Effusive-Constrictive Pericarditis: Doppler Findings

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Abstract

Purpose of Review To review the echo-Doppler findings in effusive-constrictive pericarditis (ECP). ECP corresponds to the coexistence of a hemodynamically significant pericardial effusion and markedly reduced compliance of the pericardium, manifested by constrictive physiology post-pericardiocentesis.

Recent Findings We summarize herein the recent observations regarding the prevalence of ECP based on echocardiography as well as the pre- and post-pericardiocentesis echo-Doppler features of ECP. ECP diagnosed by echocardiography was seen in approximately 15% of patients with ECP pre- and post-pericardiocentesis echo-Doppler findings sharing features with both cardiac tamponade and constrictive pericarditis.

Summary ECP post-pericardiocentesis is common but its natural history in the current era might be better than previously reported. Further studies and (particularly simultaneous echocardiography-cardiac catheterization) are still critically needed to better understand the underlying hemodynamics of ECP. Moreover, it remains to be determined whether pre- and post-pericardiocentesis echo-Doppler findings can be used to prognosticate or to guide therapy of those undergoing pericardiocentesis.

Keywords Effusive-constrictive pericarditis · Cardiac tamponade · Constrictive pericarditis · Doppler echocardiography

Introduction

Although the initial descriptions of coexistent effusive and constrictive features in an individual patient dates more than half a century [1–3], the delineation of effusive-constrictive pericarditis (ECP) as a distinct clinical entity was not formally done until the seminal work of Hancock [4] and Sagrista-Sauleda [5]. Reflecting the practice of their time, the diagnosis of ECP was predicated on an invasive hemodynamic evaluation. Transthoracic echocardiography is now the diagnostic modality of choice in patients with suspected or established pericardial diseases [6, 7] and diagnostic cardiac catheterization is reserved for a select group of patients. Our group has recently described

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the prevalence of ECP based on echocardiographic criteria [8••] as well as the pre- and post-pericardiocentesis echo-Doppler features of ECP. We will provide herein a summary of these echo-Doppler findings, contrasting them to those of cardiac tamponade and constrictive pericarditis (CP).

Pathophysiology and Epidemiology

In patients with ECP, there is concomitant hemodynamically significant pericardial effusion and significant reduction of pericardial compliance due to pericardial inflammation [9••, 10]. In these individuals, as the pericardial fluid is drained and intrapericardial pressure falls, the features of cardiac tamponade resolves and those of CP surface. As a consequence, in ECP, central venous pressure (i.e., right atrial pressure) fails to normalize post-pericardiocentesis. The persistence of elevated central venous pressure post-pericardiocentesis is the hemodynamic signature of ECP and the origin of the diagnostic criteria for ECP on cardiac catheterization: failure of the mean right atrial pressure to drop below 10 mmHg or by 50% or more post-pericardiocentesis [5]. However, this can also be observed at the bedside, and actually persistently elevated jugular venous pressure following pericardiocentesis should be the first clue that ECP is present.

Although ECP is frequently described as the conversion from tamponade to CP physiology post-pericardiocentesis, these three clinical entities are actually part of a spectrum ranging from classic cardiac tamponade (purely effusive hemodynamics) to chronic, irreversible CP (inelastic scarring of the pericardial sac). In fact, the absence of typical cardiac tamponade features in patients with ECP has been reported among both invasive and noninvasive cohorts. It is not surprising then that ECP shares hemodynamic and diagnostic features of both these entities. It should be noted that this clinical spectrum also includes transient constriction (Fig. 1), which corresponds to CP cases that are responsive to inflammatory therapy, thus foregoing the need for surgical pericardiectomy.

It remains unclear why some patients presenting with pericardial effusions will develop ECP. However, it appears that bloody effusions are more prevalent in patients with ECP [4, 5], supporting the traditional notion that the presence of blood in the pericardial space leads to a more exuberant inflammatory response, further reducing pericardial compliance. In addition, patients with tuberculosis-related pericarditis and ECP had more elevated levels of interferon-gamma and interleukin-10 in the pericardial fluid than those not showing features of ECP [11]. In a cohort of individuals with non-tuberculous pericardial effusions, we observed that neutrophil counts were higher in those with ECP versus the non-ECP group, also suggesting a more exuberant inflammatory response in the latter [8••].

The reported prevalence of ECP has varied from as low as 1–2% [5, 12] to greater than 50% [13, 14•], reflecting the heterogeneity in the populations and methodologies (invasive versus noninvasive diagnostic criteria) of the cited studies. Despite this wide range, the higher prevalence of ECP among patients with tuberculous pericarditis when compared with other etiologies has been a consistent finding. In a recently published series of 205 patients undergoing pericardiocentesis
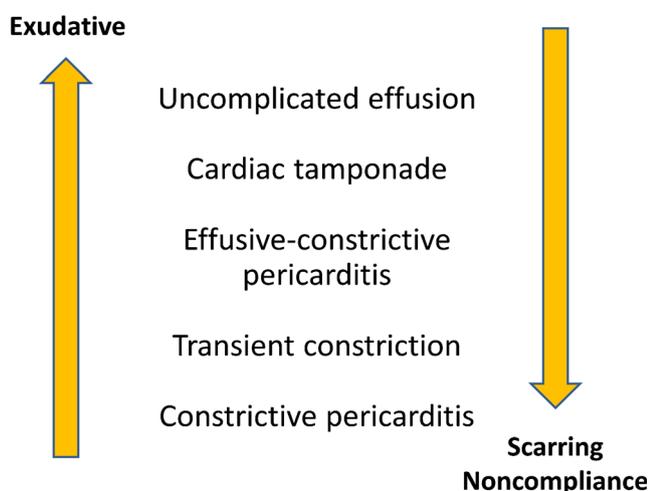
at our institution [8••], the overall prevalence of ECP diagnosed by transthoracic echocardiography was 16%. Post-cardiac surgery and percutaneous procedure-related pericardial effusions corresponded to the majority of cases, accounting for more than 50% of cases combined. Interestingly, our etiologic observations contributing to ECP closely parallel that of chronic CP among US patients undergoing pericardiectomy in the current era [10]. Other etiologies of ECP include purulent pericarditis, trauma, neoplastic involvement, and end-stage renal disease [13], but hypothetically any inflammatory disease involving the pericardium could lead to ECP.

Echo-Doppler Findings in ECP

Traditionally, the diagnosis of ECP has relied on cardiac catheterization data; however, this poses a challenge in contemporary clinical practice since right heart catheterization is no longer routinely performed for the diagnosis of cardiac tamponade at most institutions. Therefore, similar to its invasive diagnosis, it has been proposed that the presence of typical echo-Doppler features of CP following pericardiocentesis would be indicative of ECP [15–17]. In addition to a potential noninvasive diagnostic role, TTE might also add prognostic information in ECP through surveillance and disease monitoring.

The diagnostic performance of echocardiography was assessed in 32 patients with tuberculosis-related pericardial effusions undergoing pericardiocentesis and right heart catheterization [14•]. The authors defined the echocardiographic criteria as respirophasic septal shift or ≥ 25% inspiratory variation in the mitral early diastolic (E) velocities; according to these criteria, echocardiography had a sensitivity of 81% and a specificity of 75% for diagnosing ECP.

The prevalence of typical echo-Doppler features in patients of ECP was assessed in a cohort of 205 consecutive patients undergoing pericardiocentesis [8••], with ECP being present in 16% of patients. Noteworthy, the diagnosis of ECP in this study was based on post-pericardiocentesis echocardiographic findings and defined by the presence of variations in early diastolic mitral inflow velocity (E) > 25% associated with at least one of the following: expiratory diastolic flow reversal of hepatic veins, respirophasic ventricular septal shift (shifting of ventricular septum towards the right ventricle upon inspiration with the septum bulging towards the left ventricle upon expiration), increased early diastolic mitral septal annular velocity (e′) and to a level higher than that of the lateral e′. Post-pericardiocentesis, patients with ECP had shorter mitral deceleration times and higher medial and lateral e′ velocities than those without ECP. It should be highlighted that dilatation of the inferior vena cava and respirophasic septal shift were almost universal in patients with ECP (seen in 100% and 97% of individuals, respectively). Increased hepatic vein Doppler

Exudative

Uncomplicated effusion

Cardiac tamponade

Effusive-constrictive pericarditis

Transient constriction

Constrictive pericarditis

Scarring Noncompliance

Fig. 1 Diagram illustrating the clinical spectrum of pericardial disorders

diastolic flow reversals with expiration appeared highly specific and were present in 82% of ECP patients compared with only 2% of the non-ECP group. Two-dimensional data other than septal motion can also be useful: a pericardial rind (diffusely thickened, echogenic pericardium) was significantly more prevalent in those with ECP than non-ECP patients (73% versus 19%). Figure 2 illustrates post-pericardiocentesis echo-Doppler findings in patient with ECP.

We have reported similar findings in a subsequent study of 22 patients with a diagnosis of ECP defined as a clinical documentation of persistently elevated jugular venous pressure following pericardiocentesis (performed for the treatment of cardiac tamponade) [9••]. Respirophasic septal shift was seen in 91% of ECP patients along with a much higher prevalence of dilated inferior vena cava (70% in the ECP compared with 26% in those with uncomplicated tamponade). A higher E/A ratio was also identified post-pericardiocentesis in the ECP group compared with non-ECP patients.

It is worth emphasizing that mild respiratory septal shift or minor variations in mitral E velocities are not uncommon following cardiac surgery as well as among those with cardiac tamponade and normalization of jugular venous pressure post-pericardiocentesis. Therefore, clinicians and echocardiographers should be cautious diagnosing ECP in those with subtle constriction findings, especially if a normal sized inferior vena cava (or normal jugular venous pressure) is present.

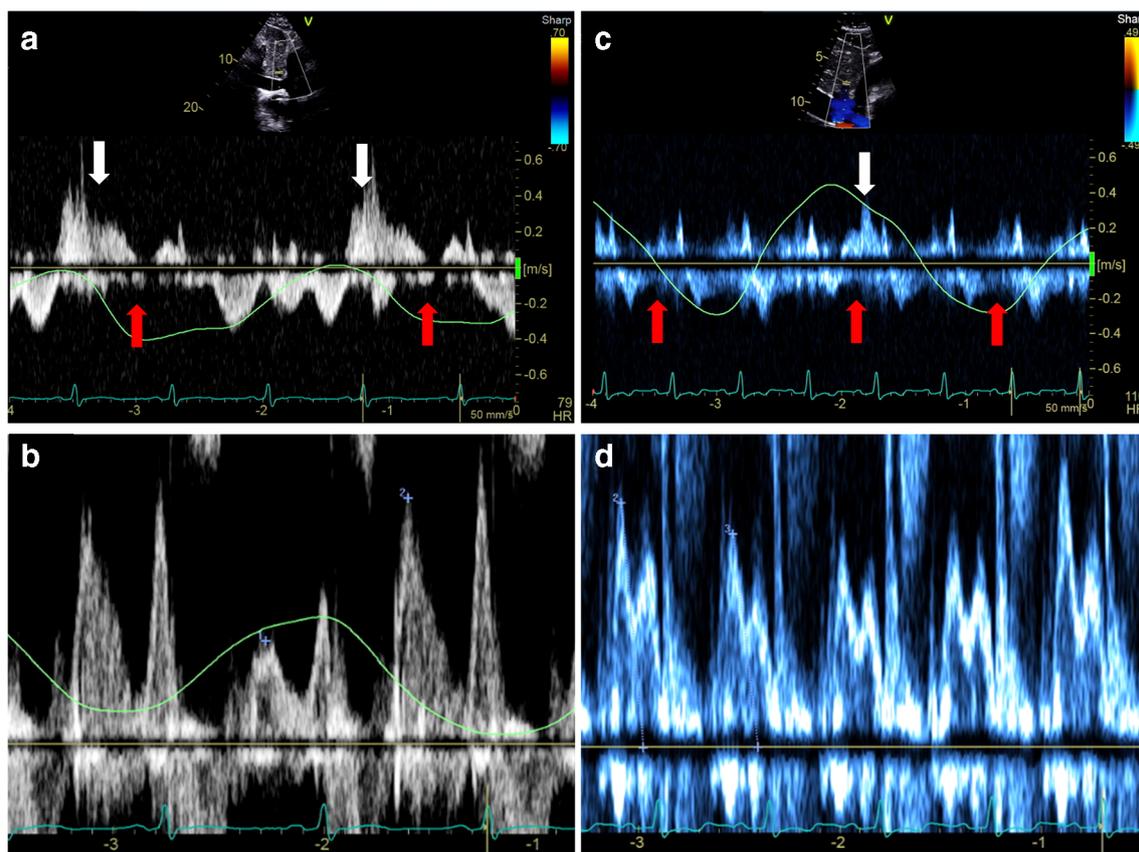## Pre-pericardiocentesis Echo-Doppler Findings in ECP

Despite not being the main focus of our initial study assessing the prevalence of ECP [8••], we noticed that not only post- but pre-pericardiocentesis findings also differed between ECP and non-ECP patients. ECP patients had higher septal e′ velocities and a higher prevalence of respirophasic shift, mitral inflow variation > 25%, and increased hepatic vein flow reversals compared with those without ECP. More complex pericardial effusions, such as loculated or fibrinous, were also more common in those with ECP. Interestingly, pericardiocentesis volume was smaller in those with ECP compared with those without ECP (median 388 ml versus 500 ml, respectively).

Prior to discussing in detail the pre-pericardiocentesis Doppler findings in ECP, a review of the underlying hemodynamics and typical Doppler features of cardiac tamponade [18, 19] and CP [15, 20] is mandatory. In cardiac tamponade, elevated intrapericardial pressure markedly impairs early diastolic ventricular filling despite elevation of both right and left atrial pressure. In
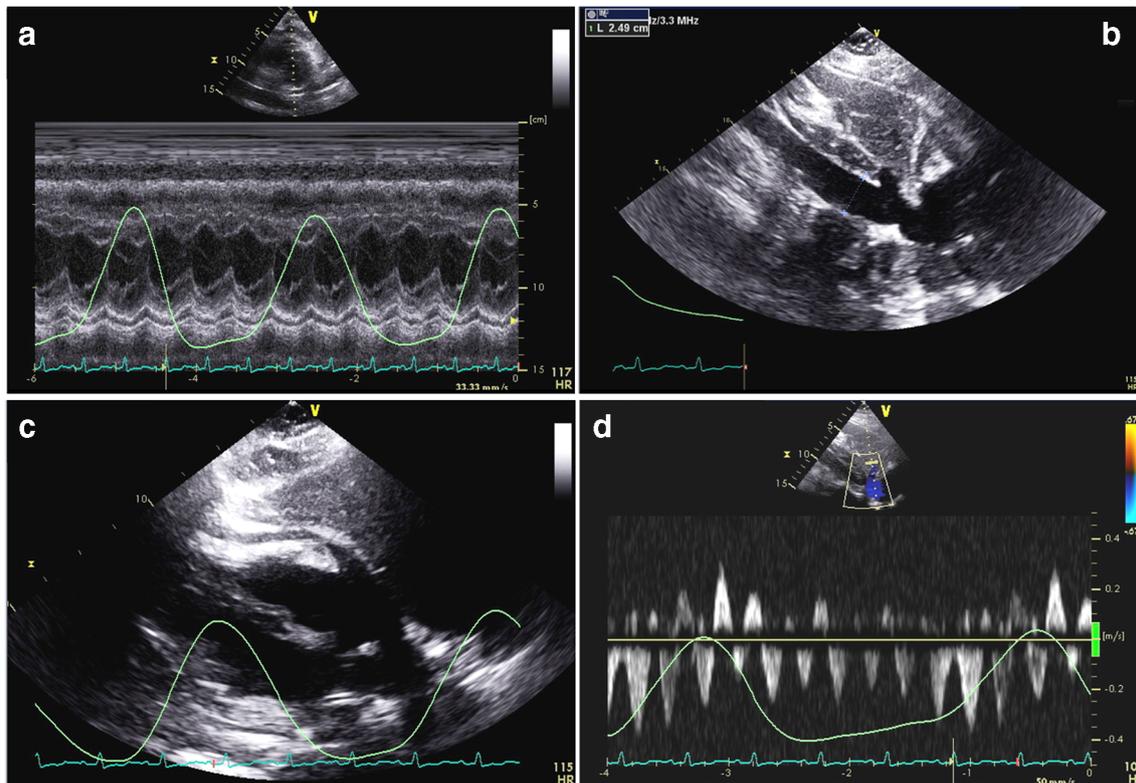
Fig. 2 Post-pericardiocentesis echo-Doppler findings in patient with ECP. M-mode demonstrates respirophasic septal shift (**a**). Subcostal imaging reveals a persistently dilated inferior vena cava (**b**) and a diffusely thickened, echogenic pericardium adjacent to the right ventricular with a residual pericardial effusion ("pericardial rind," **c**); increased expiratory reversals are seen on hepatic vein Doppler (**d**). The constellation of findings is diagnostic of effusive-constrictive pericarditis (simultaneous respirometer is shown in *green*; the upward deflection marks the onset of inspiration and downward deflection the onset of expiration)

Fig. 3 Pre-pericardiocentesis mitral inflow and hepatic vein Doppler findings in patients with cardiac tamponade and ECP. Hepatic vein Doppler shows increased expiratory reversals (*white arrows*) with markedly reduced diastolic forward flow (*red arrows*), consistent with impaired diastolic filling of the right ventricle both in cardiac tamponade (**a**) and ECP (**c**). However, mitral inflow showed an E/A ratio < 1 in the patient with tamponade (**b**) whereas diastolic filling prevails in the one with ECP (**d**) (simultaneous respirometer is shown in *green*; the upward deflection marks the onset of inspiration and downward deflection the onset of expiration)

contrast, in CP early diastolic filling of the ventricular is actually enhanced due to the elevated filling pressures but significantly decreases in mid-late diastole as pericardial reserve is reached. These differences are the origin of the classic cardiac catheterization findings in these two disorders: blunting of *y* descent in tamponade as opposed to the rapid ventricular filling waves of CP ("square root sign").

As Doppler findings are directly related to diastolic filling, patients with cardiac tamponade will show low (< 1) mitral E/A ratios [9••, 21], reflecting the underlying diminished mitral early diastolic flow; this is even more pronounced during inspiratory beats. Similarly, hepatic vein Doppler will demonstrate markedly reduced diastolic forward flow velocities, mirroring the blunted *y* descents seen on right atrial tracings (in fact, holodiastolic hepatic flow reversals are not uncommon in patients with tamponade). In contrast, patients with CP will show increased mitral E/A ratios (reflecting the predominance of mitral early diastolic flow) and prominent diastolic forward flow in the hepatic veins [22].

In our experience [9••], mitral inflow and hepatic vein Doppler data in ECP appear to be a hybrid of cardiac tamponade and CP, with ECP patients showing mitral E/A ratio and hepatic vein forward flow velocities that were intermediate to these two entities (Fig. 2). Interestingly, Hancock had described similar findings while analyzing right atrial morphology patterns, with the depth of right atrial *x* and *y* descents in ECP being intermediate between cardiac tamponade and CP. However, based on mitral inflow Doppler data, our findings suggest this to be the case not only for right but also left ventricular filling. It should also be highlighted that ECP patients had significantly reduced hepatic vein diastolic forward flow velocities and increased expiratory diastolic flow reversals, confirming that early ventricular filling is impaired despite increased venous pressure—the hallmark of tamponade physiology. The underlying hemodynamics remain to be fully elucidated, but it can be hypothesized that in ECP, the increased pericardial pressure leads to some blunting of the otherwise early prominent diastolic filling seen in CP, thus resulting in the intermediate findings between tamponade and CP. Figure 3 illustrates pre-pericardiocentesis mitral inflow and hepatic vein Doppler findings in patients with cardiac tamponade and ECP.

Fig. 4 Schematic summarizing mitral tissue Doppler, mitral inflow, and hepatic vein pulsed-wave Doppler findings in tamponade, effusive-constrictive pericarditis, and constrictive pericarditis. D, diastolic forward flow; DR, diastolic flow reversal; Exp, expiration; Insp, inspiration; S, systolic forward flow. (From: Miranda WR et al. Eur Heart J Cardiovasc Imaging 2019;20:298–306, by permission of Oxford University Press) [9••]
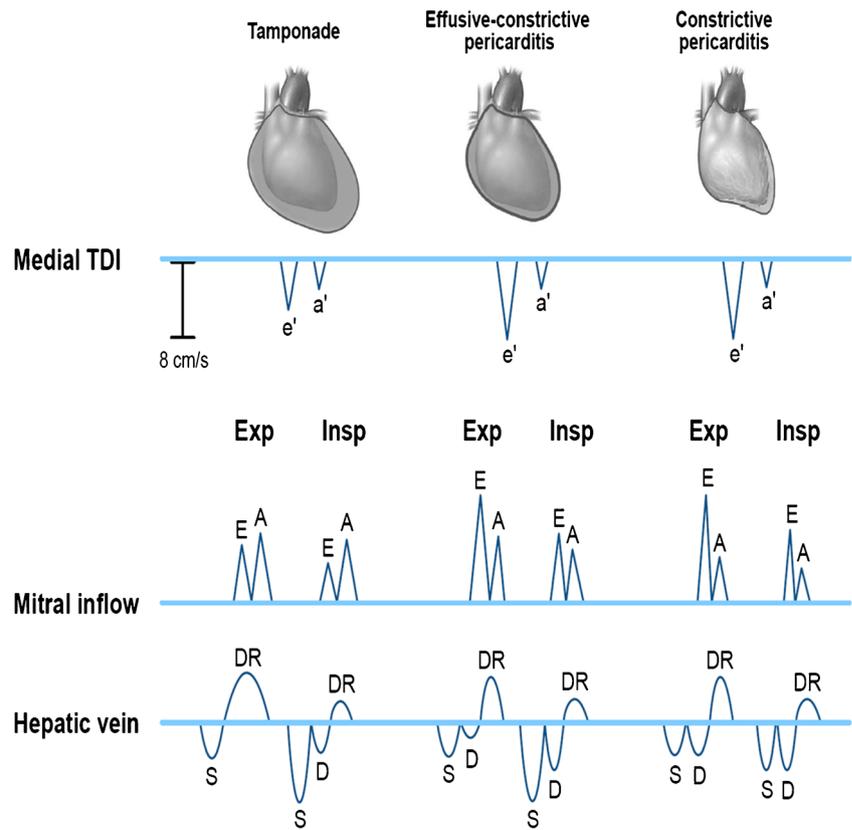
In agreement with our initial observations [8••], ECP patients showed higher medial mitral e′ velocities than those with cardiac tamponade (9.8 cm/s versus 6.2 cm/s, respectively). Although our results need to be validated in a large group of patients, they suggest that ECP patients might have a unique combination of echo-Doppler findings, including a mitral E/A ratio > 1, significantly reduced hepatic diastolic flow velocities with prominent expiratory diastolic flow reversals and preponderance of systolic forward flow, and, lastly, elevated mitral e′ velocities.

A summary of the typical echo-Doppler features of cardiac tamponade, ECP and CP are presented in Fig. 4 and Table 1.

Table 1 Summary of pre-pericardiocentesis echo-Doppler findings in cardiac tamponade and effusive-constrictive pericarditis as well in constrictive pericarditis

	Pure cardiac tamponade	Effusive-constrictive pericarditis	Pure constrictive pericarditis
Pericardial effusion	Variable in size, simple (circumferential, no strands)	Variable in size; complex (pericardial strands, sometimes loculated)	Absent
Respirophasic septal shit	Variable	Typically present	Present
Mitral inflow profile	Most often E < A	Most often E > A	E >> A
Medial mitral e′ velocity	Normal	Increased[2]	Increased[2]
Inferior vena cava[1]	Dilated; if not dilated, poorly collapsible	Dilated, poorly collapsible	Dilated, poorly collapsible
Hepatic vein expiratory diastolic reversals	Increased	Increased	Increased
Hepatic vein diastolic forward flow	Diminished, frequently absent during inspiration	Diminished	Increased

[1] Dilated inferior vena cava defined as ≥ 2.1 cm in expiration

[2] Medial mitral e′ velocity ≥ 0.09 m/s

Prognosis

Based on its initial description, ECP has been traditionally felt to be associated with a high incidence of pericardiectomy during follow-up [5] (up to 65% in some series [13]) due to persistent constrictive features. In our experience, the rates of pericardiectomy were lower than previously reported (6% in the cohort of ECP diagnosed based on echo-Doppler criteria [8••] and 14% of those with a clinical diagnosis of ECP [9••]). These findings are most likely explained by the increased recognition and more aggressive treatment of constrictive features in patients with pericardial effusions and/or tamponade in the current era. It should be noted that almost 20% of patients with an echocardiographic diagnosis of ECP were re-hospitalized for progressive dyspnea or heart failure symptoms during follow-up [8••]. Therefore, although the prognosis of ECP might be better than previously thought, these patients do require close follow-up.

Future Directions

Despite the significant advances in the diagnosis and management of pericardial diseases over the past 20 years, data regarding ECP remains very limited. Further studies and, particularly, simultaneous echocardiography-cardiac catheterization, are still critically needed to better understand the underlying hemodynamics of ECP and validate these observations. In addition, it remains to be determined whether pre- and post-pericardiocentesis echo-Doppler findings can be used to prognosticate or to guide therapy of those undergoing pericardiocentesis (for example identifying patients who will progress to pericardiectomy or who would benefit a specific therapy regimen—nonsteroidal inflammatory agents versus corticosteroids).

Conclusion

Echocardiography is currently the diagnostic modality of choice in the assessment of patients with pericardial diseases. ECP can be diagnosed by the presence of typical echo-Doppler features of CP following pericardiocentesis and might be suspected even before pericardial tap is performed based on echo-Doppler data. Although the rates of pericardiectomy appear to be lower in the modern era, patients with ECP remain at risk for future complications necessitating close follow-up and periodic echocardiographic surveillance as well as consideration of anti-inflammatory treatment after pericardiocentesis.

Compliance with Ethical Standards

Conflict of Interest William R. Miranda, Darrell B. Newman, and Jae K. Oh declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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•• Of major importance

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