified as either

inflammatory/non-inflammatory or malignant/non-malignant. This retrospective study aimed to evaluate the outcomes of patients and pathological examination of the specimens in patients who underwent surgical pericardial drainage for pericardial effusion in order to determine the underlying etiology.

MATERIALS AND METHODS

Study Population

Between January 2006 and January 2018, out of 208 patients, we reviewed the medical records of 81 patients (49 males, 32 females; mean 52.9 ± 10.6 years; range, five to 84 years) in two tertiary clinic. Of 81 patients, 51 patients underwent pericardiostomy and 30 patients underwent pericardial window. Pericardial window was performed either via subxiphoid approach (13 patients) or left anterior thoracotomy approach (17 patients). 114 patients with post-cardiotomy effusion, nine patients who underwent pericardiectomy, and four patients with insufficient clinical information were excluded. All data including the demographic and clinical features of the patients were retrieved from two tertiary clinic. All patients were evaluated with a two-dimensional echocardiography and, pericardial effusion was classified into three groups as mild (diastolic echo-free space <10 mm), moderate (effusion between 10 and 20 mm), and severe (effusion >20 mm) [4]. All patients had a history of pre-cardiocentesis prior to the surgery. The surgery was performed under either general anesthesia or local anesthesia. The patient's data including physical and laboratory examination, symptoms on admission, clinical history, underlying conditions (such as immunosuppression, collagen-vascular diseases), medication use, length of intensive care unit and in-hospital stay, pericardial fluid drainage and survey were analyzed.

Operative Technique

Subxiphoid approach was performed via a four-eight cm vertical incision, then the anterior pericardium was excised approximately two-four cm in diameter and, pericardial/peritoneal window was established with an eight mm vascular graft if needed while, left anterior mini-thoracotomy was performed via approximately 10 cm horizontal incision at the level of the 5th intercostal space by transthoracic approach. Accompanying tumors or adhesions were examined during the surgery. Biochemical and cytological examination of the pericardial fluid and pericardial samples were routinely performed during the surgery in order to determine the etiology of pericardial effusion.

Postoperative transthoracic echocardiography and chest X-Ray evaluation was performed at 1st week, 1st month, and 6th month and then every six months or once a year after discharge. The Institutional Review Board was approved (OMU KAEK 2018/92), and informed consent was obtained from all patients at the time of admission. The study was

carried out in accordance with the Helsinki Declaration principles.

Statistical Analysis

Statistical package for the social sciences windows version 21 (SPSS Inc, Chicago, IL, USA) was used to compare the data. The Kolmogorov-Smirnov test was used to analyze normally distributed continuous variables. Categorical variables were presented in percentages and frequencies. Continuous variables were presented as the mean \pm standard deviation. Independent sample t-tests were used to compare the means of dependent groups. The continuous variables were compared using t-test and the Mann-Whitney U test. The categorical data were tested with chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant.

RESULTS

Sample Sizes, Demographics, & Baseline arterial Risk Factors

Pericardiostomy or pericardial window was successfully performed in 49 males, (54.97 ± 8.7 , range 13-84 years) and 32 females (48.3 ± 7.9 , range 5-75 years). Moderate pericardial effusion was diagnosed in 14 patients (17.3%) while severe pericardial effusion was diagnosed in 51 patients (62.9%) and pericardial tamponade was detected in 16 (19.7%) patients. The most frequent symptom on admission was dyspnea in 29 patients (35.8%). 21 patients (25.9%) were presented with pleuritic chest pain, 20 patients (24.6%) were presented with other clinical signs such as fever and severe fatigue while, 11 patients (13.5%) were asymptomatic. No significant differences were noted between patients with pericardial effusion and pericardial tamponade in terms of etiology, accompanying malignancy, gender distribution, fever, erythrocyte sedimentation rate, and the levels of hemoglobin in our study ($p>0.05$).

Inflammatory signs were more commonly seen in patients with acute idiopathic pericarditis (31/39, 79.4%) ($p>0.05$). Erythrocyte sedimentation rate was elevated (above 50 mm/h) in 41 patients (50.6%). C-reactive protein was elevated (above 10 mg/dL) in 38 patients (46.9%).

Surgery was performed under local anesthesia with sedation in 59 patients (72.9%) while, general anesthesia was performed in 22 patients (27.1%). No myocardial injury was seen in any patient during surgery. All symptomatic patients were relieved after the surgery. Idiopathic pericarditis, malignancy, uremic pericarditis, tuberculous pericarditis, and non-tuberculous bacterial pericarditis were the main etiological causes of pericardial effusion in our study. Malignancy was diagnosed either with histopathological examination of the pericardial biopsy and/or fluid in 17 (80.9%) of the 21 patients who had a previous history of malignancy. Of the 21 (25.9%) patients diagnosed with malignancy, six patients (7.5%) had leukemia/lymphoma, six

Table 1. Etiological causes of pericardial effusion

	Moderate effusion		Severe effusion		Pericardial tamponade		Total	
	n	%	n	%	n	%	n	%
Idiopathic	7	18.4	25	65.7	6	15.7	38	46.9
Malignancy	3	14.2	13	61.9	5	23.8	21	25.9
Hypothyroidism	1	16.6	4	66.6	1	16.6	6	7.4
Uremic pericarditis	1	16.6	2	33.3	3	50.0	6	7.4
Tuberculous	-	-	1	100.0	-	-	1	1.2
Collagen vascular diseases	1	50.0	1	50.0	-	-	2	2.4
Non-tuberculous bacterial pericarditis	-	-	1	100.0	-	-	1	1.2
Heart failure	-	-	2	100.0	-	-	2	2.4
Miscellaneous	1	25.0	2	50.0	1	25.0	4	4.9
Total	14		51		16		81	100.0

patients (7.5%) had thyroid papillary cancer, five patients (6.1%) had lung cancer and four patients (4.9%) had breast cancer. In other etiologies, six patients (7.4%) were diagnosed with uremia, six patients (7.4%) were diagnosed with hypothyroidism, two patients (2.5%) were diagnosed with collagen-vascular disease and mycobacterium tuberculosis was identified in one patient's (1.2%) pericardial fluid culture (Table 1). Thus, these patients were considered as idiopathic pericarditis, considering broad biochemical and cytological examination via fluid cultures or serology.

Of the 81 patients, three patients were diagnosed with exudative pericardial effusion. The mean drained fluid was 750.7±305 ml (ranges, 50-3,000 ml). The mean operation time was 45.16±17.8 minutes (ranges, 20-90 minutes). The mean length of postoperative intensive care unit and in-hospital ranges 0-5 days, ranges, 4-29 days, respectively. The mean follow-up period was 2.7±2.1 years (ranges, 1-5 years). Pericardial effusion has recurred in 14 patients (17%) within the first year after the surgery. Of the 14 patients, 10 patients were undergoing pericardiostomy while four patients were undergoing pericardial window. Of the four patients, only one patient who underwent mini-thoracotomy recurred (p=0.29).

10 patients (12.3%) were passed away within the first year after the surgery. Of those, nine had malignant effusion and one had uremia thus, a significant portion of deaths were associated with the underlying disease. Of the 81 patients, 59 patients (72.8%) recovered and were discharged within a week and 39 patients (48.1%) were treated with non-steroidal anti-inflammatory drugs (NSAID) or acetylsalicylic acid and 11 patients (13.5%) were treated with corticosteroids following NSAID.

DISCUSSION

In this study, we have found that idiopathic pericarditis is the leading cause of pericardial effusion and malignancy is second most common cause of pericardial effusion.

Mycobacterium tuberculosis is the most common infectious cause (6.8%) of pericardial effusion especially in developing or under-developed countries (>60% of patients) with a 17-40% mortality rate [7-11] while viral or non-infectious causes of pericardial effusion, such as idiopathic pericarditis (up to 85%), malignancy (lymphoma, leukemia, lung and breast cancer) (10-25%), iatrogenic (15-20%) and connective tissue disorders (5-15%), systemic diseases (8.6%), post-pericardiotomy syndromes and, post-myocardial infarction have more frequently seen in developed countries [9, 12-20].

It was reported that the most common clinical manifestation of patients were dyspnea (94.3%), palpitation (59.3%), fever (38.6%), edema (37.1%), chest pain (33.6%), abdominal distention (26.4%), and faintness (21.4%), respectively [12]. However, it was reported that chest pain and dyspnea were the most common presentation [10, 17]. Our findings were consistent with [10, 17]. However, in our study dyspnea (35.8%) was less encountered rather than in [12] and chest pain was less encountered rather than in [10, 17].

Pericardial effusion can be either transudate or exudate. Cardiac, liver, and renal failure, or hypothyroidism may lead to transudative pericardial effusion [12]. However, malignancy, tuberculosis, bacteria, and fungi are more prone to severe exudative pericardial effusion and does not usually spontaneously resolve [5, 12]. Exudate pericardial effusion was detected only three patients in our study which was relatively less common to previous studies.

It was reported a series of 140 patients with pericardial effusion that 40 patients (28.5%) were diagnosed with Mycobacterium tuberculosis pericarditis [12]; however, it was reported only two patients [21], it was reported three patients diagnosed with tuberculosis pericarditis [9]. Our results were lower than in [12], which was conducted in China and, consistent with [21], which was conducted in the Western region of Turkey that we encountered only one patient with tuberculosis pericarditis. These findings showed

that the incidence of tuberculosis had decreased in our region as well as in developed countries.

In addition, it was reported a series of 31 patients [22] and it was reported a series of 148 patients with pericardial effusion and reported that [21] hypotension, cardiomegaly, accompanying pleural effusion, and severe pericardial effusion or tamponade were more frequently seen in patients diagnosed with tuberculous or malignant pericardial effusion while, fever, pericardial rub, and response to non-steroidal anti-inflammatory drugs were more often seen in patients diagnosed with idiopathic pericarditis which was reported to have a good prognosis [4, 22-24]. Our findings were consisted with previous studies that Erythrocyte sedimentation rate and C-reactive protein levels were higher in patients considered as idiopathic pericarditis ($p=0.01$, $p=0.02$, respectively).

It was evaluated 204 patients with pericardial effusion and reported that 141 patients (69.1%) were considered as idiopathic pericarditis [9]. Additionally, it was reported [23] in a 342 patient study that the most common cause of pericardial effusion was idiopathic pericarditis, which was followed by iatrogenic and, malignancy. Our findings were consistent with previous studies that idiopathic pericarditis was found the most common cause of pericardial effusion in 38 patients (46.9%). But, a large volume of patients were inconsistent with inability to detect the etiology in our study.

Malignant cells cannot be detected in more than 60% of pericardial fluid cytology in patients diagnosed with malignancy [16]. It was published a single center review of 148 patients and found that 21.6 % (32 patients) of patients had a history of malignancy [25]. Additionally, it was reported that 6.9% of patients were diagnosed with malignancy [10] and it was reported that malignancy was diagnosed in 9% of patients [23]. Our findings were higher than the previous studies that 25.9% of patients (21 patients) were diagnosed with malignancy. The reason for the relatively high incidence of malignancy, can be interpreted as a result of the Chernobyl nuclear disaster due to our geographic presence in the Black Sea coast in the Northern region of Turkey and the most frequently seen types of malignancy were including leukemia/lymphoma, thyroid papillary cancer, lung cancer and breast cancer, respectively.

The most common etiology of recurrent pericarditis was considered as idiopathic pericarditis, post-cardiotomy or systemic lupus erythematosus and 78.2% of the patients recovered without recurrence during long-term follow-up [10]. Our study demonstrates that the rate of recurrence (18.5% [15 patients]) was lower than previously published studies and 12 patients (80%) were idiopathic pericarditis.

There are some limitations to our study. First, this study had a retrospective design. Second, the number of patients in our study may seem limited compared to other studies. Third, larger studies would be required to replicate our findings.

In conclusion, pericardial effusion is usually related to an underlying disease and due to our study, tuberculosis is no longer the leading cause of pericarditis in our region. Idiopathic pericarditis is the leading cause of pericardial effusion and malignancy is the next most common cause of pericardial effusion however, we are unable to reduce the number of patients considered as idiopathic. The pathological assessment of the pericardial fluid and tissue is essential for the precise diagnosis thus, the effusion size and inflammatory signs may be helpful for diagnosing. We thought that pericardiostomy or pericardial window are useful for the assessment of the etiology.

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Ethical statement: The authors stated that the study was approved by Ethics Committee for Clinical Investigations of Ondokuz Mayıs University on July 4, 2018 with decision number 2018/92. Informed consents were obtained from the participants.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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