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Original article

Clinical and Pathological Characteristics of Pericardial Effusions: A Tertiary-Level Healthcare Center Experience

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Abstract

Introduction. Pericardial effusion represents a significant medical issue with diverse origins, often associated with malignant conditions. This study aims to comprehensively analyze the demographic, clinical, and cytological aspects of pericardial effusion in patients treated at a tertiary center.

Methods. This retrospective study included a four-year period and obtained fine needle aspiration cytology (FNAC) analysis results of pericardial effusion in 80 patients. Data covering demographics, reasons for hospitalization, and cytological analyses were collected and statistically evaluated.

Results. The average age of participants was 67±12 years, with a slight male predominance. The primary reasons for hospitalization were impending cardiac tamponade (41%), massive effusions (27%), and cardiac decompensation (9%). Hemorrhagic and malignant effusions were prevalent cytologically. Malignant effusions were noted in 20% of cases, primarily originating from lung adenocarcinoma, and in approximately 15% of cases, served as an initial indicator of hidden malignancy.

Conclusion. Understanding the demographic patterns, clinical presentations, and cytological types of pericardial effusion is crucial for timely diagnosis and treatment. This research highlights the significance of pericardial effusion as a potential indicator of an underlying malignancy and underscores the importance of early detection and intervention.

Kew words pericardial effusion, fine needle aspiration cytology (FNAC), malignant effusions

Introduction

Pericardial effusion is defined as an abnormal accumulation of liquid in the pericardial cavity. It represents a significant cause of mortality, and it can follow a wide spectrum of diseases.[1] In cases of a small pericardial effusion, typical symptoms are usually not present, although there may be a sensation of mild chest discomfort. When larger volumes of pericardial effusion occur, there is an increase in intrapericardial pressure, which leads to reduced filling of the heart's chambers on both sides, resulting in a progressive decrease in stroke volume and systemic blood pressure. It's important to note that the development of symptoms in pericardial effusion is influenced not only by the quantity of fluid but also by the rate at which it accumulates.[2] Pericardiocentesis is an invasive procedure involving the puncture of the pericardium for therapeutic evacuation of its contents, while simultaneously obtaining a sample of fluid for biochemical, cytological, microbiological, immunocytochemical, and cytogenetic analysis.[1] The analysis of pericardial effusion can represent a distinctive diagnostic challenge for cytologists,[3] as they can be sorted by different classification systems. The obtained effusion samples, following biochemical analysis, are clinically classified primarily into transudates and exudates.[4] Pericardial effusions can also be classified based on the predominance of certain cell populations into lymphocytic, macrophagic, neutrophilic-granulocytic, eosinophilic, hemorrhagic, mixed, suspicious for malignancy, malignant effusion, and transudate. Cytological analysis of pericardial effusion is a diagnostic procedure that is based on the examination of spontaneously shed cells into the pericardial cavity,[5] which entails two major groups: the first without atypical, neoplastic cells, predominantly consisting of mesothelial cells, histiocytes, and lymphocytes representing a benign type of effusion, and the second with the presence of malignant cells, indicating a malignant type. An uncertain finding, when rare abnormal cells are present, is labeled as a sample suspicious for malignancy. The main indication for performing FNAC (*Fine Needle Aspiration Cytology*) is to differentiate between benign and malignant effusions.[4]

Malignant or neoplastic findings in effusion are quite common, considering the tendency of certain tumors to metastasize to the pericardium. Most patients with malignant effusion already have knowledge of the primary neoplasm; however, in some cases, pericardial effusion is the initial manifestation of hidden malignancy, and

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sometimes pericardial effusions are often observed as an incidental finding in patients with cancer.[6-8] Primary tumors of the pericardium occur less frequently compared to secondary tumors, and they include mesothelioma, and primary lymphoma which is more commonly accompanied by effusion.[4] Metastatic tumors account for the majority of malignant pericardial effusions,[9] and the most common are adenocarcinomas, followed by squamous cell and small cell carcinoma, while melanomas and lymphomas (both Hodgkin and non-Hodgkin) are rare.[4]

The objectives of this research were to analyze the age and gender distribution of patients with pericardial effusion, determine the most common reasons for admission of patients with pericardial effusion, identify the cytological types of pericardial effusions, and analyze the frequency of malignant types of pericardial effusions and the origin of malignant cells.

Methods

This retrospective study was approved by the Ethics Committee of the Institute for Cardiovascular Diseases of Vojvodina (Sremska Kamenica, Serbia), as it included 80 participants in which fine needle aspiration cytology (FNAC) of pericardial effusion was performed during a 4-year period (2018-2022). Demographic and clinical data were extracted from the hospital's information system and included sex, age, and reason for hospitalization. To obtain a better insight into the age distribution, patients were divided into 6 categories, each one including a 10-year period from the age of 35 until the age of 94.

Samples obtained by FNAC were stained with the *May Grunwald Giemsa* (MGG) method. Based on the cytological characteristics, pericardial effusions were classified into nine categories: lymphocytic, macrophagic, neutrophilic-granulocytic, eosinophilic, hemorrhagic, mixed, suspicious for malignancy, malignant effusion, and transudate. In patients with malignant effusion, the origin of malignant cells was determined.

Collected data were statistically assessed using Jamovi version 2.4.1, a freely available statistical software. We employed descriptive statistics to summarize and present the data.

Results

Demographic data

Sex distribution has shown that our sample mainly consisted of male participants (n = 46), while 34 were female. The mean age was 67±12.6, with the youngest participant being 35, and the oldest 90. The most abundant age group, in both sexes, was 65-74, without observed statistical significance between genders. Data are presented in Figure 1.

Clinical data

The most common reason for hospitalization was impending cardiac tamponade (41.3%), as well as massive pericardial effusion (27.5%). Pulmonary edema and aortic dissection weren't noted in male patients, while no female patient was hospitalized due to cardiac arrhythmias. Data regarding reasons for hospitalization are presented in Table 1.

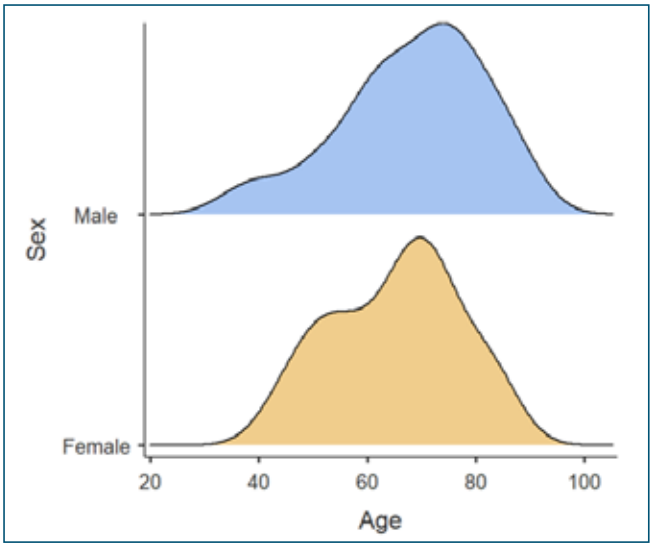

Figure 1. Age distribution based on participants' sex

Table 1. Reasons for hospitalization

Reason	Male		Female		Total	
	N	%	n	%	n	%
Impending cardiac tamponade	18	39.1	15	44.1	33	41.3
Massive pericardial effusion	14	30.4	8	23.5	22	27.5
Cardiac decompensation	2	4.3	5	14.7	7	8.8
Myocardial infarction	2	4.3	2	5.9	4	5.0
Elective admission	3	6.5	1	2.9	4	5.0
Pericarditis	3	6.5	1	2.9	4	5.0
Cardiac arrhythmias	4	8.7	0	0	4	5.0
Pulmonary edema	0	0	1	2.9	1	1.3
Aortic dissection	0	0	1	2.9	1	1.3

Type of pericardial effusion

In both sexes, the most prevalent type was hemorrhagic (33.8%) Image 1, followed by malignant (25.0%) Image 2, and mixed (13.8%) Image 3. There was not a single effusion that fulfilled the criteria of eosinophilic type (Table 2).

Table 2. Distribution of pericardial effusion types, based on cytological characteristics

Type	Male		Female		Total	
	N	%	n	%	n	%
Hemorrhagic	14	30.4	13	38.2	27	33.8
Malignant	11	23.9	9	26.5	20	25.0
Mixed	6	13.0	5	16.7	11	13.8
Transudate	5	10.9	1	5.9	6	7.5
Lymphocytic	3	6.5	2	5.9	5	6.3
Neutrophilic-granulocytic	3	6.5	2	5.9	5	6.3
Suspicious for malignancy	2	4.3	2	2.9	4	5.0
Macrophagic	2	4.3	0	0.0	2	2.5
Eosinophilic	0	0.0	0	0.0	0	0.0

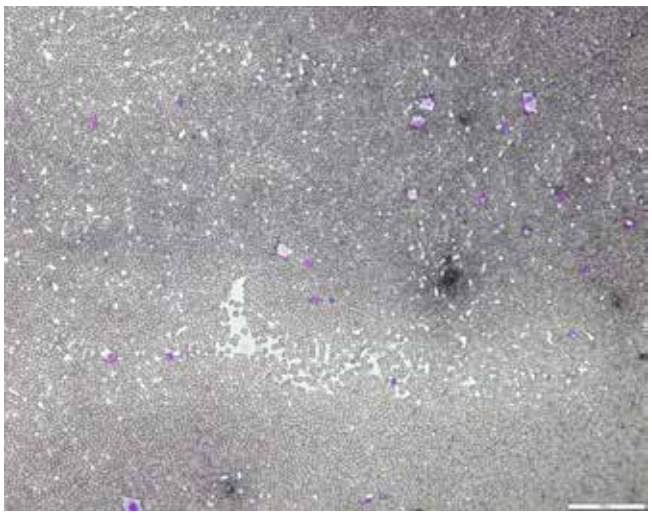

Figure 1. Hemorrhagic type pericardial effusion 20x MGG stained

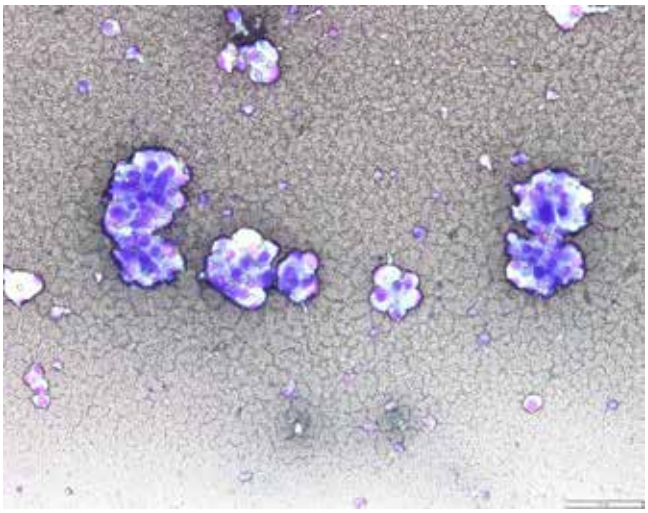

Figure 2. Malignant type pericardial effusion atypical epithel cells adenocarcinoma like 20x MGG stained

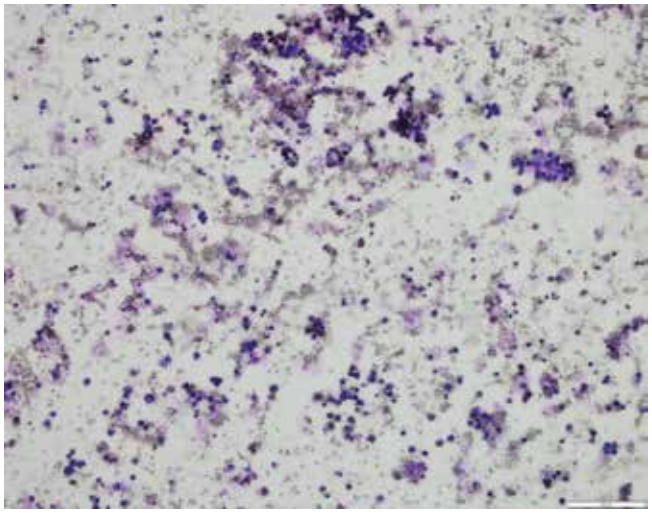

Figure 3. Mixed cellular type pericardial effusion 20x MGG stained

Origin of malignant cells

It was determined that every analyzed malignant type of effusion was a consequence of metastasis. The predominant source of malignant cells was pulmonary adenocarcinoma (n = 16), while malignant cells were much less frequently derived from diffuse gastric adenocarcinoma (n = 2), ductal breast carcinoma (n = 1), and renal cell carcinoma (n = 1). Out of 20 participants, diagnosed malignant pericardial effusion was a primary manifestation of the malignant disease in 10 of them. In each instance of pericardial effusion where the patient was unaware of an underlying tumor, the diagnosis revealed an adenocarcinoma.

Discussion

The incidence of pericardial effusions has been increasing over recent years, primarily due to prolonged survival rates among individuals with malignant diseases, chronic kidney disease patients undergoing hemodialysis, and increased use of anticoagulant therapy, and radiation therapy in tumor treatment, among other factors.[10] Cytological analysis of pericardial fluid samples represents a significant method that, in a considerable number of cases, allows for a definitive diagnosis, particularly when other standard clinical methods are insufficient and/or as support for other clinical and diagnostic approaches.[11]

Our study included 80 hospitalized patients diagnosed with pericardial effusion, and more than half of the participants were male. Although previous studies, conducted in India and in China,[10,12] have shown similar results indicating a predominance of male subjects, Kolte et al. observed a significantly higher number of women who underwent pericardiocentesis.[13] The average age of our participants was 67±12 years, with the highest number of patients aged between 65 and 74 years. The age distribution in our study is aligned with the research conducted by Gecman et al., where the average age of participants was 60±16 years.[14] In contrast, a study from India reported a much younger average age of their participants, which was 46±7 years with 25.8% of patients aged between 51 and 60 years.[12] In addition, Nataraja et al. observed that the majority of participants in their study were grouped in the range of 31 to 40 years,[15] and such significant differences could be explained by the age structure of the Indian population, where the median age is 28.7 compared to the population of Serbia, where the median age is 43.3 years.

In our study, more than a third of the participants underwent pericardiocentesis due to impending tamponade, after which they were hospitalized. The next most common reasons for admission were echocardiographically confirmed massive pericardial effusion and cardiac function disturbances such as heart failure, myocardial infarction, or severe arrhythmias. Research conducted in a tertiary care center to review pericardial effusion characteristics by Erkal et al. showed cardiac tamponade as the leading reason for admission in over 77.3% of participants, followed by massive pericardial effusions at 22.7%.[10] Similar results, with 70% of participants admitted due to impending cardiac tamponade, were observed by researchers at the Asian Medical Academic Center. Some studies, besides cardiac tamponade, cited heart diseases and arrhythmias as common reasons for admission.[16,17]

Regarding the predominance of specific cellular types, cytological findings can be categorized into several categories, and in our study, the predominant cytological findings, accounting for over 30%, corresponded to the hemorrhagic type, characterized by a multitude of red blood cells, followed by malignant and mixed types. The hemorrhagic type of effusion constituted half of the findings in studies conducted by Erkal et al., as well as Yadav and colleagues.[10,12] However, Kolte et al. in their research mentioned reactive mesothelial cells, histiocytes, and lymphocytes as the most common cellular components of pericardial effusion.[13]

Serous membranes are often sites of metastatic tumors, leading to the accumulation of fluid in the pericardial cavity.[3] According to studies conducted in Singapore, the most common cause of pericardial effusions was malignancy.[16] Cytological findings in our research are fundamentally divided into benign and malignant categories, a simple classification also used by other researchers in previous studies.[10] Malignant findings were less common in our study (20%). Similar frequencies of the malignant type of effusion were found in other studies.[6,12,17] Given that pericardium is frequently affected by metastases from malignant tumors, effusion formation is a common consequence of this process.[11] In our research, the origin of metastatic tumors resulting in pericardial effusion was primarily from lung adenocarcinoma (80%), with significantly rarer occurrences from diffuse gastric adenocarcinoma, ductal breast carcinoma, and clear cell renal carcinoma. He et al. also noted a dominant and nearly identical percentage of lung adenocarcinoma metastases in the cardiac sac, with breast carcinoma and lymphomas being other common causes of malignant effusions.[18] In their seventeen-year study encompassing 985 samples of pericardial effusion with cytological evidence of malignant cells, Dermawan et al. identified lung adenocarcinoma as the most prevalent metastatic tumor (61%), followed by infrequent occurrences from gastrointestinal tract tumors (most commonly gastric) and hematolymphoid origin (lymphomas).[9] In studies conducted by Kolte et al., lung adenocarcinoma and breast carcinoma were approximately equally responsible for pleural effusion, and a similar ratio was obtained in Saab et al.'s study.[7,13] The majority of patients who developed malignant pericardial effusion already had a diagnosed primary malignancy in their medical history. Our study observed a small percentage (4%) within the examined group, specifically 15% of participants with malignant effusion, where pericardial effusion, with or without signs of impending tamponade, was the initial manifestation of malignancy. In a study conducted by Dragoescu et al., 87% of patients with malignant pericardial effusion had a documented history of malignancy, while 13% of participants at the time of cytological examination of pericardial effusion did not have an established previous malignancy.[6] Last year's ESC guidelines on cardio-oncology recommend multimodality cardiovascular imaging (echocardiography, CMR and CT), ECG and measurement of cardiac biomarkers to confirm the diagnosis, assess the haemodynamic consequences of pericardial disease, and rule out associated myocarditis. Malignancy-related pericardial effusions caused by direct (lung, oesophageal, breast) or metastatic invasion (haematological malignancies, ovarian, melanoma) or by lymph node obstruction are generally associated with poor prognosis, and multidisciplinary discussion is needed before interrupting and restarting cancer treatment.[8]

Conclusion

The average age of participants with pericardial effusion was 67±12 years, showing no significant gender difference. The main reasons for admission were impending tamponade (41%), followed by massive effusions (27%) and cardiac decompensation (9%). Hemorrhagic and malignant types were most common in cytological findings. Malignant effusions were present in 20% of participants, primarily from lung adenocarcinoma. Notably, pericardial effusion can be an initial sign of an underlying malignancy, often marking the first manifestation of a malignant disease.

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Sažetak

Kliničko-patološke karakteritike perikardnih izliva: Iskustvo tercijarnog zdravstvenog centra

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Uvod. *Perikardijalni izliv predstavlja značajan medicinski problem sa raznovrsnim uzrocima i često prati maligna oboljenja. Ova studija ima za cilj sveobuhvatnu analizu demografskih, kliničkih i citoloških aspekata perikardijalnog izliva kod pacijenata lečenih u tercijarnom centru.*
Metode. *Ova retrospektivna studija obuhvatala je četvorogodišnji period i uključivala je citološku analizu perikardijalnog izliva putem iglene biopsije (eng. Fine Needle Aspiration Cytology, FNAC) kod 80 pacijenata. Podaci koji obuhvataju demografiju, razloge hospitalizacije i citološke analize prikupljeni su i statistički evaluirani.*
Rezultati. *Prosečna starost učesnika bila je 67±12 godina, uz blagu predominaciju ispitanika muškog pola. Glavni razlozi hospitalizacije bili su preteća srčana tamponada (41%), masivni izlivi (27%) i srčana dekompenzacija (9%). Citološki su dominirali hemoragični i maligni izlivi. Maligni izlivi su zapaženi kod 20% slučajeva, uglavnom potičući od adenokarcinoma pluća i u oko 15% slučajeva je predstavljao inicijalni znak skrivenog maligniteta.*
Zaključak. *Razumevanje demografskih obrazaca, kliničkih prezentacija i citoloških tipova perikardijalnog izliva od suštinskog je značaja za pravovremenu dijagnozu i treatman. Ovo istraživanje ističe značaj perikardijalnog izliva kao potencijalnog indikatora skrivenog maligniteta i naglašava važnost ranog otkrivanja i intervencija.*

Ključne reči: *perikardijalni izliv, "Fine Needle" aspiracija (FNAC), maligni izlivi*