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FOCUS SEMINAR: PERICARDIAL AND MYOCARDIAL DISEASE

STATE-OF-THE-ART REVIEW

Complicated Pericarditis

Understanding Risk Factors and Pathophysiology to Inform Imaging and Treatment

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ABSTRACT

Most patients with acute pericarditis have a benign course and a good prognosis. However, a minority of patients develop complicated pericarditis, and the care of these patients is the focus of this review. Specifically, we address risk factors, multimodality imaging, pathophysiology, and novel treatments. The authors conclude that: 1) early high-dose corticosteroids, a lack of colchicine, and an elevated high-sensitivity C-reactive protein are associated with the development of complicated pericarditis; 2) in select cases, cardiovascular magnetic resonance imaging may aid in the assessment of pericardial inflammation and constriction; 3) given phenotypic similarities between recurrent idiopathic pericarditis and periodic fever syndromes, disorders of the inflammasome may contribute to relapsing attacks; and 4) therapies that target the inflammasome may lead to more durable remission and resolution. Finally, regarding future investigations, the authors discuss the potential of cardiovascular magnetic resonance to inform treatment duration and the need to compare steroid-sparing treatments to pericardiectomy. (J Am Coll Cardiol 2016;68:2311–28)

Compared with other cardiovascular diseases, pericarditis has garnered relatively little interest, in part due to the appropriate focus on reducing cardiovascular mortality. In recent decades, however, as mortality related to cardiac disease has continued to decrease (1), morbidity has become increasingly important. This trend coincides with an increased emphasis on pericarditis, a disease often characterized by significant morbidity. Although most patients with acute pericarditis will have resolution, some will develop incessant, recurrent, chronic, or constrictive pericarditis. Many of these patients experience a debilitating chronic disease, and to simplify presentation throughout this review, are referred to as having complicated pericarditis.

The improved understanding of complicated pericarditis is anchored in recent clinical trials, bolstered by better characterization of pericarditis with multimodality imaging, and better delineation of the underlying pathophysiology through molecular studies. Therefore, given the need for improved diagnosis and management of patients with complicated pericarditis, this review focuses on the following questions:

1. Which patients are at risk for complicated disease after acute pericarditis?
2. Which patients with complicated pericarditis benefit from multimodality imaging?
3. What is the pathological progression of pericarditis, and how is autoinflammatory pericarditis distinct from autoimmune pericarditis?

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

CT = computed tomography

ECG = electrocardiogram

IVIG = intravenous immunoglobulin

MI = myocardial infarction

STIR = short-tau inversion recovery

4. What are the established treatments for pericarditis, and what are the emerging therapies for patients with complicated disease?

IDENTIFYING THE PATIENT WHO IS AT RISK FOR PROGRESSION BEYOND LIMITED ACUTE PERICARDITIS

Acute pericarditis is common, and when treated with appropriate anti-inflammatory medications, most symptoms resolve within days to weeks (2,3). However, a significant minority of patients will either experience adverse events related to the initial presentation or will be debilitated by recurrent attacks. To aid in the identification of these at-risk patients, an understanding of the epidemiology, etiologies, and classifications of pericarditis is necessary. With this background, risk factors for specific complications are better appreciated.

DEFINING THE STAGES OF PERICARDITIS. Pericarditis remains a clinical diagnosis with hallmark features, including precordial chest pain that is worse with inspiration and when supine, characteristic ST-segment elevation and PR deviation on electrocardiogram (ECG), a pericardial friction rub, and a pericardial effusion that is more than trivial (4). A diagnosis of pericarditis requires 2 of these 4 characteristics, usually chest pain in conjunction with either ECG changes or a pericardial effusion (5–7). Supportive findings, although not included in the diagnostic criteria, include elevated inflammatory markers or other imaging evidence of pericardial inflammation (5,8,9).

Once diagnosed, pericarditis is categorized according to the duration of symptoms. Pericarditis that persists for more than 4 to 6 weeks is termed incessant, and the presence of symptoms for >3 months is considered chronic pericarditis. If a patient is free of symptoms for at least 4 to 6 weeks, relapse is referred to as recurrent pericarditis (5). As will be discussed, this distinction may be relevant, as the underlying pathophysiology of a patient with idiopathic recurrent pericarditis is likely different from a patient with chronic pericarditis related to autoimmune disease. In general, however, these distinct time frames are admittedly arbitrary and not necessarily mutually exclusive. A patient with recurrent pericarditis may also develop incessant or chronic disease if the symptoms are not controlled. Nonetheless, the number and duration of attacks does reflect the morbidity of the disease. In addition, the distinction between acute pericarditis, a single recurrence, and multiple recurrences of pericarditis has provided a useful framework for the conduct of clinical trials (10–12).

ETIOLOGY AND EPIDEMIOLOGY OF PERICARDITIS. In the United States and Western Europe, most episodes of pericarditis (80% to 90%) are idiopathic and are often presumed to be post-viral (3). Conversely, tuberculosis is the most common cause of pericarditis in the developing world (13,14). Increasing causes of pericarditis are the post-cardiac injury syndromes, which include pericarditis after myocardial infarction (MI), percutaneous coronary intervention, electrophysiology procedures, or post-pericardiotomy (15). Less common causes of pericarditis include autoimmune diseases, chest irradiation, and active cancer.

To establish the cause of pericarditis, an extensive laboratory analysis may increase the yield (16), but is not routinely recommended (5). Currently, identification of the putative viral agent does not inform prognosis or management. Similarly, testing for antinuclear antibodies is not recommended, as low titer levels are common and nonspecific (17). In patients with a rheumatic disease, involvement of other organs is usually apparent before the onset of pericarditis (18,19).

For the clinician, a central initial question is the overall likelihood that a patient will develop complicated pericarditis. After an episode of acute pericarditis, the probability of developing incessant pericarditis or a first recurrence within 18 months is generally 15% to 30% (10,20). In patients who have had an initial recurrence of pericarditis, additional recurrence occurs in 25% to 50% (11,12). Likewise, further exacerbations will develop in 20% to 40% of patients after 2 or more previous recurrences (**Figure 1**) (21).

These data regarding the incidence of recurrence originate from randomized trials including approximately 800 patients, and 80% of patients in these trials had an idiopathic cause of pericarditis (11,12,20,21). A separate question relates to the risk of developing a first episode of pericarditis after cardiac injury. In the current era of early reperfusion for acute MI, late pericarditis (Dressler's syndrome) is uncommon (<0.5%) (22,23). Early pericarditis after ST-segment elevation MI has also decreased, with an incidence of approximately 4%, although it is more common in patients who present after at least 6 h of symptoms (14%) and in patients with percutaneous coronary intervention failure (23%) (23). After pericardiotomy, pericarditis is more common, with a likely incidence between 10% and 25% (24,25).

An additional risk of pericarditis is the development of constrictive pathophysiology. In constrictive