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CLINICAL INVESTIGATION

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Recurrent pericarditis in older adults: Clinical and laboratory features and outcome

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Abstract

Background: Current guidelines for the diagnosis and treatment of pericarditis refer to the general adult population. Few and fragmentary data regarding recurrent pericarditis in older adults exist.

Objective of the Study: Given the absence of specific data in scientific literature, we hypothesized that there might be clinical, laboratory and outcome differences between young adults and older adults affected by idiopathic recurrent pericarditis.

Materials and Methods: We performed an international multicentric retrospective cohort study analyzing data from patients affected by recurrent pericarditis (idiopathic or post-cardiac injury) and referring to tertiary referral centers. Clinical, laboratory, and outcome data were compared between patients younger than 65 years (controls) and patients aged 65 or older.

Results: One hundred and thirty-three older adults and 142 young adult controls were enrolled. Comorbidities, including chronic kidney diseases, atrial fibrillation, and diabetes, were more present in older adults. The presenting symptom was dyspnea in 54.1% of the older adults versus 10.6% in controls ($p < 0.001$); pain in 32.3% of the older adults versus 80.3% of the controls ($p < 0.001$). Fever higher than 38°C was present in 33.8% versus 53.5% ($p = 0.001$). Pleural effusion was more prevalent in the older adults (55.6% vs 34.5%, $p < 0.001$), as well as severe pericardial effusion (>20 mm) (24.1% vs 12.7%, $p = 0.016$) and pericardiocentesis (16.5% vs 8.5%,

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$p = 0.042$). Blood leukocyte counts were significantly lower in the older adults (mean + SE: 10,227 + 289/mm^3 vs 11,208 + 285/mm^3, $p = 0.016$). Concerning therapies, NSAIDS were used in 63.9% of the older adults versus 80.3% in the younger ($p = 0.003$), colchicine in 76.7% versus 87.3% ($p = 0.023$), corticosteroids in 49.6% versus 26.8% ($p < 0.001$), and anakinra in 14.3% versus 23.9% ($p = 0.044$).

Conclusions: Older adults affected by recurrent pericarditis show a different clinical pattern, with more frequent dyspnea, pleural effusion, severe pericardial effusion, and lower fever and lower leukocyte count, making the diagnosis sometimes challenging. They received significantly less NSAIDs and colchicine, likely due to comorbidities; they were also treated less commonly with anti-IL1 agents, and more frequently with corticosteroids.

KEYWORDS
anakinra, dyspnea, older adults, pericarditis, pleural effusion

INTRODUCTION

Idiopathic pericarditis represents the most common form of pericardial pathology in industrialized countries.[1] Recent studies allowed progress in defining the underlying pathological process, with involvement of the inflammasome and production of IL-1 and other inflammatory mediators that cause inflammation of the pericardium.[2–4] Several causes have been implicated as triggers of the inflammatory event, including mainly viral infections, which are likely to be placed on a terrain prone to the out-of-control autoinflammatory response, that tends to perpetuate even after the viral infection has been eradicated.[5,6] Most cases are characterized by high values of C-reactive protein (CRP), high neutrophil values, with the ratio of neutrophils to lymphocytes markedly in favor of neutrophils both during the first acute episode and during relapses.[7–10] At present, the diagnostic criteria for pericarditis, codified by the 2015 European Society of Cardiology (ESC) guidelines,[1] refer to the general population, which includes both young and older adults. Few data are currently available, and only in patients with a first attack of acute pericarditis, regarding clinical, diagnostic, and laboratory peculiarities of the older adults population,[11] suggesting that the younger population more often presents with chest pain, fever, ST elevation, and PR depression on ECG, higher CRP values, and a higher rate of recurrences. Similarly, there are few data regarding differences in therapy approach between adult and older adult subjects.[11,12] The older adult population is characterized by frequent comorbidities that may affect the access to care.[1] The use of non-steroidal anti-inflammatory drugs (NSAIDs) in the older adults is often precluded by comorbidities such as renal failure, gastrointestinal bleeding, or concomitant use of anticoagulant drugs, and this may adversely affect the outcome of older adult patients with idiopathic pericarditis. Due to limited data on the older adult population with recurrent pericarditis, we collected clinical, laboratory, and treatment features of this population in an international observational study, in order to develop a more tailored diagnostic and therapeutic approach.

Key points

- Older adults affected by recurrent pericarditis often showed a unique pattern, with more frequent dyspnea, pleural effusion, severe pericardial effusion, and lower fever and lower leukocyte counts.
- Older adults underwent pericardiocentesis more frequently.
- Older adults were significantly less treated with NSAIDs and colchicine, likely due to comorbidities, less commonly with anti-IL1 agents, and more frequently with corticosteroids.

Why does this paper matter?

The data in the literature regarding common clinical, laboratory, therapy and outcome characteristics of the population of older adults affected by recurrent idiopathic pericarditis are fragmentary. This study may help identifying characteristics that should be considered in order to rapidly diagnose and establish appropriate treatment.

MATERIALS AND METHODS

We performed a multicenter international retrospective study including a consecutive cohort of patients diagnosed with recurrent pericarditis (idiopathic or post-cardiac injury), followed from January 2019 to July 2023. All patients provided informed consent and the study was approved by our ethical committee.

This study followed the STROBE reporting guideline. Consecutive individuals 65 years or older with recurrent pericarditis who fulfilled the ESC diagnostic criteria[1] were eligible in eight centers (seven in Italy and one in Greece). Subjects with secondary form of pericarditis (autoimmune diseases, neoplasms, and bacterial infections) were excluded; patients with Post Cardiac Injury Syndrome (PCIS) were included. Of 153 eligible patients 13 were excluded for incomplete minimal clinical data set, 6 were unavailable, 1 denied consent; 133 were included. For each of these, each center provided at least one control younger than 65 years matched for gender. As also specified in the ESC guidelines, patients who had a suspicion of a specific etiology or any predictor of poor prognosis (fever >38°C, subacute onset, large pericardial effusion, cardiac tamponade, myopericarditis, immunosuppression, trauma, or use of oral anticoagulants) were further screened for specific etiology through further investigations related to the suspicion, including antinuclear antibodies, interferon-gamma release assay (quantiferon test) for tuberculosis, Chest CT scan, appropriate virological test, blood and pericardial or other biological fluid cultures and polymerase-chain-reaction search for viral or mycobacterial genome.

The following variables were then compared in the two groups (cases aged 65 years and older; controls younger than 65): age at onset; number of relapses and duration of disease; clinical presentation at first attack; absolute number of blood leukocyte count; percentage and absolute number of blood neutrophil counts; percentage and absolute number of lymphocyte count; maximum CRP value; comorbidities and possible use of anticoagulant drugs; need for pericardiocentesis; medical therapy for pericarditis assigned at first diagnosis of pericarditis (NSAIDs, colchicine, corticosteroids, anakinra).

Statistical analysis

Assuming a prevalence of chest pain of 80% in young subjects and a prevalence of 50% in older adults in the first attack of acute pericarditis according to previous data,[11] with a case: control ratio of 1, a sample of patients equal to 110 allows to obtain a probability of error of Type I (alpha) equal to 0.05 and Type II (beta) equal to 0.10 with a power of the study equal to 90%. Similarly, assuming a prevalence of dyspnea of 50% in young subjects and a prevalence of 70% in older adults with a case: control ratio of 1, a sample of patients equal to 248 allows to obtain a probability of error of Type I (alpha) equal to 0.05 and Type II (beta) equal to 0.10 with a power of the study equal to 90%. Thus, a total population of at least 124 older adults and 124 young adult patients is appropriate and consistent with the study primary aims. Statistical analysis of the data was performed using the SPSS computer program (version 28.0.1.0, IBM, New York, NY, USA). The assignment of missing values, especially for some laboratory variables such as leukocyte count and its differential formula, is based on a Predictive Mean Matching model of multiple imputation, performing up to 50 iterations. In the descriptive analysis, continuous variables with a normal distribution were expressed by the mean and standard error (SE), continuous variables with a non-normal distribution by the median and interquartile range (IQR), and categorical variables by absolute and relative frequency, unless otherwise stated. To remark the differences between the two populations for each variable, the chi-square test for categorical variables and the Mann–Whitney *U* test for continuous variables were performed. Univariate correlation with the two groups under study for each categorical variable was studied with the Cochran–Mantel–Haenszel test, while Student's *t*-test was used for continuous ones. The statistical significance threshold used was 0.05. As a sensitivity analysis, we also defined correlations between continuous variables in the presence of missing values for comparison. Confidence intervals were not adjusted for multiplicity. Next, having defined the individual correlations for each variable under study and after identifying those that were statistically significant, a multivariate analysis was set up to define the independence for each variable in correlation with patient age: therefore, the variables were included in a generalized linear model (GLM) with binomial distribution with a prohibit function, setting a significance level of 0.95.

RESULTS

We analyzed 133 patients aged 65 years and older affected by recurrent pericarditis (cases) and 142 controls (younger than 65 years). The samples (cases and controls) were homogeneous by gender: respectively 73 men (55%) in cases and 74 men (52%) in controls; median age at first attack (IQR) was 73 (68–78) years in cases versus 39 (34–50) in controls. Median follow-up (IQR) from the first

TABLE 1 Comparison of cases (patients aged 65 years and older) and controls (younger than 65 years) according to comorbidities.

	Cases ($N = 133$), N (%)	Controls ($N = 142$), N (%)	p value[a]
Comorbidities[b]	115 (86.5%)	55 (38.7%)	**<0.001**
COPD	24 (18.0%)	5 (3.5%)	**<0.001**
Type 2 diabetes	30 (22.6%)	4 (2.8%)	**<0.001**
Hypothyroidism	22 (16.5%)	9 (6.3%)	**0.013**
AH	98 (73.7%)	19 (13.4%)	**<0.001**
AF	44 (33.1%)	2 (1.4%)	**<0.001**
Acute MI	19 (14.3%)	7 (4.9%)	**0.008**
CKD	34 (25.6%)	7 (4.9%)	**<0.001**
Previous cancer	18 (13.5%)	10 (7.0%)	0.075
IBD	1 (0.8%)	1 (0.7%)	0.963
HF	22 (16.5%)	4 (2.8%)	**<0.001**
Oral anticoagulants	35 (26.3%)	3 (2.1%)	**<0.001**
GI bleeding	10 (7.5%)	1 (0.7%)	**0.004**
Previous heart surgery	18 (13.5%)	8 (5.6%)	**0.025**
Smoking habit	18 (13.5%)	34 (23.9%)	**0.040**
Creatinine mg/dL—median (IQR)	1.02 (0.90–1.22)	0.81 (0.70–0.96)	**<0.001**
eGFR mL/min—median (IQR)	69.68 (51.35–81.60)	106.91 (88.32–115.64)	**<0.001**

Abbreviations: AF, atrial fibrillation; AH, arterial hypertension; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; GI, gastro intestinal; HF, heart failure; IBD, inflammatory bowel disease; IQR, interquartile range; MI, myocardial infarction.

[a]For categorial variables, Pearson's chi-square test, $p < 0.05$; for continuous variables, Mann–Whitney U test, $p < 0.05$.

[b]Expressed as absolute number (%); significant p values are highlighted in bold type.

attack to the last observation was 12 months[7–24] in the older adults and 22 months (10–52) in the younger ($p < 0.001$). As expected, comorbidities were preponderant in older adults: respectively 86.5% versus 38.7% ($p < 001$) (Table 1). Among the comorbidities analyzed, chronic obstructive pulmonary disease (COPD), Type 2 diabetes mellitus, hypothyroidism, arterial hypertension, atrial fibrillation, clinical history of acute myocardial infarction, chronic renal failure, previous diagnosis of malignancy, congestive heart failure, use of anticoagulants, previous gastrointestinal bleeding, and previous cardiac surgery were significantly more prevalent in the elderly. Cigarette smoking was more frequent in controls. As expected, creatinine values were higher in the older adults and consequently eGFR was lower in the older adults: respectively 69.68 mL/min versus 106.91 mL/min ($p < 0.001$). Idiopathic recurrent pericarditis was the most common etiology in the majority of cases in both samples (respectively 87.2% in cases vs 88.7% in controls), while PCIS was recorded in 12.8% of cases and 11.3% of controls. Twenty-eight patients (10.2% of patients), 18 in older adults (13.4%) and 10 in younger adults (7.1%), experienced cardiac tamponade at clinical presentation ($p = 0.082$, OR = 2.03, 95% CI 0.9–4.58); 6 more patients underwent pericardiocentesis due the severity of the condition and diagnostic purposes; pericardiocentesis was significantly more common in older adults (Table 2).

In all patients who underwent pericardiocentesis, the general chemistry and cellular characteristics of the pericardial fluid were characterized by high levels of nucleated cells, protein, albumin and LDH, at levels consistent with inflammatory exudates.[13] No significant differences were observed in the quality of pericardial fluid between young and older adults, but the small number of samples analyzed does not allow definitive conclusions. Four or more recurrences were more frequent in controls (respectively 29.6% in younger patients vs 14.3% in older adults, $p = 0.003$) (Table 2). Mean number of recurrences (95% CI) was 7.7 (6.0–9.4)/100 patients-months in subjects younger than 65 years, versus 6.3 (5.3–7.2) in subjects 65 years and older ($p = 0.128$). Mean time (95% CI) from the first attack to the first recurrence was 193.8 (63.6–323.9) days in subjects younger than 65 years, versus 83.7 (52.5–114.9) days in subjects 65 years and older ($p = 0.093$). We then considered the clinical presentation of pericarditis in the first attacks, that is usually the more intense, in the two samples (Table 2). Particularly in the older adults, the onset symptom was mainly represented by dyspnea (respectively 54.1% vs 10.6%; $p < 0.001$) while

TABLE 2 Comparison of patients aged 65 years and older and younger than 65 years by number of recurrences, by symptoms at onset, by type of effusion, for the severity of pericardial effusion, and by therapies.

Variables[a]	Cases ($N = 133$), N (%)	Controls ($N = 142$), N (%)	Odds ratio (95% CI)	p value[b]
Number of recurrences				
1 recurrence	45 (33.8%)	38 (26.8%)	1.40 (0.83–2.35)	0.202
2 recurrences	34 (25.6%)	32 (22.5%)	1.18 (0.68–2.05)	0.557
3 recurrences	35 (26.3%)	30 (21.1%)	1.33 (0.76–2.33)	0.312
4 or more recurrences	19 (14.3%)	42 (29.6%)	**0.40 (0.22–0.73)**	**0.003**
Symptoms				
Dyspnea	72 (54.1%)	15 (10.6%)	**9.99 (5.30–18.85)**	**<0.001**
Chest pain	43 (32.3%)	114 (80.3%)	**0.12 (0.07–0.20)**	**<0.001**
Both	18 (13.5%)	13 (9.2%)	1.55 (0.73–3.31)	0.254
Fever	46 (33.8%)	76 (53.5%)	**0.44 (0.27–0.72)**	**0.001**
Pleural effusion	74 (55.6%)	49 (34.5%)	**2.38 (1.46–3.87)**	**<0.001**
Pericardial effusion	120 (90.2%)	119 (83.8%)	1.78 (0.86–3.69)	0.118
Grade of pericardial effusion				
Mild (<10 mm)	35 (26.3%)	58 (40.8%)	**0.52 (0.31–0.86)**	**0.011**
Moderate (10–20 mm)	53 (39.8%)	43 (30.3%)	1.53 (0.93–2.51)	0.097
Severe (>20 mm)	32 (24.1%)	18 (12.7%)	**2.18 (1.16–4.12)**	**0.016**
Cardiac tamponade	18 (13.4%)	10 (7.1%)	2.03 (0.90–4.58)	0.082
Pericardiocentesis	22 (16.5%)	12 (8.5%)	**2.15 (1.02–4.53)**	**0.042**
Ascites	11 (8.3%)	10 (7.0%)	1.19 (0.49–2.90)	0.702
Therapy at the first attack				
NSAIDs	85 (63.9%)	114 (80.3%)	**0.44 (0.25–0.75)**	**0.003**
Colchicine	102 (76.7%)	124 (87.3%)	**0.48 (0.25–0.90)**	**0.023**
Steroids	66 (49.6%)	38 (26.8%)	**2.70 (1.63–4.46)**	**<0.001**
Anakinra	19 (14.3%)	34 (23.9%)	**0.53 (0.28–0.98)**	**0.044**

Note: The bold values represent statistically significative differences.
Abbreviation: NSAIDs, non-steroidal anti-inflammatory drugs.
[a]Expressed as count (%).
[b]Cochran–Mantel–Haenszel test, $p < 0.050$.

TABLE 3 Comparison of patients aged 65 years and older and younger than 65 years according to laboratory data.

Laboratory test[a]	Cases ($N = 133$)	Controls ($N = 142$)	Differences (95% CI)	p value[b]
Leukocytes at onset (/mm^3) (IQR)	10,227 (289)	11,208 (285)	**981 (185 to 1777)**	**0.016**
Neutrophils at onset (/mm^3) (IQR)	7611 (295)	8325 (272)	713 (−73 to 1500)	0.076
Lymphocytes at onset (/mm^3) (IQR)	1666 (90)	1759 (65)	92 (−127 to 312)	0.435
CRP (mg/L) (IQR)	92.72 (6.65)	100.15 (7.40)	7.43 (−12.07 to 26.93)	0.457

Note: The bold values represent statistically significative differences.
Abbreviations: CRP, C-reactive protein; IQR, interquartile range.
[a]Expressed as mean (ES).
[b]*T*-Student test for paired data, $p < 0.050$.

chest pain prevailed in controls (respectively 80.3% vs 32.3%; $p < 0.001$). In a few cases, both were present (13.5% of the older adults and 9.2% of the young adults; $p = 0.254$). In contrast, fever (>38°C) was more present in the younger patients. In the older adults, there was also a higher occurrence of pleural effusion and moderate (10–20 mm) to severe pericardial effusion (>20 mm maximal telediastolic size) with a higher prevalence of mild

TABLE 4 Multivariate analysis performed using significant variables identified in univariate analysis.

Variables used as predictors	Adjusted odds ratio	95% CI	*p* value[a]
Prevalent symptoms			
Dyspnea	**3.45**	**1.06–11.25**	**0.040**
Chest pain	**0.19**	**0.21–0.55**	**0.002**
Fever >38°C	**0.44**	**0.21–0.94**	**0.034**
Grade of pericardial effusion			
Mild (<10 mm)	0.45	0.20–1.00	0.051
Severe (>20 mm)	1.76	0.63–4.89	0.278
Pleural involvement	1.94	0.92–4.10	0.082
Four or more recurrences	**0.34**	**0.14–0.85**	**0.021**
Need for pericardiocentesis	0.80	0.24–2.73	0.725
Therapies			
NSAIDs	1.43	0.57–3.55	0.444
Colchicine	**0.36**	**0.14–0.90**	**0.028**
Steroids	**4.44**	**1.94–10.15**	**<0.001**
Anakinra	0.53	0.21–1.31	0.167
Leukocytes at onset	**1.01**	**1.00–1.01**	**0.010**

Note: The bold values represent statistically significative differences.
Abbreviation: NSAIDs, non-steroidal anti-inflammatory drugs.
[a]Generalized linear model, binomial distribution, logit function, $p < 0.050$.

pericardial effusion in younger patients (Table 2). Pericardiocentesis was more frequently performed in the older adults than in the young adults. In contrast, there was no statistically significant difference regarding ascites. Regarding laboratory data (collected at the first pericarditis attack), leukocytes were higher in the younger, with a prevalence of neutrophils (Table 3). There was no statistically significant difference regarding CRP values in the two samples, although this value was slightly higher in the younger subjects (100.15 ± 7.40 mg/L in the <65 vs 92.72 ± 6.65 mg/L in the >65). NSAIDs were less commonly used in the older adults compared with young adults, as well as colchicine; on the other hand, corticosteroids were more frequently administered in the older adults. Mean initial dosage of corticosteroids (95% CI) was significantly higher in subjects younger than 65 years: 27.5 (23.3–31.8) mg prednisone/equivalent, versus 22.4 (20.1–24.7) mg in subjects 65 years and older ($p = 0.024$). Tapering was usually similar, and according the guidelines.[1] Finally, the use of anakinra was higher in controls (Table 2). In multivariable analysis (Table 4), we confirmed the differences in clinical presentation between the two groups: younger patients were more prone to four relapses (aOR 0.34, 95% CI 0.14 to 0.85, $p = 0.021$), with fever (aOR 0.44, 95% CI 0.21 to 0.94, $p = 0.034$) and chest pain (aOR 0.19, 95% CI 0.21 to 0.55, $p = 0.002$) as the most frequent onset symptoms; in the older adults dyspnea (aOR 3.45, 95% CI 1.06 to 11.25, $p = 0.040$) was the most common complaining symptom. However, the degree of pericardial effusion and the presence of pleural effusion did not differ between the two groups. For management and prophylaxis of new episodes, colchicine was more commonly administered to younger patients (aOR 0.36, 95% CI 0.14 to 0.90, $p = 0.028$) while steroid therapy was more commonly administered in the older adults (aOR 4.44, 95% CI 1.94 to 10.15, $p < 0.001$).

The outcomes were similar in both groups in term of death (0 vs 0) and permanent pericardial constriction requiring pericardiectomy (0 vs 0), while a higher prevalence of cardiac tamponade and pericardiocentesis was observed in older adults (see Table 2); all the patients are still on active pharmacological treatment at the last follow-up.

DISCUSSION

Our study is the first to address recurrent pericarditis in the older adults. We found that older adults affected by recurrent pericarditis show a different clinical pattern compared to younger subjects, with more frequent dyspnea, pleural effusion, severe pericardial effusion, and lower fever and lower leukocyte count, sometimes making the diagnosis challenging. They underwent pericardiocentesis more frequently. Older adults received

significantly less NSAIDs and colchicine, likely due to comorbidities; they were also treated less commonly with anti-IL1 agents, and more frequently with corticosteroids. We also observed no significant gender differences in cases versus controls. These results are in line with what has been observed in the first attack of pericarditis.[11,14]

As expected, comorbidities were more commonly represented in the older adults. In particular, chronic kidney disease was predictably more represented in cases, where creatinine levels were significantly higher. In our opinion, this inevitably led to repercussions at the time of therapeutic choice and could underlie what was observed in the differences between therapeutic approaches in the two samples: the high percentage of older adults treated with corticosteroids instead of NSAIDs. The more frequent use of corticosteroids in older patients is not related to a more severe disease course (mean number of recurrences/100 patients-months not significantly different) but in our practice is related to the difficulty in using high-dose of NSAIDs and colchicine in these subjects. On the other hand, we observed that the initial dosage of steroids administered to older adults was significantly lower than that administered to younger adults, and this, in our practice, is related to comorbidities that prevented the use of higher doses of steroids.

The observation of a higher number of recurrences in patients under younger than 65 could be related to several factors: their longer life expectancy after the first attack and longer duration of follow-up, but also to a different individual response with a stronger inflammatory component in the young. The shorter duration of follow-up in the older adults we observed might be related to several factors, including age-related difficulties and comorbidities that likely affected negatively the possibility of attending regular follow-up visits, particularly if the referral center was located in a distant area.

An important finding that emerged is the peculiar presentation of pericarditis in older adults. Differently from what is reported in the 2015 ESC Guidelines on the general population,[1] older adults showed a lower prevalence of chest pain (32.3%) and a greater frequency of dyspnea and pleural involvement. Although it should be noted that in the older adults there are numerous factors that may contribute to the development of pleural effusion and dyspnea, particularly heart failure and renal failure, it is necessary to take dyspnea into account as a possible presenting symptom of pericarditis in the evaluation of these patients.

In clinical presentation, fever exceeding 38°C appears to be more common in younger patients. This could be explained by the reduction in the immune response seen in the older adults, as evidenced by recent works on immunosenescence.[15] Correlating this finding with laboratory results (lower levels of leukocytes and neutrophils in the older adults), it can be assumed that the older adults group is more prone to develop forms of systemic involvement characterized by dyspnea, pleural effusion, and a lower tendency to develop fever than in young individuals, making the clinical condition more difficult to identify. This highlights the difficulty in diagnosing pericarditis with systemic involvement in older adults and underscores the need for a specific evaluation for this subgroup of patients aged 65 years and older.

Therefore, in older adults with dyspnea, even in the absence of chest pain, but with pleural effusion (often accompanied by moderate-to-severe pericardial effusion), elevated CRP with or without leukocytosis, with or without fever, the diagnosis of pericarditis should be considered. This presentation may represent a unique profile of pericarditis more typical of the older adults.

The finding of a lower frequency of fever, lower levels of leukocytes and different/atypical clinical presentation does not represent an unexpected finding, and is common in geriatric medicine, where it is known that presentations of many types of diseases may differ in older adults as compared to younger subjects (autoimmune, infectious, cardiovascular, etc.).[16–21]

It also emerges that there was a greater use of corticosteroids in cases compared with controls, and NSAIDs and colchicine were administered less frequently. This finding could reflect both the inability to administer NSAIDs and colchicine to patients with chronic renal failure and other comorbidities or polypharmacy with potential drug interactions with colchicine,[22] which are more frequently encountered in the older adults. We also observed that anakinra was administered less frequently in the older adults, even though anti-IL-1 agents might have a specific role in older adults with comorbidities[12] as they can be used in subjects with concomitant renal failure, heart failure, ischemic heart disease, fluid overload, recent surgery, anticoagulation, or gastrointestinal hemorrhages.[23] Considering the comorbidities of the older adults, it is important to note that low-dose colchicine has been approved by the FDA to reduce the risk for cardiovascular events in adult patients with established atherosclerotic cardiovascular disease, based on the results of the COLCOT and LODOCO2 studies.[24,25] Overall, the cardiovascular safety profile of anti-IL-1 agents and colchicine is superior to that of NSAIDs other than aspirin and corticosteroids.[23–26]

A recent review[27] highlighted how pericardial effusion is practically ubiquitous in isolated pericarditis of viral etiology, affecting all patients, and giving rise to conditions of cardiac tamponade, especially in older adults; in agreement with these findings, we found a

higher prevalence of cardiac tamponade and pericardiocentesis in older patients.

In the era of the progressive development of antibiotic resistance, it is also important to observe some differences between what was observed in our case series and what was reported by a recent review on cases of bacterial pericarditis, specifically caused by Methicillin-Resistant *Staphylococcus aureus*. In this review the authors observed a peak incidence around 48 ± 16 years in the adult population. In pericarditis of bacterial origin, not only is pericardial effusion almost ubiquitous, but tamponade is also a particularly frequent event. Similarly, age-related comorbidities may impact the clinical course in Methicillin-Resistant *Staphylococcus aureus* Pericarditis.[28]

We observed that in older adults the leukocytosis is not as pronounced as in younger adults. This is in line with what has been observed in immunosenescence phenomena[15] but also is similar to what has been recorded in tuberculous pericarditis.[18] Patients suffering from tuberculous pericarditis, contrary to what is observed in older adults suffering from recurrent idiopathic pericarditis, often present weight loss and frequent HIV co-infection. Another peculiar aspect that recurrent idiopathic pericarditis in older adults has in common with tuberculous pericarditis is the presence of dyspnea; however, dyspnea is often accompanied by cough in patients with Mycobacterium Tuberculosis infection, which however is not frequently found in patients with idiopathic pericarditis.[29] Tuberculosis should always be considered in the differential diagnosis of recurrent pericarditis in older patients, since atypical presentations of both conditions may overlap. Detailed clinical history collection, physical examination and appropriate tests should be considered, including interferon-gamma release assay (quantiferon test), culture and polymerase chain reaction (PCR) for genome in sputum and other available biological fluids, adenosine deaminase testing in pericardial or pleural fluid, eventually chest CT scan.

This study has some strengths and limitations. The retrospective nature can be listed among the limitations of this study, which included Caucasian patients only. In addition, the data were drawn from a sample able to attend visits in an outpatient service, i.e., patients who are not bedridden, at least self-sufficient, and not burdened with other comorbidities necessitating hospitalization or a high care burden.

Despite these drawbacks, this is the first study specifically focusing on the older adults with recurrent pericarditis. Our data allowed us to identify the most frequent clinical and laboratory features in the older adults, useful for clinicians dealing with older adults with recurrent pericarditis.

Although pericarditis is still considered a relatively rare condition, probably because of an underestimation of its true incidence,[4,5] larger multi-ethnic studies are needed also in the older adults group.

CONCLUSIONS

Data from this study suggest the clinical and laboratory characteristics of older adults patients with recurrent pericarditis are distinct from those seen in younger subjects, based on the largest sample of geriatric patients analyzed to date. The most typical features in the group of patients aged 65 and older appear to be dyspnea as a symptom of onset (even without chest pain), pleural effusion (a clinical and radiological sign), often accompanied by moderate-to-severe pericardial effusion, elevated CRP with milder leukocytosis, and a lower frequency of fever compared to younger individuals. This profile of pericarditis presentation should be considered during the evaluation of older adults with dyspnea and pleural effusion, as well as in the follow-up of patients with known recurrent pericarditis as they age.

AUTHOR CONTRIBUTIONS

All authors contributed significantly to this work.

CONFLICT OF INTEREST STATEMENT

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