Chapter

Pericardial Diseases in Elderly Patients

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Abstract

The pericardium is a double-walled, fibrous sac typically containing 20–50 mL of fluid surrounding the heart and great vessels. In addition to its known anatomical and physiological functions, the pericardium also serves an active immunological role that is the focus of interest pertaining to inflammatory cardiac conditions such as pericarditis and myocarditis. In the geriatric population, the pericardium also undergoes age-related changes similar to other anatomical structures; however, in contrast to common cardiac diseases such as coronary artery disease, heart failure, valvular disease, etc., data from randomized trials regarding the management of pericardial diseases are limited, especially in the elderly population. In this chapter, we will discuss age-related pericardial anatomical changes, various pericardial diseases (acute, recurrent and constrictive pericarditis, pericardial effusion, cardiac tamponade, etc.) along with their clinical impact, and evidence-based management.

Keywords: pericardial disease, elderly, acute pericarditis, constrictive pericarditis, recurrent pericarditis, cardiac tamponade, pericardium, myocarditis

1. Age-related pericardial anatomical changes

The pericardium is subject to age-related changes just like any other organ in the human body although available literature regarding pericardial anatomy and pericardial disease etiology related to aging is very limited. One study examining bovine pericardium for age-dependent differences in collagen alignment showed higher elasticity, higher tensile strength, and thin pericardium in neonatal compared to adult bovine pericardium [1]. Despite such noted anatomical changes in the pericardial structure with age, the spectrum of pericardial disease remains similar among younger and older populations. Although most guidelines have not discussed specific age-related pericardial disease management, diagnostic evaluation and treatment of pericarditis in the geriatric population should take comorbidities into consideration for optimal management [2].

2. Pericardial effusion

The pericardial space contains 20–50 mL of fluid in the pericardial sac which works as a lubricant between two layers of pericardium. Pericardial effusion is defined by an excess fluid collection over the normal physiological amount within this space. Pericardial fluid accumulation can be secondary to increased fluid

production (i.e., any inflammatory condition) or from reduced fluid reabsorption (i.e., heart failure, pulmonary hypertension, and pericardial lymphatic obstruction). The fluid starts accumulating according to gravitational forces, initially in the posterior-inferior site then circumferentially resulting in moderate to large effusion.

Pericardial effusion can be classified based on various characteristics such as size (mild, moderate, and large), onset (acute, subacute, and chronic), distribution (localized or circumferential), composition (transudate, exudate, blood, or rarely gas from bacterial infections), and hemodynamic effects (without tamponade, with tamponade, effusive-constrictive) [2, 3]. (**Table 1**).

The normal pericardium is made up of a high content of collagen fibers, which creates a relatively inelastic sac that contains the heart. The pressure-volume curve of the normal pericardium is a J-shaped curve, which allows a limited stretch of the pericardium in response to physiological events such as posture or volume status without significant change in the intrapericardial pressure; however, after reaching a certain intrapericardial volume, the intrapericardial pressure rises suddenly and can cause sudden systemic hemodynamic derangements. The rapid rate of the fluid collection also plays a role in the pressure-volume curve; a sudden rise in intrapericardial volume (such as with aortic dissection or trauma with hemopericardium) of 100–200 mL significantly raises the intrapericardial pressure, whereas the slow collection of fluid may allow the development of a large pericardial effusion (1–2 L) without signs of cardiac tamponade [3, 4].

2.1 Etiology

Among the elderly, the spectrum of etiologies for pericardial effusion does not differ significantly from the rest of the population. The underlying cause of effusion can usually be inferred from the clinical picture. One study in 322 patients

Size of fluid collection in TTE*	Less than 10 mm—mild
	10–20 mm—moderate
	More than 20 mm—large
Onset of fluid collection	<1 week—acute
	>1 week to <3 months—subacute
	>3 months—chronic
Fluid distribution	Localized
	Circumferential
Fluid composition	Infectious—exudative Non-infectious—transudate
	Hemopericardium—blood
	Pneumopericardium—air
	Chylopericardium—chylous
Hemodynamic effects	No tamponade effect
	Tamponade effect
	effusive-constrictive

TTE, transthoracic echocardiography.

Table 1.
Classification of pericardial effusion.

has reported around 60% of cases had a known cause of pericardial effusion [5]. A varying amount of effusion can be seen in other conditions such as malignancy (with or without direct pericardial involvement), renal failure, pregnancy, aortic or cardiac wall rupture, trauma, heart failure, cirrhosis of the liver, nephrotic syndrome, autoimmune diseases, radiation, etc. One study incorporated demographics in their review of pericarditis etiology by comparing a younger patient population (age 15–65, n = 221) to a geriatric population (age 66–88, n = 101) and found no statistically significant differences in the incidence of idiopathic (33 vs. 38%) versus neoplastic (14.4 vs. 10.8%) pericarditis or the incidence of tamponade (36 vs. 38.6%) [6]. The cause of effusion may also vary by geographical area and clinical setting. For example, effusions related to viral pericarditis or idiopathic pericarditis are more common in outpatient populations of the western world, whereas bacterial and tuberculous inflammation and effusion are more common in sub-Saharan Africa and the developing world. Effusions associated with uremic pericarditis or malignancies are frequently found in hospital settings [3, 7].

According to one study with a mean participant age of 56, when determining the cause of moderate to severe pleural effusions, it is important to consider three major factors: (1) size of effusion; (2) presence of tamponade; and (3) inflammatory signs (defined as two or more from: fever >37°C, pericardial friction rub, characteristic chest pain, and diffuse ST-segment elevation). The presence of inflammatory signs was associated with acute idiopathic pericarditis (likelihood ratio = 5.4, $P < 0.001$), a large effusion without any inflammatory signs or tamponade was found to be associated with chronic idiopathic pericardial effusion (likelihood ratio = 20, $P < 0.001$), and the features of tamponade without inflammatory signs were associated with malignant effusions (likelihood ratio = 2.9, $P < 0.01$) [5].

2.2 Clinical presentation

The presentation of pericardial effusion varies according to the speed of accumulation, size of effusion, and etiology. The rate of fluid collection plays a critical role in clinical presentation as rapidly accumulating pericardial effusion causes a quick rise in intrapericardial pressure, which results in cardiac tamponade, while slowly accumulating fluid accommodates comparatively larger volume before signs of tamponade [2, 3]. The cases of isolated pericardial effusion can be asymptomatic or can have symptoms related to the underlying etiology or to the effusion itself. The classically reported symptom is dyspnea on exertion; however, the wide spectrum of symptoms related to compressive effect includes cough, weakness, fatigue, palpitations (from compressive effect of the pericardial fluid or reduced blood pressure), nausea (diaphragm), dysphagia (esophagus), hoarseness of voice (recurrent laryngeal nerve), etc. Patients may present with fever from underlying disease (infectious or systemic inflammatory disease), pleural effusion, ascites, or hepatic dysfunction from long standing pericardial constriction [2, 8].

Physical examination may remain normal without any significant findings in patients with no hemodynamic compromise. Pulsus paradoxus is an inspiratory drop in systolic BP >10 mmHg due to the augmentation of right ventricular preload causing impaired left ventricular filling resulting in abnormal decrease in stroke volume [9] and is a phenomenon commonly seen with large pericardial effusion or cardiac tamponade. Pericardial friction rub is rarely heard but is a usual finding of pericarditis.

2.3 Diagnostics

Upon clinical suspicion of pericardial effusion, the diagnostic approach should consider three major steps: (1) confirm the presence of effusion; (2)

assess the hemodynamic impact; and (3) effort to identify the underlying etiology. Transthoracic echocardiography (TTE) is recommended in all patients with suspected effusion as a class I, level C recommendation. Further imaging modalities such as computed tomography (CT) scan, cardiac magnetic resonance imaging (CMRI), pericardial fluid analysis, or biopsy can be considered in cases where loculated effusion, masses, or thickening of the pericardium are suspected. Basic diagnostic work up, including blood counts, chemistry, thyroid function tests, cardiac biomarkers, inflammatory markers such as C-reactive protein (CRP) and sedimentation rate (ESR), electrocardiogram (ECG), and chest X-ray, should be done [2, 10]. ECG findings in pericardial effusion include low QRS voltage and electrical alternans, a finding of large pericardial effusion or tamponade that is usually associated with sinus tachycardia.

TTE is recommended as the first modality to determine the hemodynamic significance of pericardial effusion and is highly sensitive and specific. The pericardial fluid appears as echo-lucent space between the pericardium and epicardium on TTE. The semi-quantitative assessment for largest echo-free space in echocardiographic views provides an assessment of severity. Mild pericardial effusion is considered <10 mm, moderate between 10 and 20 mm, and large effusion is any collection >20 mm. The collection of effusion follows gravity initially in the inferolateral position close to right atrium in the apical four chamber view with the patient in a supine-left lateral position. The pattern of collection changes to circumferential in the pericardium with increasing amount of fluid (**Figure 1**). After the development of a large amount of effusion, the heart can be seen swinging in the pericardial cavity, a finding that correlates with electrical alternans on ECG [2, 3, 11].

Cardiac CT and CMRI are useful imaging modalities for the evaluation of pericardial effusion and tamponade especially for more detailed assessment and the localization of the effusion and associated abnormalities in the mediastinum, lungs,

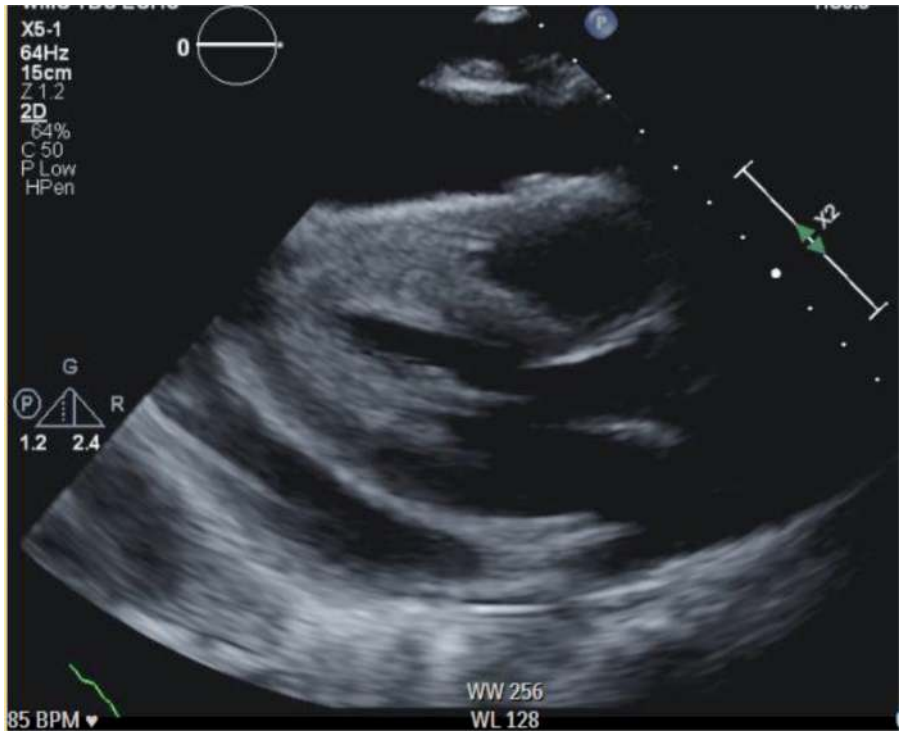

Figure 1.
Large circumferential pericardial effusion.

and adjacent structures. They are useful for the guidance of pericardiocentesis since loculated effusions or calcified pericardium can be identified. CMRI is superior to CT in differentiating fluids especially highly exudative fluid from thickened pericardium. CT detects a minimum amount of pericardial calcium and is relatively quick [2, 11].

Pericardial fluid analysis is often performed when the patient requires pericardiocentesis. Routine fluid studies include measuring fluid protein level, protein fluid/serum ratio, lactate dehydrogenase (LDH), LDH fluid/serum ratio, glucose, cell counts, and specific gravity. Fluid cytology and tumor markers (carcinoembryonic antigen, cancer antigen 19-9, adenosine deaminase, and interferon gamma) are useful measures in malignancy. Polymerase chain reaction and fluid cultures help in infectious etiologies.

2.4 Treatment

For small-to-medium sized, asymptomatic pericardial effusion without signs of hemodynamic instability, regular outpatient follow-up with clinical examination and/or echocardiography should be preferred. Management of pericardial effusion with signs of inflammation (pericarditis) should follow the standard or treatment for pericarditis; however, in the absence of any inflammation, anti-inflammatory drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and corticosteroids, are generally not effective. Such cases as well as cases with large effusion that failed empiric anti-inflammatory therapy would require pericardiocentesis. Recurrence of effusion is fairly common and further management options include pericardial window formation or pericardiectomy. A study comparing patients age 15–65 to a group of patients age 66–88 years showed elderly people had more persistence of effusion (6.3 vs. 14%; $P < 0.05$) but no statistically significant difference in mortality (24 vs. 30%) or evolution of cardiac constriction (4 vs. 2%) during median follow up time of 11 months [6]. There is no standard guideline available for elderly patients regarding pleural effusions; however, the expert consensus suggests adjusting the type and dosages of medications with special attention to drug interactions and renal function given the prevalence of polypharmacy and renal dysfunction in the geriatric population [2]. A proposed management algorithm for pericardial effusion of unknown origin is depicted in **Figure 2** [2, 3].

2.5 Prognosis

The prognosis of pericardial effusion is related to its etiology and size. Moderate-to-large size effusions are more commonly associated with bacterial infection, systemic inflammatory disease, or malignancy. Idiopathic pericardial effusion has a good prognosis, but effusion related to bacteria, post-radiation, or pericardial injury has a higher rate of developing either early (cardiac tamponade) or late complications (constrictive pericarditis). Large effusion (>3 months) carries a 30–35% risk of progression to cardiac tamponade. The follow-up of pericardial effusion is mainly based on symptomatic evaluation with the follow-up of inflammatory biomarkers and echocardiography [3]. A recent meta-analysis regarding prognosis of pericardial effusion in an elderly population with mean age > 60 reported that pericardial effusion can be considered as a marker of severity of the underlying disease as evidenced by a higher hazard ratio (HR) in patients with pericardial effusion with myocardial infarction (HR 2.65, 95% CI: 1.4–4.99; $P = 0.003$, 15 months follow-up) versus those with chronic heart failure (HR 1.53, 95% CI: 1.22–1.92; $P < 0.0001$, 31 months follow-up) [12].

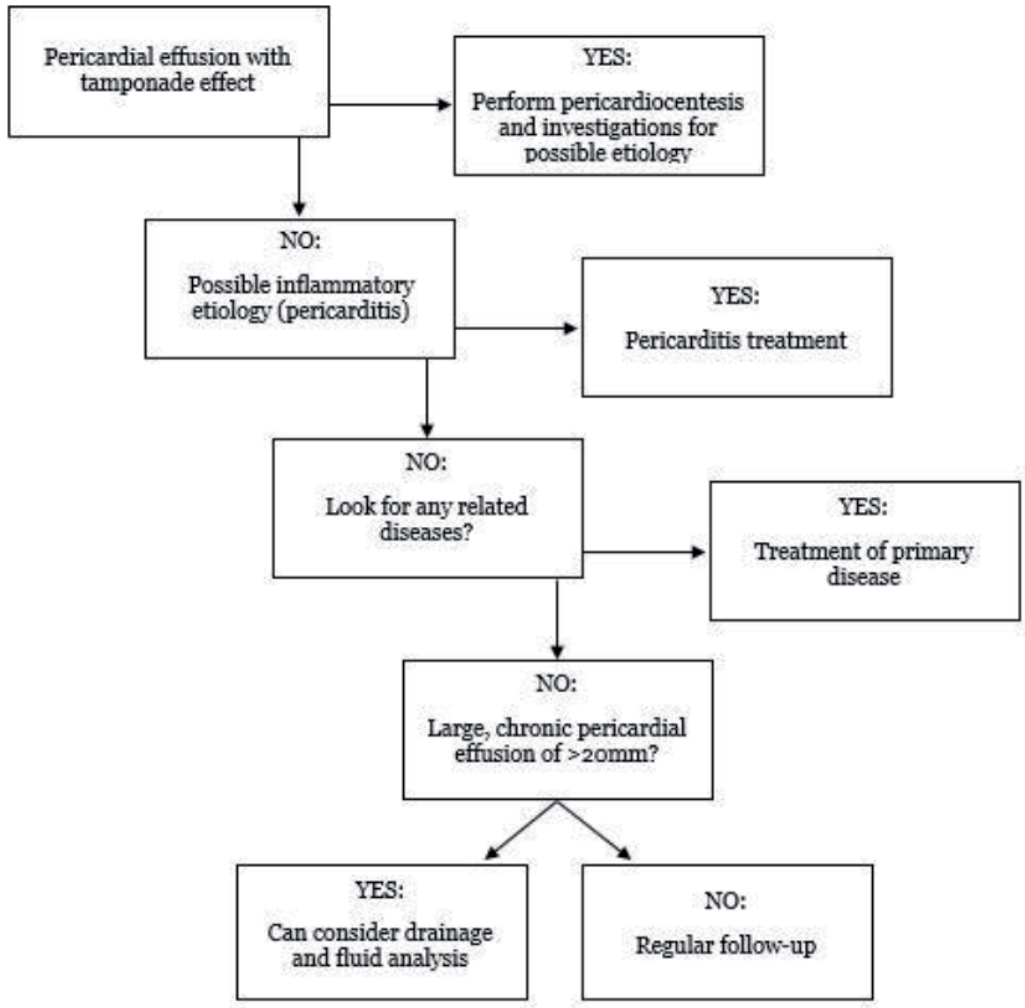

Figure 2.
Management algorithm for pericardial effusion with unknown origin.

3. Acute pericarditis

Acute pericarditis is a condition defined by the inflammation of the pericardial sac that can take place in the setting of a systemic disease (infectious, malignant, inflammatory, etc.) or independently of any other condition [2, 5, 13–15]. Among the elderly, it is important to consider malignancy in the evaluation of etiology as it is more common in this population and may prompt appropriate testing leading to a faster diagnosis and potential earlier intervention.

3.1 Etiology

Various infections (viral, bacterial, fungal, and tick-borne) have been known to cause the inflammation of the pericardium. In fact, prior to the widespread distribution of anti-retroviral medications, pericarditis was found to be the most common cardiovascular manifestation of human immunodeficiency virus/acquired immunodeficiency syndrome [16, 17] and, in conjunction with tuberculosis, remains the most common cause of pericardial inflammation in the developing world [18], whereas coxsackievirus maintains its status as the most common viral etiology of pericarditis overall. Malignancy, independent of other systemic diseases, has also been associated with acute pericardial disease and

accounts for about 6% of cases without another explanation [19, 20]. Systemic diseases, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), have been found to cause pericardial inflammation with approximately 50% of patients with SLE experiencing pericarditis. Other established etiologies of acute pericardial disease include post-myocardial infarction pericardial inflammation and/or effusion [21–24], post-radiation pericarditis with or without pericardial effusion [25], and uremic pericarditis usually in the setting of advanced renal failure and inadequate dialysis [26, 27]. Hypothyroidism severe enough to result in myxedema can result in a large, slowly accumulating pericardial effusion but rarely causes acute pericarditis [28].

3.2 Clinical presentation

There are four major distinctive features of acute pericarditis (at least two of which are required to make a clinical diagnosis): chest pain, pericardial friction rub, characteristic ECG changes, and pericardial effusion. The predominant presenting symptom is chest pain that is usually pleuritic in nature, sharp and alleviated by sitting up and leaning forward due to the positional shift of the pericardium, a feature which distinguishes it from the typical chest pain caused by myocardial ischemia [29, 30]. Pericardial chest pain is also often associated with nonproductive cough and dyspnea [29]. A scratchy, squeaking sound heard over the left sternal border upon auscultation known as a pericardial friction rub is the second of four major clinical features of pericarditis and is reported to be found in approximately 85% of patients with acute pericarditis in the absence of a pericardial effusion [20]. It is an extra heart sound resulting from the friction between the parietal and visceral pericardium coming into contact in the presence of inflammation. The presence of a pericardial effusion is the third of the four major signs of acute pericarditis and can best be appreciated on an echocardiogram. The last of the four major signs of pericarditis is new, diffuse ST-elevation, PR segment depressions, and PR segment elevation in lead aVR found on ECG (discussed further under *Diagnostics*) [15, 29, 31]. Other secondary features of pericarditis that may or may not be present are fever, subacute course of chest pain, elevated troponin (suggestive of myocardial involvement), and hemodynamic instability (suggestive of cardiac tamponade) [32, 33].

3.3 Diagnostics

Various laboratory tests and imaging modalities play role in establishing the diagnosis of acute pericarditis. Inflammatory markers, such as white blood cell count (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels although nonspecific, may help distinguish pericarditis from a condition with overlapping features given appropriate clinical criteria. Troponin levels, usually elevated in acute coronary syndrome, may also be elevated in pericarditis indicating myocardial involvement [34].

The chest X-ray may show cardiomegaly in the presence of a significant pericardial effusion but otherwise has limited utility in the diagnosis of pericardial disease. An echocardiogram can be similarly useful although the absence of pericardial effusion would not necessarily exclude the diagnosis of acute pericarditis. Cardiac CT imaging can serve a dual purpose in the diagnosis of acute pericarditis in that it may also help elucidate the underlying pathology responsible for the inflammatory changes. Pericardial thickening and effusion in the absence of calcification along with the enhancement of the visceral and parietal pericardium with intravenous contrast are indicative of active inflammation consistent with pericarditis [35]. CMRI can confirm inflammation but is likely not necessary in the diagnostic

workup of acute pericarditis unless the presumed etiology is a systemic inflammatory or autoimmune disease with characteristic cardiac findings.

The ECG may be perhaps the most useful diagnostic modality when considering acute pericarditis. The ECG progresses through a distinctive, four stage pattern although the evolution can be variable with up to 40% of patients showing atypical changes [30–32]. Stage 1 is characterized by widespread ST elevation with reciprocal ST depression in leads aVR and V1 as well as PR segment elevation in lead aVR accompanied by PR segment depression in the remaining limb leads and V5–6. Within 1 week of onset, normalization of ST and PR segments on the ECG comprises Stage 2. Stage 3 of the ECG is marked by diffuse T-wave inversions, while Stage 4 consists of normalization of the ECG. However, not all forms of pericarditis result in the characteristic ECG pattern as the pericardium itself is an inert tissue and only inflammatory changes involving the epicardium or myocardium would be reflected in acute pericarditis [36]. In fact, one review found that of 100 patients studied, only seven arrhythmias were identified all resulting from underlying heart disease [37], while a separate study comparing acute pericarditis to myopericarditis found arrhythmias more frequently associated with myopericarditis [38].

3.4 Treatment

Medical treatment of acute pericarditis utilizes one or a combination of two out of three different medications: NSAIDs, colchicine, and glucocorticoids. Treatment duration is usually guided by the resolution of symptoms and etiology of disease in the absence of confounding factors such as acute kidney or liver injury.

A combination of NSAIDs and colchicine is the mainstay of therapy for acute viral or idiopathic pericarditis. NSAIDs alone have been shown through multiple studies to effectively treat up to 80% of pericarditis cases [20, 32, 39]. No one particular NSAIDs has been shown to be more effective than another except in the case of post-myocardial infarction pericarditis for which aspirin is recommended and other NSAIDs should be avoided in order to prevent the disruption of myocardial scar formation [40]. Patients taking NSAIDs for pericarditis should concurrently take a proton-pump inhibitor for ulcer prophylaxis in the absence of any direct contraindication to do so. Treatment can be tapered once the patient is symptom-free for at least 24 hours (typically 1–2 weeks). Alternatively, one study recommends following weekly CRP levels along with symptom resolution and beginning tapering, once the patient is symptom-free for 24 hours and CRP levels have returned to normal [41].

In 2005, the Colchicine for Acute Pericarditis (COPE) trial suggested colchicine as an effective adjunct for treating acute pericarditis when combined with NSAIDs therapy for patients with non-bacterial, non-malignancy-related pericardial disease [39]. The addition of colchicine was further shown to reduce symptom burden and decrease the rate of recurrent pericarditis by a subsequent, randomized-control trial (RCT) [42], a finding, which was later supported by a meta-analysis in 2014, that demonstrated a reduced risk of recurrence at 18 months in patients undergoing treatment for acute pericarditis [43]. The management of acute pericarditis with a combination of NSAIDs and colchicine is also currently supported by the 2015 European Society of Cardiology (ESC) guidelines [2].

For patients with contraindications to NSAIDs therapy (kidney failure, GI bleeding, pregnancy, etc.), glucocorticoids may be used in combination with colchicine for the initial treatment of acute pericarditis. Treatment duration is then guided by symptom resolution and the normalization of CRP levels with tapering usually started 2–4 weeks thereafter. Glucocorticoids have also been utilized in patients with pericarditis refractory to NSAIDs and colchicine though one study shows a trend toward higher rate of recurrent pericarditis with steroid use [44].

Geriatric patients appear to have a higher risk of mortality when admitted and treated for pericarditis in the hospital. Although data regarding treatment of specifically elderly patients are sparse, one study examined the relationship between pericarditis, age, hospital admission, and mortality. They analyzed 45,504 patients above the age of 65 from 1999 to 2012 and found that hospitalization for the treatment of pericarditis is associated with increased risk of 1-year all-cause mortality despite a decrease in 1-year mortality rate from 19.7% (95% confidence interval (CI) 18.8–20.8) in 1999 to 17.3% (95% CI 15.3–20) in 2012 [45]. While it is possible that this association is in part due to a higher prevalence of significant comorbidities and compromised immune systems among the elderly, it nevertheless remains an aspect of pericardial disease that warrants further investigation as advanced therapies and support devices continue to enable longer lifespans with time.

4. Recurrent pericarditis

Recurrent pericarditis is a syndrome defined by the reemergence of pericarditis after the treatment of the initial inflammatory event [31, 46–48]. A minimum 4–6 week symptom-free interval post anti-inflammatory treatment is required to differentiate recurrent pericarditis from incessant pericarditis.

4.1 Etiology

Acute pericarditis has been found to have recurrence rates as high as 30% in patients treated without colchicine [32, 39, 47, 49]. Some cases of recurrent pericarditis appear to reflect localized inflammation given the detection of certain cytokines (interleukin (IL)-6, IL-8, and interferon gamma) in the pericardial fluid and their absence in the serum [50]; however, most cases are considered to be of autoimmune etiology [2, 51].

4.2 Clinical presentation

Chest pain appears to be the most common recurring symptom; however, the clinical diagnosis of recurrent pericarditis requires the presence of at least one of the following in addition to pleuritic chest pain: fever, pericardial rub, ECG changes, pericardial effusion, elevated WBC, ESR, CRP, or evidence of active pericardial inflammation on imaging [15]. Patients with previously treated pericarditis may experience multiple recurrences over the course of months to years following the initial event [52–54].

4.3 Diagnostics

The selection of the initial treatment regimen can directly impact the potential for the recurrence of acute pericarditis and may serve as an independent predictor of risk. For instance, a prior response to NSAIDs therapy is associated with the reduced risk of recurrence [32], whereas treatment with glucocorticoids is associated with increased recurrence [55]. It is difficult to rely upon ECG changes for the diagnosis for recurrent pericarditis as they are non-specific in the majority of cases. Chest X-ray and TTE also have limited utility as both will appear to be normal without a significant pericardial effusion. CT and CMRI imaging have proven to be of benefit in elucidating the diagnosis of recurrent pericarditis as contrast-enhanced CT can detect active pericardial inflammation while CMRI may reveal the evidence of edema via pericardial gadolinium enhancement [2, 35].

4.4 Treatment

Recurrent viral or idiopathic pericarditis is typically managed with an outpatient medical regimen [2, 52, 54] initially consisting of an NSAIDs and colchicine [15] as glucocorticoids are known to increase the risk of recurrence despite multiple recurrences of pericarditis [56]. Glucocorticoid therapy is, therefore, reserved for patients who are either unable to tolerate NSAIDs or have failed NSAIDs therapy in the past [2].

It is important to ensure an adequate trial of NSAIDs was given prior to labeling a patient as refractory. Common agents such as Aspirin and Ibuprofen should be attempted first followed by Indomethacin for treatment resistant cases. Medication should be administered in three doses over 24 hours to ensure consistent therapeutic levels, and dosage should be titrated up as needed to achieve symptom control until the daily maximum is reached or symptoms have subsided [10, 32, 39, 52, 54, 57].

Patients with recurrent pericarditis are often times designated as refractory to colchicine therapy after having received inappropriate dosing or rapid tapers [43]. In addition, colchicine should be given twice a day in order to reduce the risk of poor compliance due to gastrointestinal discomfort [10, 57, 58].

In cases of recurrent pericarditis refractory to treatment with NSAIDs, colchicine, and glucocorticoids, patients found to have the evidence of systemic inflammation may benefit from anti-interleukin-1 therapy. A recent trial in 2016 demonstrated a significant reduction of recurrence (90–18%) in patients with pericarditis resistant to colchicine and dependent on corticosteroids with the addition of anakinra, an IL-1B antagonist [59]. Although promising, this study's results were limited by a small sample size and inconsistent colchicine dosing across trial participants warranting further investigation.

5. Constrictive pericarditis

Constrictive pericarditis is a condition that occurs when a thickened or calcified pericardium loses elasticity resulting in the reduction of diastolic filling. It is a syndrome that is the end result of chronic pericarditis and pericardial effusion gradually progressing to fibrosis [2, 15, 29, 60]. Such impairment overtime causes the reduction of pericardial space, which in turn uncouples intrathoracic and intracardiac pressures generating increased interventricular interdependence visible on echocardiogram [2, 35, 61, 62].

5.1 Etiology

Constrictive pericarditis can occur as a result of inflammation and effusion from any pericardial disease [2, 31, 63]. A combination of studies has found that 42 to 61% of cases were idiopathic or viral, 11 to 37% postcardiac surgery, 2 to 31% postradiation, 3 to 7% due to connective tissue disorders, 3 to 15% bacterial or tuberculous, and 1 to 10% related to malignancy, trauma, drug toxicity, sarcoidosis, or uremic pericarditis [64–69]. Tuberculosis remains a major global cause of constrictive pericarditis especially in endemic nations [2, 70].

5.2 Clinical presentation

Patients with constrictive pericarditis usually present with symptoms of right heart failure in the absence of ventricular function impairment. Symptoms are consistent with volume overload, such as edema, pleural effusion, dyspnea, ascites,

or low output states such as exertional dyspnea and fatigue [2]. As high as 93% of patients present with elevated jugular venous pressure (JVP) [65], while only approximately 20% of patients present with pulsus paradoxus or Kussmaul's sign [64, 65, 71]. A pericardial knock has been noted in 47% of patients with constrictive pericarditis [65].

5.3 Diagnostics

Although the diagnosis of constrictive pericarditis can be made by echocardiography [72], an ECG and chest X-ray should also be obtained as part of the initial evaluation. There are no specific ECG changes consistently indicative of constrictive pericarditis; however, an ECG may be helpful in ruling out other cardiac pathology. The chest X-ray may show the evidence of pericardial calcification in which the presence of right heart failure would be strongly suggestive of constrictive pericarditis; however, the absence of such a finding would not rule out the disease [2].

All patients with suspected pericardial disease should be evaluated with echocardiography [2, 73]. Septal bounce and pericardial thickening on M-mode and 2-dimensional echocardiography would be suggestive of a constrictive pattern. On Doppler echocardiography, increased interventricular interdependence is associated with pericardial fibrosis, and the ratio of the right ventricular (RV) area to the left ventricular (LV) area, known as systolic area index (SAI), is virtually diagnostic of constrictive pericarditis when the SAI is >1.1 [74].

CT imaging can show pericardial thickening and calcification but is not necessary to diagnose constrictive pericarditis. However, the identification of important vascular structures on CT can prove useful if planning for pericardiectomy [75]. Positron emission tomography (PET)/CT can also be helpful in predicting response to corticosteroid therapy [76]. CMRI may show characteristic changes of constrictive pericarditis, such as pericardial thickening, dilation of the inferior vena cava, or ventricular interdependence, but is usually necessary unless investigating other related cardiac pathology.

5.4 Treatment

Treatment of constrictive pericarditis is dependent on the course of the disease at the time of evaluation. For early subacute disease in patients who are hemodynamically stable, medical therapy similar to that used for acute pericarditis is recommended. Patients who present with the evidence of late chronic disease (cachexia, pericardial calcifications, and hepatic dysfunction) or those who have failed conservative management with anti-inflammatory therapy can be treated with pericardiectomy [63]. The majority of patients achieve symptomatic relief with early surgical removal of the inflamed pericardium [69] with one study reporting up to 69% of patients being symptom-free at 4 year follow-up [65].

6. Cardiac tamponade

Cardiac tamponade is characterized by the accumulation of pericardial fluid causing significant impairment in cardiac function due to the pressure effect of external pericardial content causing compression of all cardiac chambers. Increase in intrapericardial pressure reduces the myocardial transmural pressure with a reduced ventricular wall diastolic compliance and a decrease in cardiac output and blood pressure. In cardiac tamponade, unlike constrictive pericarditis, most of the inspiratory decline in the intrathoracic pressure is transmitted through

the pericardium to the right ventricle and results in increased venous return and right ventricular distention. The higher intrapericardial pressure limits the right ventricular free wall expansion, resulting in bulging of the right ventricular septum to the left ventricle. This bulge diminishes the compliance of the left ventricle, which results in decreased filling and cardiac output [4, 77]. A similar mechanism contributes to pulsus paradoxus, an abnormal decline in systolic blood pressure (>10 mmHg) with inspiration. Cardiac tamponade is a treatable cause of cardiogenic shock that can be rapidly fatal.

Usually, cardiac tamponade is seen after pericarditis, tuberculosis, iatrogenic (secondary to cardiac interventions), trauma, neoplasm, with other uncommon causes including, collagen vascular disorder, radiation therapy, post-myocardial infarction, uremia, aortic dissection, and a bacterial infection.

6.1 Etiology

Cardiac tamponade could be acute, subacute, low-pressure type, or regional. Acute cardiac tamponade is sudden in onset and acutely life-threatening if not treated. Subacute cardiac tamponade is less dramatic compared to acute, but once the intrapericardial pressure reaches the threshold, patients experience classical tamponade symptoms related to decreased cardiac function. Low-pressure tamponade is a condition that appears in hypovolemic patients (such as traumatic hemorrhage, over diuresis, etc.). Correction of volume status reveals a typical tamponade pattern. Regional tamponade occurs from loculated effusion or a localized hematoma causing compression of only selected chambers. It is usually seen after myocardial infarction or pericardiotomy [77].

6.2 Clinical presentation

Depending on the severity of the tamponade, a variety of clinical findings are seen. Sinus tachycardia as a physiologic response to maintain the cardiac output is common. Elevated jugular venous pressure, muffled heart sounds, and systemic hypotension together referred to as Beck's triad is a pathognomonic sign for tamponade.

6.3 Diagnosis

The diagnostic approach and the evaluation of cardiac tamponade are similar to that for patients with suspected pericardial effusion. The ECG findings include sinus tachycardia, low voltage of QRS complex, and frequently electrical alternans, which is beat-to-beat changes in the position of the heart with relation to cardiac tamponade. The presence of total electrical alternans, including P wave, QRS complex, and ST segment alternans, is highly specific for cardiac tamponade, but sensitivity is very low with findings present in only 5–10% of cases. The presence of lone QRS alternans is more common but is not very specific for tamponade. The presence of QRS vector alternans (axis shift) is more specific than QRS amplitude alternans for the cardiac tamponade [77, 78].

TTE is the standard first-line imaging technique recommended for the evaluation of cardiac tamponade with excellent safety and efficacy. The size of the pericardial effusion does not indicate significance. Since respiration has an impact on intracardiac pressures, mainly on the right side of the heart, this respirophasic flow pattern becomes more evident in tamponade, which can be measured by Doppler echocardiographic variations in blood flow across the mitral (>25% variation) (**Figure 3**) and tricuspid valves (>40% variation) as well as pulmonary and

systemic outflow. Right atrial collapse and RV collapse on diastole (**Figure 4**) are usual signs of cardiac tamponade, but in the setting of severe pulmonary hypertension, right-sided chamber collapse may be delayed and preceded by left atrial collapse. In most cases, the thickness of the left ventricular wall and lower compliance prevents LV collapse. As the tamponade worsens, there are progressive impairments in hemodynamics and intracardiac flows. Elevated pressures in the right atrium can

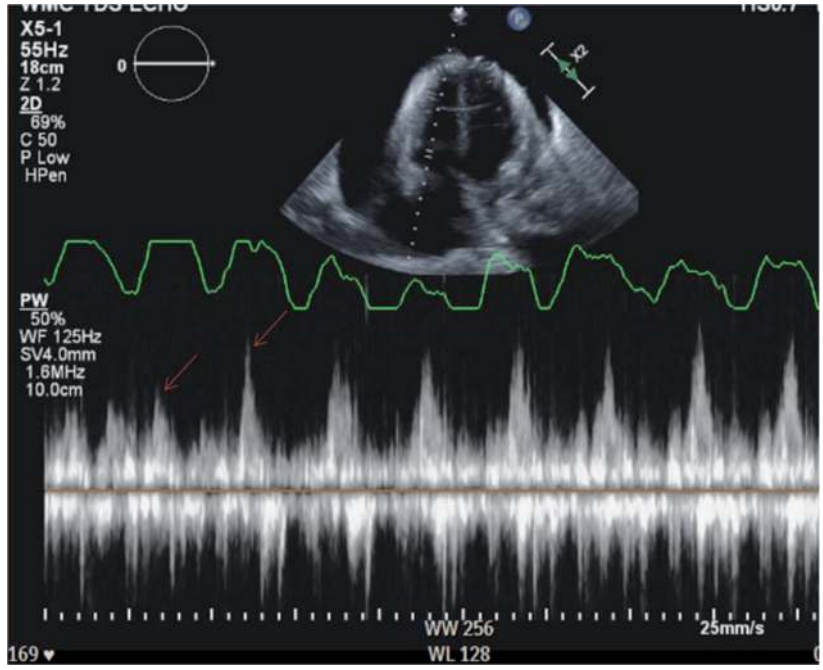

Figure 3.
Doppler echocardiographic variations in blood flow across the mitral valve.

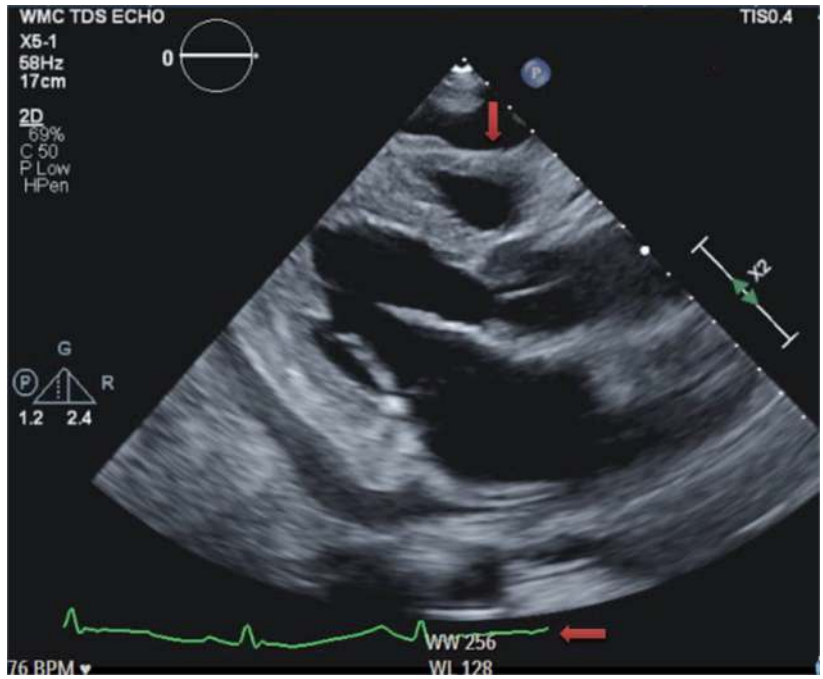

Figure 4.
Diastolic collapse of the right ventricular wall (top arrow) and diastolic period of cardiac cycle (bottom arrow).

be assessed from a plethora of the inferior vena cava (IVC) which is a lack of change in IVC caliber in response to respiratory flow pattern (<50% reduction in IVC diameter during inspiration). The swinging movement of the heart within the pericardial sac is another echocardiographic sign. These TTE findings in cardiac structural and functional change with a decline in cardiac function often occur well before the onset of pulsus paradoxus and significant clinical deterioration, and thus, they are an important indicator in cardiac tamponade [11, 79]. Cardiac CT and CMRI may provide valuable information about the functional and structural change of the heart and pericardium, but they are only required in special conditions such as localized tamponade, loculated pericardial effusion, or hematoma [61, 79].

6.4 Treatment

The treatment of cardiac tamponade is decompression with pericardiocentesis which can be done by percutaneous catheter pericardiocentesis or open surgical drainage with or without a pericardial window or video-assisted thoracoscopic pericardiectomy. Catheter pericardiocentesis under echocardiographic or fluoroscopic guidance is a more rapid and less invasive technique. Surgical pericardiocentesis is usually performed in purulent pericarditis bleeding into the pericardium or when pericardial biopsies and pericardiectomy are needed [2, 77]. A triage system proposed by the ESC Working Group on Myocardial and Pericardial Diseases can be used to guide the timing of the pericardiocentesis in non-emergent cases [80]. Fluid removal and decompression of the pericardial cavity rapidly improve the clinical hemodynamic status. Positive pressure mechanical ventilation should be avoided as it increases the intrathoracic pressure that deteriorates cardiac filling. The use of vasodilators and diuretics that reduce the preload is not recommended in the presence of cardiac tamponade [2].

Disclosure

None of the authors have any conflicts of interest to disclose.

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