Original Article

Prevalence and Prognostic Significance of Pericardial Effusion in Native Valve Endocarditis Based on Data From the Iranian Registry of Infective Endocarditis (IRIE)

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ABSTRACT

Background: The presence of pericardial effusion (PE) in the setting of infective endocarditis (IE) may be a sign of more severe IE. In this study, we aimed to determine the prevalence and prognostic significance of PE in patients with native valve IE.

Methods: The Iranian Registry of Infective Endocarditis (IRIE) is a single-center observational hospital-based study of patients with IE. Between 2002 and 2015, all patients with a diagnosis of IE who had been enrolled in the IRIE were evaluated.

Results: A total of 445 patients (68.3% male) were enrolled in this registry, and 221 (49.7%) patients had PE. PE was more prevalent in the patients with native valve IE and those with right-heart involvement (65% in right-heart IE vs 50% in left-heart IE; *P*=0.002). The rate of in-hospital mortality was 20% and 19.2% in the patients with and without PE, respectively, and the presence of PE was not a predictor of in-hospital death in our multivariate analyses. Additionally, there was no relationship between the rates of IE-related complications and the severity of PE. However, the prevalence of PE was higher in the patients with right-sided IE as well as in those with aortic root abscess and systemic emboli at presentation.

Conclusions: The prevalence of PE in the setting of IE was relatively high in the present study. Most cases of PE had mild effusion, and there was no relationship between the severity of PE and IE-related complications as well as in-hospital mortality. ***(Iranian heart Journal 2018; 19(2): 36-43)***

KEYWORDS: Infective endocarditis, Pericardial effusion

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Infective endocarditis (IE) is an infection of the myocardial tissue which predominantly involves the heart valves. IE has a poor prognosis, with an in-hospital mortality rate of 15% to 20%. [1-3] IE may cause several types of cardiac complications such as heart failure as the result of valvular insufficiency, perivalvular abscesses, intracardiac fistulae, myocardial infarction, aneurysms, and aortic dissection. [3,4] The pericardium can also be involved in IE. The presence of pericardial effusion (PE) in the setting of IE may be a sign of more severe IE. The prevalence of pericardial involvement has been reported from 20% in pathologic studies to more than 50% in echocardiographic-based studies. Although PE is a prevalent finding in IE, tamponade and purulent PE are very rare. The inflammatory process, peri-annular invasion, development of heart failure, and infection itself can cause PE in the setting of IE. [5-12]

In patients with native valve IE, PE is more common in younger patients and those who suffer from renal insufficiency. It has been shown that intravenous drug abuse and right-sided endocarditis are more common in patients with mild-to-moderate PE than in other groups of patients with IE. [6]

The Iranian Registry of Infective Endocarditis (IRIE) is a single-center observational hospital-based study of IE patients admitted to Rajaie Cardiovascular, Medical, and Research Center—a tertiary center for cardiovascular medicine in Tehran, Iran. In the present study, we aimed to determine the prevalence and prognostic significance of PE in patients with native valve IE enrolled in the IRIE

METHODS

Between 2002 and 2015, all patients with a definitive diagnosis of IE who had been admitted to our center were enrolled in the IRIE. Data on admission and throughout the hospital course were collected by an expert registry team. The presence of PE on admission or its development during the hospital course was checked via echocardiographic data. The assessment of the severity of PE was based on the recommendations of the American Society of Echocardiography. [13]

All the data were recorded in dedicated software designed by the Medical Intelligent Technology Team of Rajaie Cardiovascular, Medical, and Research Center. The recorded data were controlled by a trained team and expert cardiologists every day.

The study was approved by the institutional ethics and research committee, and informed consent was obtained from all the participants.

Statistical Analysis

IBM SPSS statistics, version 19, for Windows (IBM Corp, Armonk, NY, US) was applied for all the statistical analyses. The Kolmogorov–Smirnov test was used to assess the normal distribution of the variables. The categorical data were presented as counts (percentages) and the continuous variables as means (standard deviations [SDs]).

The Student *t*-test was used to compare the continuous data, and the χ^2 test was applied for the categorical data. The logistic regression analysis (binary regression analysis/low likelihood with backward elimination) was employed for multivariable analysis. A *P* value smaller than 0.05 was considered statistically significant.

RESULTS

A total of 445 patients (68.3% male) with a definitive diagnosis of IE were enrolled in the current study. The mean (SD) of age was 45.1 (16.3 [between 17 and 93 y]). Detailed data regarding the IRIE will be presented later.

Among the 445 patients suffering from IE, 221 (49.7%) had PE. Table 1 depicts the demographic and clinical characteristics of the IE patients with PE. Approximately, 55% of the patients had PE on admission and the rest had developed PE during their disease course. The

mean (SD) of age in the patients with PE was 43.4 (15.9), and 70% of them were male.

PE was significantly more prevalent in the patients with native valve IE than in those with prosthetic valves or device-related endocarditis (54% vs 36.5%, respectively; *P*=0.01).

Among the 221 patients with PE, 34 (15.4%) had IE of the prostatic valve or the intracardiac device and 187 (84.6%) had native valve IE. Twenty of the 187 patients had a history of rheumatic heart disease, and 58 of them had congenital heart disease.

Bicuspid aortic valve and patent ductus arteriosus were the most common diagnoses among the patients with congenital heart disease. The rest of the patients had diagnoses of degenerative valve diseases, including mitral valve prolapse or non-rheumatic valvular dysfunction (stenosis or regurgitation). Eleven patients had multi-valve IE.

Figures 1 to 3 depict the pattern of the cardiac abnormalities in the patients with or without PE. The pattern of the valvular disorders (rheumatic or non-rheumatic) as well as the congenital heart anomalies was not different between the patients with PE and those without PE. However, the prevalence of PE was significantly higher in the patients with degenerative valvular heart disease than in the other groups (*P*=0.03).

Table 2 presents comparisons of the vegetation locations in the patients with and without vegetation. PE was significantly more prevalent in the patients who had vegetation on their tricuspid valve (*P*<0.001).

Table 1. Demographic and clinical characteristics of the infective endocarditis patients with pericardial effusion (N=221)

Characteristic	Value
Gender, number (%) (male/female)	155(70)/ 66(30)
Age, y, mean (SD)	43.4(15.9)
Left-sided native valve endocarditis, n (%)	139(62.9)
Right-sided native valve endocarditis, n (%)	57(25.8)
Left-sided prosthetic valve endocarditis, n (%)	24(10.9)
Right-sided prosthetic valve endocarditis, n (%)	7(3.2)
Device-related endocarditis, n (%)	3(1.4)
Endocarditis in intravenous drug abusers, n (%)	41(18.6)

Table 2. Comparisons of vegetation locations between the patients with pericardial effusion and those without it

Vegetation Location	Pericardial Effusion number (%)		*P* value
	Yes, n=187	No, n=224	
Mitral valve	71(37.9)	92(41)	0.1
Aortic valve	72(38.5)	93(41.5)	0.5
Tricuspid valve	47(25.1)	24(10.7)	<0.001
Pulmonary valve	7(1.3)	4(1.7)	0.6

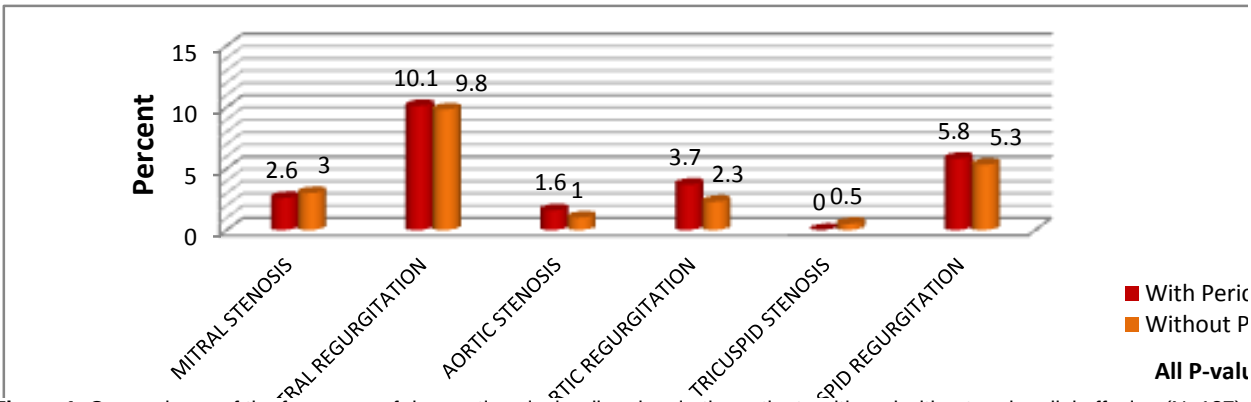

Figure 1. Comparisons of the frequency of rheumatic valvular disorders in the patients with and without pericardial effusion (N=187)

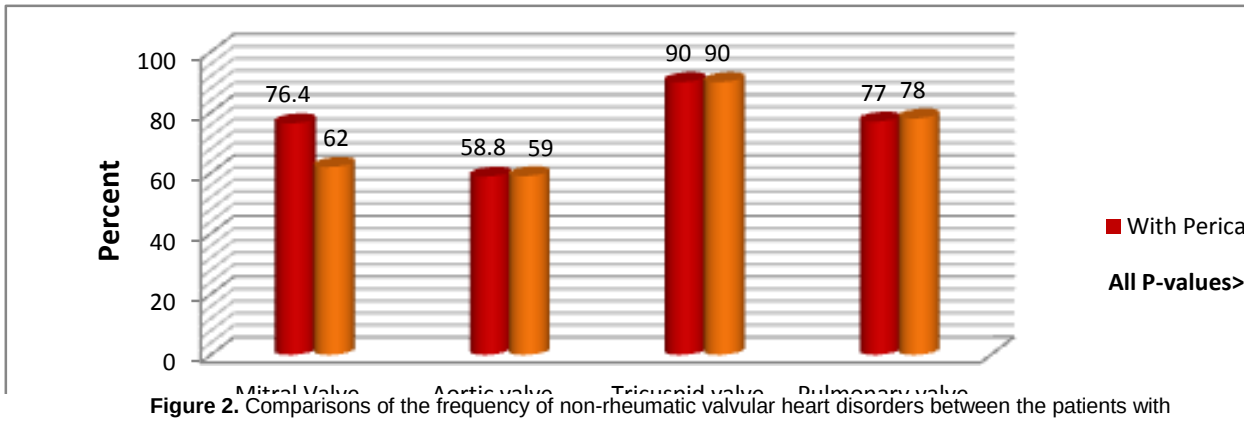

Figure 2. Comparisons of the frequency of non-rheumatic valvular heart disorders between the patients with pericardial effusion and those without it (N=187)

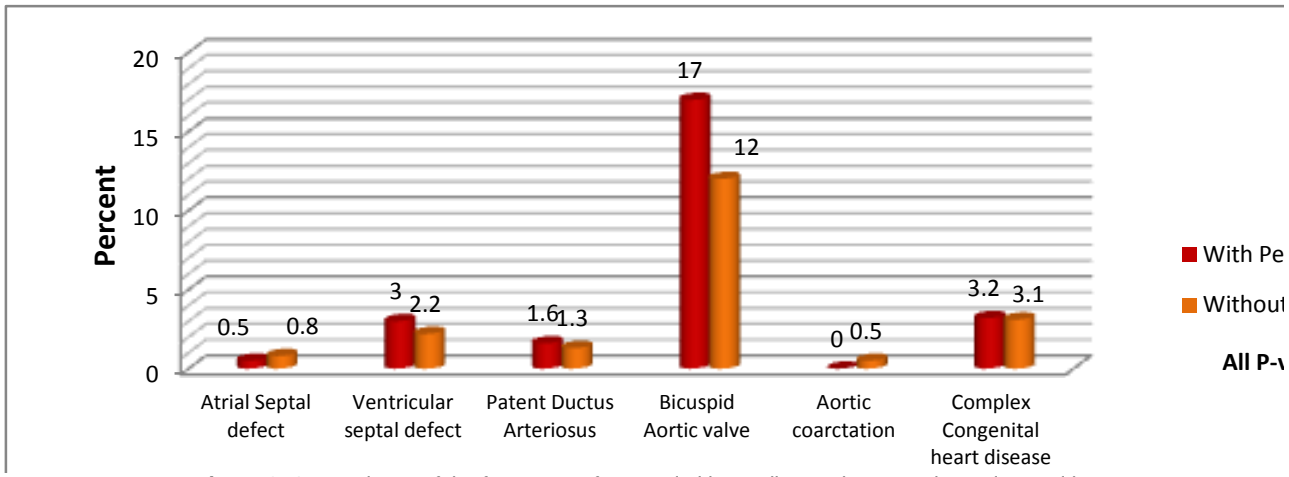

Figure 3. Comparisons of the frequency of congenital heart disease between the patients with pericardial effusion and those without it (N=187)

Severity of PE

PE was mild in 73% of the patients, moderate in 20%, and severe in 7%. Tamponade was diagnosed in 15 (3.4%) patients.

PE was significantly more prevalent in the patients with right-heart involvement (65% in right-heart IE vs 50% in-left heart IE; *P*=0.002). Nonetheless, moderate-to-severe and severe PE (more-than-moderate PE) was 1.8 times more prevalent in the patients with left-heart involvement than in those with right-heart involvement (28.3% vs 15.7%; *P*<0.001). More-than-moderate PE was more commonly seen in the patients with aortic and mitral valve IE. The prevalence of aortic and mitral valve IE in the patients with more-than-moderate PE was 40% and 34%, correspondingly. Regarding right-heart involvement, moderate-to-severe PE and severe PE were seen in 11 (22%) and 2 (4%) patients with tricuspid and pulmonary valve IE, respectively.

The incidence of tamponade was also higher in the patients with left-heart IE. (87.5% of the patients with tamponade had left-heart IE.)

Complications of native valve IE in the patients with PE

Table 3 shows the rate of native valve IE complications in the patients with or without PE. The rates of 4 complications—namely embolic events (*P*=0.002), aortic root abscesses

(*P*=0.004), lung abscesses (*P*=0.005), and need for surgical interventions (*P*<0.001)—were significantly higher in the patients with PE than in the rest of them.

There was no significant difference regarding the other complications such as renal failure, cardiac fistulae, myocardial aneurysm, pseudoaneurysms, heart failure, splenic or brain abscesses, brain emboli, and death between the 2 groups. Moreover, in-hospital mortality was not different between the patients with and without PE (20% vs 19.2% in the patients with and without PE, respectively).

However, there was no relationship between the severity of PE and the development of complications, and the rates of the complications mentioned in Table 3—including in-hospital death—were not higher in the patients with more-than-moderate PE (All *P*s>0.05).

Table 3. Comparisons of native valve infective endocarditis-related complications between the patients with pericardial effusion and those without it

Complication	Pericardial Effusion , number(%)		*P* value
	Yes	No	
Dehiscence	7(3.6)	10(5.4)	0.3
Abscess	24(12.8)	11(4.9)	0.02
Embolic event on presentation	68(36.3)	41(18.3)	0.002
History of renal failure	15(8)	10(10.8)	0.3
Renal failure during admission	63(33.6)	56(25)	0.4
Cardiac fistula	12(6.4)	8(3.6)	0.3
Aortic root abscess	22(11.7)	7(3.1)	0.004
Intramyocardial abscess	0	1(0.5)	0.4
Pseudoaneurysm	21(11.2)	16(7.1)	0.3
Heart failure	17(9)	24(10.7)	0.2
Splenic abscess	14(7.4)	13(5.8)	0.8
Brain abscess	4(2.1)	3(1.3)	0.7
Lung abscess	26(15)	10(4.5)	0.005
Mycotic aneurysm	6(3.2)	3(1.3)	0.3
Brain emboli	20(10.6)	17(7.6)	0.5
Surgical intervention	136(72.7)	88(39.3)	<0.001
Death	39(20)	43(19.2)	0.6

Independent predictors of more-than-moderate PE

A binary logistic regression model was applied to find the independent predictors for more-than-moderate PE. It showed that mitral valve involvement, aortic valve involvement, history of intravenous drug abuse, valvular dehiscence, and presence of fistulae were the predictors of more-than-moderate PE (Table 4). Additionally, the logistic regression analysis revealed that the presence of more-than-moderate PE could be an independent predictor of need for surgery (β=1.48, *P*=0.03, OR [95% CI]=4.4 [1.1 to 17.4]). However, many of the surgeries were due to pericardial drainage in the patients with impending to tamponade. The multivariate analysis also showed that the presence of more-than-moderate PE could not be an independent predictor for in-hospital mortality. Table 5 shows the independent predictors of mortality in the patients with native valve IE.

Table 4. Independent predictors of more-than-moderate pericardial effusion in the patients with infective endocarditis

No	Variable	Beta	Sig.	Odds Ratio (95% CI)
1	Intravenous drug abusers infective endocarditis	1.212	.035	3.359(1.1-10.3)
2	Vegetation site mitral valve	-1.417	.008	0.24(0.09-0.7)
3	Vegetation site aortic valve	-1.214	.026	0.29(0.1-0.9)
4	Dehiscence	2.059	.036	7.8(1.1-53.6)
5	Cardiac fistula	1.575	.020	4.8(1.2-18.3)

Table 5. Independent predictors of mortality in the patients with infective endocarditis

No	Variable	Beta	Sig.	Odds Ratio (95% CI)
1	Left-sided native valve infective endocarditis	-1.351	.007	0.26(0.09-0.7)
2	Intravenous drug abusers	-2.323	.002	0.09(0.02-0.4)
3	Presence of vegetation	-1.452	.009	0.23(0.07-0.7)
4	Mitral vegetation	1.229	.010	3.4(1.3-8.6)
5	Renal failure	1.366	.002	3.9(1.7-9.1)
6	Heart failure	1.466	.025	4.3(1.2-15.5)

DISCUSSION

In our study, the prevalence of PE in patients with IE was approximately 50%. The prevalence of PE was higher in the patients with native valve IE than in those with prosthetic valve IE. There are limited studies regarding PE in the setting of IE, and most of them are case reports or case series with small sample sizes. In these studies, the prevalence of PE was between 8% and 50%. [4,6-12,14,15] Considering the large sample size of our study, the current prevalence may be more acceptable.

In the present study, most cases of PE were mild and the involvement of the right-heart valves may be a predisposing factor for PE. We also found a high prevalence of PE among the patients who had intracardiac abscesses secondary to their IE. It seems that right-sided heart failure secondary to the presence of abscesses and inflammatory processes in the heart tissue may increase the chance of the development of PE. In a study by Reid et al, [7] the prevalence of PE was 54% and inflammatory response, heart failure, periannular complications, and infection itself were considered the predisposing factors of PE.

Regarding in-hospital mortality and IE-related complications, we found no relationship between PE and in-hospital mortality of IE in the current study. The rate of in-hospital mortality was 20% and 19.2% in the patients with and without PE, respectively, and the presence of PE was not a predictor of death in the multivariate analyses. We also found no relationship between the rates of IE-related complications and the severity of PE; however, the prevalence of PE was higher in the patients with right-sided IE as well as in those with aortic root abscesses and systemic emboli at presentation. Further, the chance of surgical interventions showed an increase in the patients with PE—particularly during the first days of admission.

There are conflicting data regarding the severity of PE and the rate of mortality and/ or complications in the setting of IE. Regeurio et al [6] studied 457 patients with IE between 1990 and 2007 and found that massive PE could be a predictor for late mortality (mortality after a year). In their study, 23% of the patients with IE had mild-to-moderate PE and massive PE was seen in only 2% of the study population. The authors also found a high rate of intravenous drug abuse and right-sided IE among the patients with PE and reported that the rates of periannular abscesses and systemic emboli were higher in the patients who had massive PE. The predisposing factors of PE in the study by Regeurio and colleagues included native valve involvement, renal failure, and lower age.

The prevalence of PE in a study by Reid et al [7] was 54%. The authors reported no in-hospital mortality in their patients with PE. They had 2 cases of surgical drainage of tamponade, and there was no difference between the patients with or without PE in terms of IE-related complications except for more prolonged fevers in those with PE.

In a case report, Chang et al [9] reported a patient with aortic valve IE and massive PE. In our study, although the prevalence of PE was higher in the patients with aortic root abscesses, there was no relationship between the severity of PE and aortic valve involvement.

Study Limitations

The utilization of registry-based data is the strength of the present study. Nevertheless, the absence of long-term follow-up information is a limitation of this study. The IRIE is an ongoing registry, and the patients who have been included since 2015 have been followed up for 2 years now. Comprehensive data regarding this registry, including the follow-up information, will be presented later.

In conclusion, the prevalence of PE in the setting of IE was relatively high in the current study. Still, most of the cases were mild and there was no relationship between the severity of PE and IE-related complications and/or in-hospital mortality. Further studies are needed to clarify the prognostic significance of PE in the long term.

Conflict of Interest: None declared.

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This study was approved by the Ethics Committee of Rajaie Cardiovascular, Medical, and Research center, and the patients gave informed consent.

This paper has not been published or submitted in any other journal, and all the authors have read and approved the manuscript and have no disclosures to admit.

The authors herewith disclose that this study has no relationship with industry and financial associations and no competing interest has been declared.

REFERENCES

1. Hoen B, Duval X. Infective Endocarditis. New England Journal of Medicine. 2013;368(15):1425-33. PubMed PMID: 23574121.

2. Cahill TJ, Prendergast BD. Infective endocarditis. The Lancet. 2016 2016/02/27/;387(10021):882-93.

3. Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG, Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis–Prospective Cohort Study. Archives of internal medicine. 2009;169(5):463-73.

4. Mocchegiani R, Nataloni M. Complications of Infective Endocarditis. Cardiovascular & Hematological Disorders-Drug Targets. 2009;9(4):240-8.

5. Perdekamp M, Serr A, Hench J, Mattern D, Bohnert M. Hemopericardium caused by endocarditis ulcerosa: an unusual cause of sudden death in adolescence. Archiv fur Kriminologie. 2001;210(5-6):158-66.

6. Regueiro A, Falces C, Cervera C, del Rio A, Paré JC, Mestres CA, et al. Risk factors for pericardial effusion in native valve infective endocarditis and its influence on outcome. The American journal of cardiology. 2013;112(10):1646-51.

7. Reid CL, Rahimtoola SH, Chandraratna P. Frequency and significance of pericardial effusion detected by two-dimensional echocardiography in infective endocarditis. The American journal of cardiology. 1987;60(4):394-5.

8. Alió-Bosch J, Tornos-Mas M, Soler-Soler J. Cardiac tamponade as an initial clinical presentation of infective endocarditis. International journal of cardiology. 1987;14(3):373-6.

9. Chang K, Seung K-B, Shin W-S, Kim P-J, Ihm S-H, Lee D-G, et al. Infective endocarditis of the aortic valve complicated by massive pericardial effusion and rupture of a sinus of valsalva into the right atrium. Journal of the American Society of Echocardiography. 2004;17(8):910-2.

10. Katz LH, Pitlik S, Porat E, Biderman P, Bishara J. Pericarditis as a presenting sign of infective endocarditis: two case reports and review of the literature. Scandinavian journal of infectious

diseases. 2008;40(10):785-91.

11. Ribeiro P, Shapiro L, Nihoyannopoulos P, Gonzalez A, OAKLEY CM. Pericarditis in infective endocarditis. European heart journal. 1985;6(11):975-8.

12. Rose RL, Higgins LS, Helgason AH. Bacterial endocarditis, pericarditis and cardiac tamponade∗. The American journal of cardiology. 1967;19(3):447-51.

13. Klein AL, Abbara S, Agler DA, Appleton CP, Asher CR, Hoit B, et al. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. Journal of the American Society of Echocardiography. 2013;26(9):965-1012. e15.

14. Arita M, Kusuyama Y, Takatsuji M, Kawazoe K, Masuyama Y. Septal myocardial abscess and infectious pericarditis in a case of bacterial endocarditis. Japanese circulation journal. 1985;49(4):451-5.

15. Arnett EN, Roberts WC. Valve ring abscess in active infective endocarditis. Frequency, location, and clues to clinical diagnosis from the study of 95 necropsy patients. Circulation. 1976;54(1):140-5.