Preliminary report
Preliminarno izvješće

PERICARDIAL FEATURES OF IN-HOSPITAL RHEUMATOLOGY PATIENTS: AN OBSERVATIONAL STUDY

OBILJEŽJA PERIKARDA U HOSPITALIZIRANIH REUMATOLOŠKIH BOLESNIKA: OPSERVACIJSKA STUDIJA

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Abstract

Rheumatic disorders can be associated with pericarditis, but severe forms of pericarditis are rare. The aim of this observational study was to evaluate pericardial features in patients with different rheumatic diseases. Thirty-five patients hospitalized at the Clinic of Rheumatology, University Clinical Center of Kosovo, from October 1 to October 21, 2014 were included in the study. Demographic data, history, laboratory, ECG, and echocardiography data, with special emphasis on the analysis of the pericardium, were obtained from each patient. Echocardiography was especially focused on the amount of pericardial fluid and pericardial thickness in the posterior wall of the heart.

Mean patient age was 51.5 ± 13.8 years. 65.7% of the patients were women. Out of the patients that we analyzed, 88.6% had an inflammatory rheumatologic disease. 11.3% of the patients had mild symptoms, in 68.7% the symptoms were moderate, and in 20% severe. In all patients, pericardial hyperechogenicity was marked, with a mean pericardial thickness of 4.68 ± 1.66 mm. Pericardial effusion in a small amount was present in 57.1% of patients, with a mean pericardial fluid amount of 3.3 ± 1.9 mm. The severity of rheumatic disease had a positive and significant correlation with the presence of pericardial effusion (r= 0.29, p=0.04) and its amount (r= 0.28, p=0.05). The patients had not been aware of the pericardial involvement and did not have any clinical symptoms.

In conclusion, in this short-term small observational study pericardial changes were a frequent finding in the rheumatology patients. In general, the pericarditis was subclinical and with small amounts of effusion. The disease activity of rheumatic disorders can be associated with pericarditis. Further studies with larger samples of patients and of longer duration are needed to further explore this issue.

Keywords: Rheumatic diseases – complications; Pericarditis – etiology, ultrasonography; Pericardial effusion – etiology, ultrasonography; Pericardium – ultrasonography; Cross-sectional studies

Sažetak

Reumatske bolesti mogu biti povezane s perikarditisom, ali su teži oblici te bolesti rijetki. Cilj ovog opservacijskog istraživanja bio je proučiti obilježja perikarda u bolesnika s različitim reumatskim bolestima. Uključeno je trideset i pet bolesnika hospitaliziranih u Klinici za reumatologiju Sveučilišnoga kliničkog centra Kosova od 1. do 21. listopada 2014. Prikupljeni su demografski podaci, anamnestički podaci, učinjeni su EKG i ehokardiografija s posebnim naglaskom na perikard. Ehokardiografija je bila posebno usmjerena na količinu perikardijalnog izljeva i njegovu debljinu u stražnjoj srčanoj ovojnici.

Srednja dob bolesnika bila je 51,5 ± 13,8 god., a 65,7% njih bile su žene. Među analiziranim bolesnicima bilo je 88,6% s upalnim reumatskim bolestima, od čega njih 11,3% s blagim simptomima, 68,7% s umjerenim i 20% s teškim

simptomima. U svih je bolesnika naglašena perikardijalna hiperehogenost sa srednjom debljinom perikarda od 4,68 ± 1,66 mm. Perikardijalni izljev manje količine bio je prisutan u 57,1% bolesnika s količinom od 3,3 ± 1,9 ml. Težina reumatske bolesti bila je značajno i pozitivno povezana s prisutnošću perikardijalnog izljeva (r = 0,29; p = 0,04) i količinom perikardijalnog izljeva (r = 0,28; p = 0,05). Bolesnici nisu znali da imaju perikardijalni izljev niti su imali kliničke simptome u tom smislu.

Zaključno, u ovome kratkotrajnom malom opservacijskom istraživanju promjene perikarda bile su čest nalaz u bolesnika s reumatskim bolestima. Ipak, najčešće se radilo o perikarditisu supkliničkog oblika i s malom količinom izljeva. Aktivnost bolesti može biti povezana s perikarditisom. Potrebne su studije s većim brojem bolesnika i dužeg trajanja da bi se dalje istražilo ovo područje.

Ključne riječi: Reumatske bolesti – komplikacije; Perikarditis – etiologija, ultrasonografija; Perikardni izljev – etiologija, ultrasonografija; Perikard – ultrasonografija; Presječna istraživanja

Introduction

Rheumatic disorders are often associated with pericarditis, but severe forms of pericarditis are rare (1). Based on various methods of assessment (echographic or postmortem studies), pericarditis occurs in 30–50% of patients with rheumatoid arthritis (2). Nevertheless, studies also reveal that clinically evident pericarditis is much less frequent, even in patients with severe RA (3). Early diagnosis of RA is important, as effective treatment improves the outcome of affected patients (4). Thus, along with antibody screening, the use of an etiological evaluation strategy in patients with pericardial effusion may be helpful in diagnosing RA and possibly other most common inflammatory rheumatic diseases (5).

The aim of our study was to determine the prevalence of pericardial effusion in patients with rheumatic diseases hospitalized at the Department of Rheumatology during a three-week period, and to watchfully analyze the pericardium, in regard to its echogenicity and thickness. Furthermore, we wanted to evaluate the relationship between the severity and duration of the rheumatic disease and the confirmed pericardial changes.

Patients and methods

We present the results of a cross-sectional observational study conducted in the University Clinical Center of Kosovo in the period from October 1 to October 21, 2014. The study included 35 consecutive patients with different rheumatic disorders hospitalized at the Clinic of Rheumatology. Exclusion criteria were: acute myocardial infarction, cardiac surgery, trauma, neoplasia, end-stage renal failure and/or hypothyroidism.

The study was approved by the Ethical Committee of the University Clinical Center, and written informed consent had been obtained from each patient before he/she entered the study.

Demographic data, a thorough history, physical examination, laboratory tests, ECG, and echocardiography were obtained from each patient, with a special emphasis on the pericardium.

Rheumatic disorders

Rheumatic disorders were divided into two major groups, inflammatory and degenerative. Diagnosis was established by using the criteria issued by the American College of Rheumatology (ACR). Thus, for rheumatoid arthritis and systemic sclerosis the criteria endorsed by the ACR and the European League Against Rheumatism (EULAR) (ACR/EULAR Criteria) were used (6, 7). The severity of inflammatory rheumatic diseases was determined based on their activity. For rheumatoid arthritis we used the six rheumatoid arthritis disease activity markers: Clinical Disease Activity Index (CDAI), Disease Activity Score 28 CRP/ESR (DAS28 CRP/ESR), Patient Activity Scale (PAS), Patient Activity Scale II (PASII), Routine Assessment of Patient Index Data 3 (RAPID3), and Simple Disease Activity Index (SDAI). Disease activity for systemic sclerosis (SSc) was measured according to the European Scleroderma Study Group (ESSG), whereas for Systemic Lupus Erythematosus we used the Disease Activity Index (SLEDAI) (8).

Echocardiography

Echocardiography (Phillips iE 33) examinations and measurements were performed according to the recommendations of the American Society of Echocardiography (9). Left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and septal and posterior wall thickness were measured from parasternal M-mode recordings according to standard criteria. LV ejection fraction (EF %) was determined from apical views with the modified Simpson's rule.

Echocardiographic examination of the pericardium

The pericardium was analyzed by echocardiography in different views, with the main focus on the posterior left ventricular wall depicted by the parasternal long axis view. Additionally, we examined the pericardium from the short axis view and apical four-chamber view.

Pericardial effusion was defined as the presence of echo-free space on M-mode detected between the epicardium and pericardium. The echo-free space was then measured and classified as a small amount of pericardial effusion if the posterior echo-free space was less than 10 mm, as moderate if the posterior space was 10 to 20 mm, and as large if the pericardial effusion in the posterior wall was above 20 mm. In patients without pericardial effusion we measured the pericardial thickness of the posterior wall.

Statistical analysis

All data were expressed as mean ± standard deviation (SD) and percentages. The correlation of selected variables was estimated using the Pearson correlation test. Simple regression analysis was performed to determine if the severity of rheumatic disorders and their duration were related to the pericardial changes. Variables with a value of $p \leq 0.05$ in simple regression were considered significant. Statistical analysis was performed using the statistical software SPS, version 2.80, 2005. Significance was set up at $p<0.05$.

Results

The mean patient age was 51.5 ± 13.8 years. 65.7% of the patients were women. Other baseline patient characteristics are presented in Table 1.

Table 1. Baseline patient characteristics*
*Tablica 1. Osnovna obilježja bolesnika**

Patient characteristics	n=35
Age, yr	51.46 ± 13.76
Female (%)	23/35 (65.71)
Current smokers (%)	6/35 (17.14)
Alcohol users (%)	1/35 (2.86)
Hypertension (%)	11/35 (31.43)
Diabetes mellitus (%)	6/35 (17.14)
Chronic bronchitis (%)	2/35 (5.71)
Dyslipidemia (%)	3/35 (8.57)
Anemia (%)	1/35 (2.86)

** Data are presented as mean ± SD or No. (%) / Podaci su prikazani kao srednja vrijednost ± SD ili kao broj (%)*

Inflammatory rheumatic disorders were present in 88.6% of our in-hospital rheumatology patients, whereas the rest were degenerative disorders (Table 2).

The mean duration of the disease in these patients was 6.2 ± 7.8 years. As for disease activity, 20% of the patients had a high disease activity, while 68.7% and 11.3% had a moderate and mild activity, respectively.

The mean erythrocyte sedimentation rate (ESR) was above referent values, being 35.3 ± 25.1 after the first hour. The mean value of rheumatoid factor was 41.8 ± 77.9 IU/mL (0.0–14 IU/mL, referent value). There were no major deviations in the results of the routine laboratory tests.

Table 2. Types of rheumatic disorders in the study population*
*Tablica 2. Tipovi reumatskih poremećaja u istraživanoj populaciji**

Rheumatic condition	n=35
Rheumatoid arthritis (%)	13/35 (37.14)
Reactive arthritis (%)	2/35 (5.71)
Systemic lupus erythematosus (%)	4/35 (11.43)
Erythema nodosum (%)	1/35 (2.86)
M. Behçet (%)	3/35 (8.57)
Polyarthritis chronica (%)	6/35 (17.14)
Progressive systemic sclerosis (%)	1/35 (2.86)
Vasculitis (%)	1/35 (2.86)
Cervical syndrome (%)	1/35 (2.86)
Lumbar syndrome (%)	3/35 (8.57)

** Data are presented as mean ± SD or No. (%) / Podaci su prikazani kao srednja vrijednost ± SD ili kao broj (%)*

Basic echocardiography measurements were within normal limits (Table 3), with the exception of mean pulmonary artery systolic pressure (PSAP), which was mildly elevated, being 30.1 ± 7.8 mmHg. Mitral and aortic regurgitation was detected rather frequently, although it was mostly low-grade. Table 4 presents the frequency of observed valvular regurgitation, as well as its grade.

In all patients pericardial hyperechogenicity was pronounced. The mean pericardial thickness was 4.68 ± 1.66 mm. An example of pericardial thickness is

Table 3. Basic echocardiographic data of the study population*
*Tablica 3. Osnovni ehokardiografski podaci u istraživanoj populaciji**

	n=35
IVSd, mm	10.2 ± 1.6
PWd, mm	9.8 ± 1.6
LVEDD, mm	50 ± 4.9
LVESD, mm	32.1 ± 5.8
LVEF, %	64.9 ± 9
LA, mm	36.4 ± 4.8
Aorta, mm	31.9 ± 4.8
RV, mm	23.9 ± 4.8
PSAP, mmHg	30.1 ± 7.8

** Data are presented as mean ± SD / Podaci su prikazani kao srednja vrijednost ± SD*
Legend / Legenda: IVSd: diastolic interventricular septum / interventrikularni septum u dijastoli; PWd: diastolic posterior wall / stražnji zid u dijastoli; LVEDD: left ventricular end-diastolic diameter / promjer lijevog ventrikula na kraju dijastole; LVESD: left ventricular end-systolic diameter / promjer lijevog ventrikula na kraju sistole; LV: left ventricle / lijevi ventrikul; EF: ejection fraction / ejekcijska frakcija; LA: left atrium / lijevi atrij; RV: right ventricle / desni ventrikul; PSAP: pulmonary systolic aortic pressure / plućni sistolički aortalni tlak

Table 4. Basic valvular echocardiographic data of the study population

Tablica 4. Osnovni ehokardiografski podaci zalistaka u istraženoj populaciji

MR			AR			TR		
0–1	1–2	2	0–1	1–2	2	0–1	1–2	2
45.7%	14.3%	5.71%	51.4%	8.57%	2.86%	21.9%	8.6%	2.9%
65.71%			62.83%			33.4%		

Legend / Legenda: MR: mitral regurgitation / mitralna regurgitacija; AR: aortic regurgitation / aortalna regurgitacija; TR: tricuspid regurgitation / trikuspidalna regurgitacija

shown in Figure 1. The presence of pericardial effusion was detected in 20 (57.14%) patients, with a mean pericardial effusion diameter of 3.3 ± 1.3 mm, i.e., a small amount according to the pericardial effusion classification. The small amount of pericardial effusion is confirmed by the fact that the maximum separation that was found was only 7 mm. Two (10%) of the patients with pericarditis had degenerative rheumatic diseases. Small-amount pericardial effusions detected by 2D and M-mode echocardiography are shown in Figures 2 and 3. None of our patients had been aware of the pericardial involvement nor had any clinical symptoms suggesting it.

Regarding the association of severity of symptoms and pericardial features, in a simple regression analysis we found a significant positive correlation with the presence of pericardial effusion (r=0.29, p=0.04) and the amount of pericardial effusion (r=0.28, p=0.05), whereas there was no significant relationship with the pericardial thickness (r=–0.08, p=NS). Concerning the duration of the rheumatic symptoms and the pericardial features, we were unable to find any significant correlation.

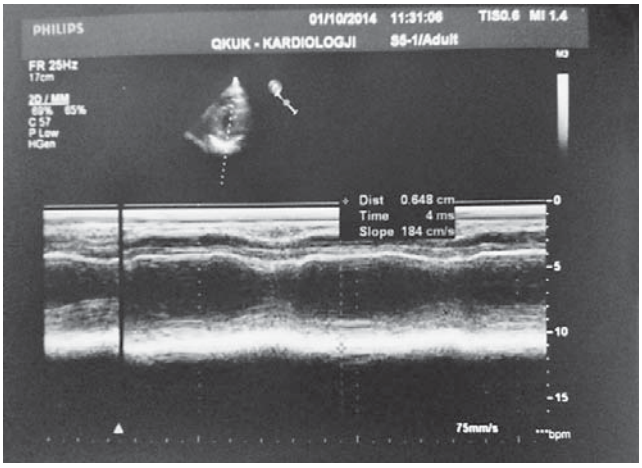

Figure 1. Echocardiography image showing pericardial hyperechogenicity and thickness of the posterior wall of approx. 6.5 mm

Slika 1. Ehokardiografija koja pokazuje hiperehogenost u području perikarda i zadebljanje stražnjeg zida, oko 6,5 mm

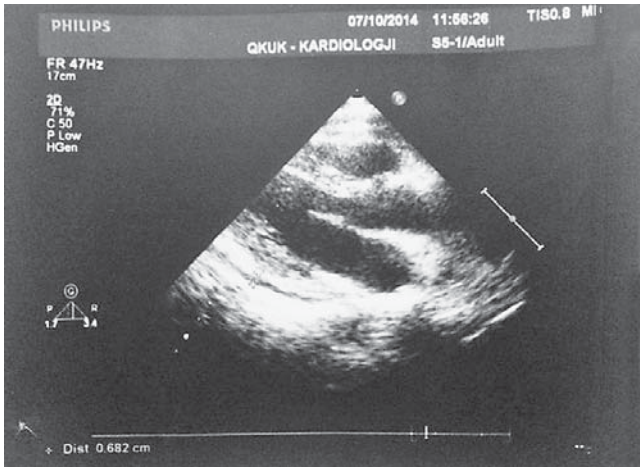

Figure 2. 2D echocardiography showing pericardial effusion of approx. 6.8 mm on the posterior LV wall

Slika 2. 2D ehokardiografija koja pokazuje perikardijalni izljev od oko 6,8 mm³ na stražnjem zidu lijevog ventrikula

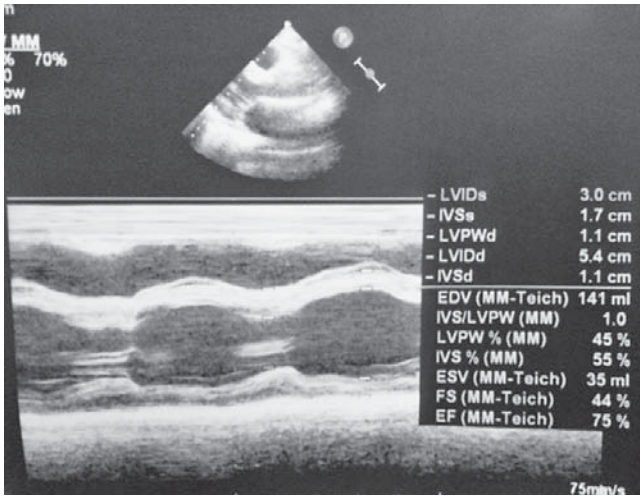

Figure 3. M-mode echocardiography showing separation of pericardial layers of the posterior LV wall

Slika 3. M-mode ehokardiografija koja pokazuje odjeljivanje slojeva perikarda stražnjeg zida lijevog ventrikula

Discussion

Rheumatic disorders may be associated with various cardiovascular diseases, including myocardial ischemia, arterial stiffness, systolic and diastolic heart failure, pericardial disease, valvular disease, conduction abnormalities, arrhythmias, et cetera (10, 11). In patients with rheumatoid arthritis, pericarditis is seen predominantly in male patients with a severely destructive and nodular form of the disease (12). This finding is in concordance with our results, as patients with severe forms of rheumatic disease had a significant positive correlation with the presence and amount of pericardial effusion. In rheumatoid arthritis, fibrinous pericarditis has been found at autopsy, but generally it was not of clinical relevance, although in rare cases constrictive pericarditis had developed (13, 5). In patients with systemic lupus

erythematosus pericarditis is also the most common clinical cardiovascular manifestation (14, 15), and it is usually presented as a small amount of pericardial effusion, although moderate to large pericardial effusions have been found in up to 7% of cases (15).

Though pericarditis is a frequent finding in patients with rheumatic diseases, it is rarely manifested clinically; however, when it is present as clinical pericarditis, its prognosis appears to be worse (14). Whether pericarditis itself contributes significantly to the overall mortality is unknown, except in the few cases with constrictive pericarditis or rapidly progressive effusive pericarditis that are known to be associated with a high morbidity and mortality (14).

The majority of patients develop pericarditis after the onset of rheumatic disease; however, in some patients pericarditis may precede the diagnosis of rheumatic disease (3). Pericarditis of rheumatic etiology may be found by coincidence on echocardiography or due to pericarditis symptomatology. Thus, as pericarditis may be the initial finding of a rheumatic condition, we consider it an important manifestation that may lead to early and effective treatment of rheumatic disorders. Hence, even a small degree of pericarditis found incidentally on echocardiography might be an indication to refer the patient for a detailed rheumatologic workup.

There are several limitations of this observational study, the most obvious ones being the study design and the small sample of patients. Nevertheless, we consider it a good starting point for a larger study.

In conclusion, pericardial changes were frequently found in our sample of patients with different but mainly inflammatory rheumatic disorders. They were mostly presented as small amounts of pericardial effusion and as subclinical manifestations. Severe forms of rheumatic disorders were more strongly associated with pericarditis. On the other hand, the duration of rheumatic disorders does not seem to be related to pericardial changes, probably due to the small sample of study subjects. Further studies with a larger sample and an appropriate follow up are warranted to help elucidate the significance of pericardial changes in the etiology and course of rheumatic disorders.

Disclosure: The authors declare no conflict of interest.

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