JACC: CARDIOVASCULAR IMAGING VOL. 11, NO. 4, 2018

PUBLISHED BY ELSEVIER

EDITORIAL COMMENT

Ephemeral Effusive Constrictive Pathophysiology*

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Over 4 decades ago, Dr. Hancock reported a surgical series of patients with effusive constrictive pericardial disease, described as constriction involving the visceral pericardium in the presence of a tense pericardial effusion (1). In a patient with pericardial tamponade, the hallmark of effusive constrictive pathophysiology (ECP) has been a persistently elevated right atrial pressure after pericardiocentesis. Often, successful treatment required pericardiectomy and, if possible, included removal of the visceral pericardium.

Typically, the visceral pericardium (or epicardium) consists of only a single layer of mesothelial cells that rests on a basement membrane supported by fibrous tissue and elastic fibers (2). In effusive constrictive pericarditis, fibrosis can lead to adhesions between the parietal and visceral pericardium, a pathology similar to typical constrictive pericarditis. This inflammatory response can resolve or progress, which may lead to transient or permanent constrictive pathophysiology, respectively. Therefore, as opposed to being labeled as a separate disease, it is simpler to consider effusive constriction as one end of the spectrum of pericarditis with effusion and epicardial involvement as the predominant features (**Figure 1**).

From a clinical perspective, several important questions arise after pericardiocentesis for frank or impending tamponade. First, how should we diagnose ECP, and how do different diagnostic criteria influence the incidence? Second, what is the expected clinical course for these patients, and how many will require pericardiectomy? Finally, does a diagnosis of ECP inform subsequent anti-inflammatory treatment and outcome?

In this issue of *iJACC*, the paper by Kim et al. (3) provides insights into these important questions. The investigators performed a retrospective cohort study of 205 consecutive patients with pre- and post-pericardiocentesis echocardiograms at the Mayo Clinic between January 2006 and December 2007. From this cohort, 33 patients (16%) were diagnosed with effusive constrictive pericarditis. In these patients, echocardiographic features of constrictive pathophysiology were more common prior to pericardiocentesis, and only 2 patients eventually required pericardiectomy.

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First, Kim et al. (3) highlight that echocardiographic features of constrictive pathophysiology are more common prior to pericardiocentesis in patients eventually diagnosed with effusive constrictive pericarditis. In constrictive pathophysiology, distinguishing features can be classified into 2 domains—accentuated early diastolic filling and respirophasic ventricular interdependence (**Figure 1**). For patients with ECP, echocardiographic correlates of accentuated early diastolic filling, such as higher early diastolic medial mitral annular velocities (e′), and ventricular interdependence, such as respirophasic ventricular septal shift, are more common prior to pericardiocentesis. Of note, this association has not been previously described with invasive hemodynamics. These data highlight that a dedicated echocardiogram with a respirometer may be more sensitive for constrictive pathophysiology when compared with a standard right heart catheterization. Consequently, if clinical stability permits, echocardiography prior to pericardiocentesis may identify patients at risk for ECP.

Another interesting issue raised in this paper is a high reported incidence of ECP, approximately

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

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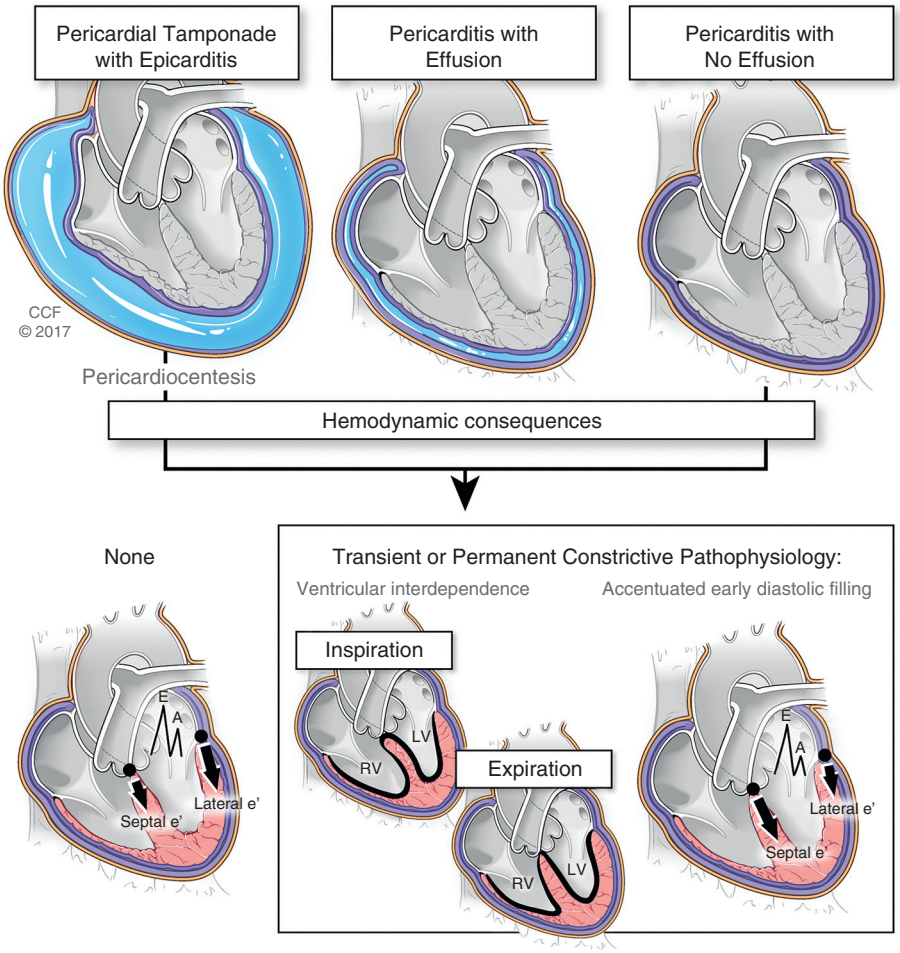
ISSN 1936-878X/$36.00 https://doi.org/10.1016/j.jcmg.2017.10.028

FIGURE 1 **Spectrum of Pericarditis**



A simplified approach to pericardial disease considers patients on a spectrum and approaches inflammation and hemodynamics separately. In pericarditis, the presence and size of the pericardial effusion may vary, as can the degree of visceral and parietal pericardial involvement. Pericarditis may result in either no hemodynamic consequences or lead to constrictive pathophysiology, characterized by ventricular interdependence and accentuated early diastolic filling. The constrictive pathophysiology may be transient, resolving spontaneously or with anti-inflammatory therapy, or may be permanent, possibly requiring pericardiectomy for successful treatment of heart failure. Reprinted with permission from the Cleveland Clinic Foundation for Medical Art & Photography © 2017. All Rights Reserved.

twice that of a previous report from a large cohort of patients with pericardial tamponade (4). In fact, the incidence of ECP has ranged widely, from 2% to 15%, in part reflecting differences in patient populations, methodologies, and definitions (5). Importantly, the current study is generalizable only to large referral centers in the developed world, not to practices with predominant tuberculous pericarditis, where ECP may be more common (6).

However, the patients in this cohort were generally similar to the previous report by Sagrista-Sauleda et al. (4), though the incidence in that study was slightly <8%. Most likely, this difference is attributable to different diagnostic criteria. In the study from Barcelona, patients had pericardial tamponade, and ECP was defined as failure of the right atrial pressure to decrease by 50%, or to a level below 10 mm Hg, after intrapericardial pressure was lowered to nearly 0 mm Hg with removal or pericardial fluid. In addition, patients had persistently elevated end-diastolic pressures and a characteristic dip and plateau morphology on heart catheterization after pericardiocentesis.

In the current Mayo study, not all patients had tamponade, and constrictive pathophysiology was defined by echocardiographic criteria. These criteria

are evolving, and in this study, ECP was defined as >25% respiratory variation in mitral inflow plus 1 of the following: expiratory diastolic flow reversal of hepatic veins; respirophasic interventricular septal shift; or augmented early diastolic septal e′ to a level higher than the lateral e′ annular velocity. Of note, this definition differs from previously proposed criteria from this group (7). More recently, respiratory variation in mitral inflow has not been emphasized for diagnosis, and specific thresholds have been used for mitral medial e′ velocities as well as ratios of expiratory diastolic hepatic vein reversal (8). The earlier period for this study (2006 to 2007) may explain the deviation from current criteria, but in general, echocardiographic definitions may be more sensitive than heart catheterization. Inevitably, the tradeoff for this increased sensitivity is less specificity, especially if less stringent criteria are employed.

This increased sensitivity may lead to a higher incidence of ECP with echocardiography, possibly identifying patients with mild or early disease. However, this hypothesis remains putative as only 1 patient in the current study had concomitant heart catheterization. Nonetheless, different diagnostic criteria will have implications regarding outcomes within a specific cohort. In the current study, only 2 of 33 patients with ECP eventually required pericardiectomy (3), compared with about one-half of ECP patients in the previous study by Sagrista-Sauleda et al. (4). If echocardiographic diagnosis identifies patients with less severe ECP, then the rate of pericardiectomy will also be less. In this respect, more information regarding symptoms after pericardiocentesis would have been helpful. Specifically, are there patients with ECP on echocardiography that remain without heart failure symptoms throughout clinical follow-up? These data would better delineate whether ECP on echocardiography is occasionally an imaging finding of uncertain clinical significance.

Moreover, these patients can develop symptoms related to active inflammation, right-heart failure, or both. After pericardiocentesis, as this paper highlights (3), the strength of echocardiography is related to the hemodynamics of constrictive pathophysiology, not the degree of pericarditis. For this assessment, even though cardiac magnetic resonance imaging is often informative (9), clinical criteria, such as underlying diagnosis, pleuritic chest pain, and elevated inflammatory markers are most helpful (10).

In the current study, anti-inflammatory therapy was prescribed in more than one-half of the patients. All but 2 of these patients, as well as all of the patients without anti-inflammatory therapy, had resolution of constrictive pathophysiology on follow-up echocardiography. These results highlight 2 important points. First, the risks for progression from transient to permanent constrictive pathophysiology are not well understood. Second, patients should not be taken prematurely to pericardiectomy as follow-up echocardiography after appropriate anti-inflammatory therapy often demonstrates resolution of constrictive pathophysiology.

In conclusion, the study by Kim et al. (3) provides valuable insights regarding echocardiography in patients after pericardiocentesis. Specifically, echocardiography seems particularly sensitive in diagnosing constrictive pathophysiology, though test characteristics compared directly with an invasive hemodynamic diagnosis have yet to be defined. Given the higher reported incidence of ECP in the current study by Kim et al. (3), echocardiography also likely identifies patients with more subtle hemodynamic perturbations. After successful pericardiocentesis, these patients may be especially likely to have a benign course with standard guideline-based therapies (10), and fortunately, many may never develop clinical sequelae of their ephemeral effusive constrictive pathophysiology.

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KEY WORDS echocardiography, effusive-constrictive pericarditis, pericardiocentesis