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RESEARCH LETTER

Adverse Prognosis in Patients With Postcardiac Injury Syndrome–Related Recurrent Pericarditis

Effect of Gender

Postcardiac injury syndrome (PCIS) is a common cause of recurrent pericarditis (RP).[1] RP secondary to PCIS, especially if untreated, can lead to complications such as further recurrences, constriction, and cardiac tamponade.[2] Therefore, the aim of this retrospective cohort study is to report a detailed analysis of factors associated with poor outcomes in PCIS-related RP.

Consecutive patients (n = 77) seen at our center from January 1, 2012, through December 31, 2019, with a history of RP secondary to PCIS (electrophysiology procedures, myocardial infarction, and postcardiotomy) were included. RP was diagnosed in patients who had a recurrence of pericarditis symptoms after a 4- to 6-week symptom-free interval following an initial episode of acute pericarditis. The primary outcome was clinical remission. Clinical remission was defined as cessation of nonsteroidal anti-inflammatory drugs, colchicine, immunotherapy (steroids, biologics, and disease-modifying antirheumatic drugs) and no further recurrences as defined by the absence of clinical, laboratory, echocardiographic, and electrocardiographic findings of pericarditis for at least 90 days. Therapy duration and intensity were based upon serial imaging (echocardiography, cardiac magnetic resonance imaging) and serial inflammatory markers (C-reactive protein, erythrocyte sedimentation rate) in conjunction with clinical response. This study was approved by the institutional review board at the Cleveland Clinic.

Multivariable Cox proportional hazard models were used to examine associations with outcomes. Covariates were chosen based on biological plausibility and univariate analysis with $P < 0.10$. Included covariates were sex, steroids, PCIS etiology, and number of prior recurrences. A 2-sided P value of <0.05 was considered statistically significant, and the assumption of proportional hazards was satisfied.

The mean age of our cohort was 51 ± 15 years with 57% being females (n = 44). The cohort was composed of primarily postcardiotomy patients (n = 39, 51%) followed by post-electrophysiology (n = 34, 44%) and post-myocardial infarction (n = 4, 5%) patients. The median duration of follow-up was 18 (Q1, Q3: 11, 36) months. The median number of recurrences was 3 (Q1, Q3: 2, 5). The median high-sensitivity C-reactive protein was 1.2 (Q1, Q3: 0.5, 4.4) mg/L. None to mild late gadolinium enhancement on cardiac magnetic resonance was seen in 86% of patients (n = 57), whereas moderate to severe late gadolinium enhancement was present in 14% of patients (n = 9). At baseline, 62 (81%) patients were on nonsteroidal anti-inflammatory drugs, 68 (88%) patients were on colchicine, and 34 (44%) were on corticosteroids. The total number of patients who achieved clinical remission was 37 (48%) in a median time of 43 months. After multivariable adjustment, female sex (HR: 0.41, 95% CI: 0.20-0.82, $P = 0.012$), number of prior recurrences (HR: 0.80, 95% CI: 0.64-0.99, $P = 0.038$), and corticosteroid use (HR: 0.41, 95% CI: 0.19-0.91, $P = 0.027$) were associated with less clinical remission (Table 1).

Limited data are available regarding risks associated with worse outcomes in PCIS-related RP, and this analysis demonstrated that females, the number of prior recurrences, steroids, and cardiotomy are associated with higher risk. To our knowledge, this is the first description of the association of female sex with adverse outcomes in PCIS-related RP. The pathophysiology of PCIS-related RP is not well understood and is likely related to an inappropriate innate immune response following pericardial injury. Given the morbidity associated with PCIS-related RP, there is a need to identify patients at increased risk to guide appropriate prophylaxis and management.[3,4] Limitations of the current study include the small sample size and single-center retrospective cohort study design. Furthermore, due to the relatively small sample size, there is some concern for possible overfitting, however, our study is the largest to date of RP in PCIS patients. Further studies with larger sample sizes are needed to confirm our findings.

TABLE 1 Baseline Clinical Characteristics and Outcomes

Baseline Characteristics	Overall (n = 77)	Female (n = 44)	Male (n = 33)	*P* Value[a]
Age, y	51 (15)	53 (17)	47 (10)	0.060
Total pericarditis episodes	3.00 (2.00-5.00)	3.00 (2.00-5.00)	3.00 (2.00-5.00)	0.51
PCIS etiology				0.59
Postcardiotomy	39 (51)	20 (45)	19 (58)	
Post-EP	34 (44)	21 (48)	13 (39)	
Post-MI	4 (5.2)	3 (6.8)	1 (3.0)	
Pericardial window	12 (16)	8 (19)	4 (12)	0.44
Pericardiocentesis	15 (19)	11 (25)	4 (12)	0.16
Hypertension	30 (40)	16 (37)	14 (44)	0.57
Diabetes mellitus	4 (5.3)	3 (7.0)	1 (3.1)	0.63
Congestive heart failure	6 (8.0)	3 (7.0)	3 (9.4)	>0.99
COPD	1 (1.3)	1 (2.3)	0 (0)	>0.99
Atrial fibrillation	16 (21)	9 (21)	7 (22)	0.92
Chronic kidney disease	2 (2.7)	2 (4.7)	0 (0)	0.50
MRI – LGE				0.72
None or mild	57 (86)	32 (84)	25 (89)	
Moderate or severe	9 (14)	6 (16)	3 (11)	
NSAIDs	62 (81)	34 (77)	28 (85)	0.41
Colchicine	68 (88)	39 (89)	29 (88)	>0.99
Steroids	34 (44)	21 (48)	13 (39)	0.47
DMARDs	5 (6.5)	3 (6.8)	2 (6.1)	>0.99

Outcome (Clinical Remission)	HR	95 CI	*P* Value
Sex (female)	0.41	0.20-0.82	0.012
Total pericarditis episodes	0.80	0.64-0.99	0.038
Steroids	0.41	0.19-0.91	0.027
PCIS etiology (post-EP)	2.25	1.06- 4.77	0.034

Values are n (%) or median (IQR) unless otherwise indicated. [a]Wilcoxon rank sum test; Fisher's exact test; Pearson's chi-squared test.

COPD = chronic obstructive pulmonary disease; DMARD = disease-modifying antirheumatic drug; LGE = late gadolinium enhancement; MRI = magnetic resonance imaging; NSAID = nonsteroidal anti-inflammatory drug; PCIS = postcardiac injury syndrome; post-EP = post-electrophysiology procedures.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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