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A contemporary look at pericardiocentesis☆

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ABSTRACT

Percutaneous drainage is the default strategy for evacuating a pericardial effusion. A pericardiocentesis can be necessary or required in a wide variety of clinical settings ranging from urgent tamponade to relieve in iatrogenic hemorrhagic effusions in the electrophysiology or catheterization room, to planned diagnostic procedures in patients with suspected or known malignancy or infections. With the help of several procedural improvements over the past decades, echocardiography and fluoroscopy-guided percutaneous pericardiocentesis has become the standard intervention for evacuating pericardial effusions, as well as an essential tool in the diagnostic work-up of an unexplained pericardial effusion. When performed by skilled physicians assisted by appropriate imaging it is a very safe procedure, and provided that an indwelling catheter is placed, it is also very effective with an acceptably low risk of recurrences. In this review, the indications and standard techniques for pericardiocentesis are discussed, as well as their consequences for patients with iatrogenic and malignant effusions.

Introduction

Percutaneous drainage is the default strategy for evacuating a large pericardial effusion. In addition, the procedure is often performed during the diagnostic work-up of a pericardial effusion, giving access to fluid samples for further tests in patients without a clear etiological cause. Less frequently, a pericardial puncture is performed for intrapericardial administration of therapeutic agents, or for epicardial electrophysiological procedures. Taken together, this implies that a pericardial puncture can be necessary or required in a wide variety of clinical settings, ranging from the urgent relief of tamponade in iatrogenic hemorrhagic effusions in the electrophysiology or catheterization room, to planned diagnostic procedures in patients with suspected or known malignancy or infections.

Accessing the pericardium is relatively straightforward, but it is nevertheless essential to be familiar with its function and relation to the heart. The pericardium is a relatively tight sac surrounding the heart and the roots of the aorta and pulmonary artery, serving as an anatomical anchor and physical barrier of the heart [1]. It consists of two layers, the visceral and parietal pericardium, separated by a small amount of serous fluid that lubricates the external surface of the heart. Pericardial serous fluid is continuously produced from parietal and epicardial capillaries and drained by the epicardial lymphatic system. On average, the pericardial sac contains only about 25 mL of fluid, with physiological amounts ranging between 20 and 60 mL [1]. Increased production, impaired drainage, or both, will lead to excessive fluid accumulation, sometimes requiring percutaneous aspiration, a technique termed pericardiocentesis. In this review, both the indications and technical options for pericardiocentesis are discussed, as well as the consequences of the diagnostic work-up after a pericardial puncture.

Reasons for pericardiocentesis

The causes of a pericardial effusion are abundant (Table 1). Fluid accumulates in the pericardial space as the result of direct pericardial damage due to inflammation, infection or trauma, or after iatrogenic injury to the myocardium, coronary arteries or valvular structures. Other causes include malignancy, reduced fluid clearance such as in congestive heart failure and mediastinal processes, and metabolic disturbances. In clinical practice, the most likely cause of a pericardial effusion highly depends on the clinical setting and presentation. It has been reported that using a structured step-wise approach, based on the patient's history and clinical presentation, lab testing, cardiac ultrasound and, in deliberately selected cases, pericardial fluid sampling, will establish a clear diagnosis in about 70% of patients, leading to a tailored management [2].

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Table 1
Causes of pericardial effusion.

Pericardial inflammation
Pericarditis
Viral, Bacterial, Fungal, Protozoal
Auto-immune and auto-inflammatory diseases
Post-surgery – postcardiotomy syndrome
Dressler syndrome – Postmyocardial infarction
Reduced pericardial fluid clearance
Congestive heart failure
Nephrotic syndrome
Cirrhosis
Trauma
Blunt and penetrating chest trauma
Iatrogenic
Post-cardiac and thoracic surgery
Percutaneous Coronary Intervention
Electrophysiological procedure
Aortic dissection
Malignancy
Pericardial primary tumor
Pericardial metastasis
Mediastinal malignancy
Post-radiation
Chemotherapy-related effusion
Metabolic
Uremic
Hypothyroidism
Drugs

Data on the frequency of different etiologies vary widely between populations studied. In the past decades, only a handful prospective series on the etiology of pericardial effusions have been reported [3–10]. Some of these included distinct populations in which tuberculosis and HIV are common. As a consequence, published frequencies of causes of pericardial effusions might not necessarily be universally representative or relevant for practices in industrialized countries. Still, tuberculous pericardial effusions, and effusions due to other infectious diseases, can be common in distinct migrant populations [11]. In the pediatric setting, the etiology of pericardial effusions requiring drainage appears to be somewhat different as well [12]. In a large series of pericardial effusions or tamponade in children ($n = 9920$), the effusion was most often labeled as 'idiopathic' (36%), or secondary to neoplasia (24%), pneumonia (20%) or autoimmune diseases (19%).

In a contemporary tertiary care setting, the causes of pericardial effusion have heavily shifted from infectious diseases to iatrogenic and malignant causes [13]. Malignancy is indeed frequently the underlying cause of pericardial effusions in contemporary practices. Pericardial disease can be the first manifestation of an underlying malignancy, especially in those presenting with a cardiac tamponade, represent progression of disease, or be the result of cancer therapies [14]. As cancer has hence become an important issue in the management of pericardial disease, malignancy-related pericardial effusion and its implications are discussed in more detail below.

In the past decade, the booming of complex invasive procedures including pulmonary vein ablations, valvular interventions and chronic total coronary occlusion interventions have also led to more procedure-related acute pericardial effusions [15]. As these procedures are often performed under full anticoagulation or antiplatelet therapy, they not only present a significant risk for acute tamponade but also add to the risk of need for an urgent pericardial drainage [4]. Acute tamponade is a feared complication in the catheterization and electrophysiology lab, or after a cardiac device implantation or lead extraction. In a recent series, detectable coronary artery perforations occurred in 0.7% of percutaneous coronary interventions (PCI) [16]. About half of these cases required an urgent pericardiocentesis. In chronic total occlusion interventions (CTO), a perforation even occurred in 4% of the cases in a recent report, but only 14% of these required a pericardiocentesis [17]. Although there is not always an absolute need for an acute pericardial drainage, the mortality associated with a perforation-associated tamponade requiring a pericardiocentesis was found to be very high (17%) [17]. These figures also suggest that every interventionalist and electrophysiologist should be well trained and comfortable with urgent pericardiocentesis procedures in addition to interventional techniques to evacuate the pericardial fluid, as there is often no time to waste. Importantly, pericardial effusions are often initially missed in the catheterization laboratory, when an incessant bleeding only causes symptoms after the patient has moved to the ward. This indicates that physicians and nurses always should remain vigilant in such patients, especially after complex procedures.

Evaluating the need for a pericardiocentesis

A pericardial puncture or drainage is most frequently performed when fluid needs to be removed from the pericardial sac, both for therapeutic and diagnostic purposes. In addition to effusions, a tamponade can also be caused by air; a tension pneumopericardium is rare but can be the result of blunt or penetrating chest trauma, or due to air aspiration during a pericardiocentesis. The pericardial space sometimes needs to be accessed in the absence of significant fluid, with the use of dedicated devices, e.g. for electrophysiological assessment of the epicardium, administering pericardial therapeutics or additional diagnostic procedures such as a pericardioscopy [18].

The clinical presentation of a pericardial effusion often varies greatly for the same given amount of fluid, from asymptomatic cases, to causing only dyspnea, to tamponade or acute hemodynamic collapse. Excessive pericardial fluid can cause a tamponade, but the amount of fluid that causes symptoms critically depends on the rate of fluid accumulation and systemic hemodynamic factors. At physiological pericardial fluid volumes, the pericardium is highly compliant, but compliance decreases steeply with abrupt fluid additions. while a very gradual accumulation of volume increases pericardial compliance [19]. As a result, sudden relatively small effusions can be immediately life-threatening, while a paucisymptomatic large effusion has likely accumulated over a longer period and is usually well tolerated.

Not all pericardial effusions need a pericardiocentesis, and the benefits and risks associated with such a procedure should always be balanced carefully. Small effusions, especially when the cause is known, can almost always be left untreated. Modest effusions secondary to treatable conditions like congestive heart failure or acute idiopathic pericarditis also generally do not require pericardiocentesis. Even larger asymptomatic chronic effusions, such as those observed in patients with a systemic inflammatory disease, can often be managed medically. Still, it is essential to repeatedly assess the absence of progression or the effect of non-invasive therapies on the extent of the pericardial effusion. In prospective series of large chronic idiopathic pericardial effusions in patients who received regular follow-up (3–6 months), about 40% of effusions regressed completely, while 8% developed a tamponade and 30% required a pericardiocentesis during a mean follow-up period of 4 years [20]. This indicates that sudden deterioration can occur in some patients and hence that regular re-assessment remains essential to identify patients who will require a pericardiocentesis.

When a pericardiocentesis is needed to relieve a cardiac tamponade, there is often little time to lose. However, in hemodynamically stable patients, a pericardial drainage can be delayed for 12–24 h if necessary. Often, the difficulty lies in judging whether an intermediate pericardial effusion requires a pericardiocentesis. Hemodynamic instability and uncertainty about the etiology of

Table 2
Indications for pericardiocentesis, using a comprehensive score (Ref [20], Ristic et al.). A score of 6 or above suggests that an urgent pericardiocentesis is be warranted. Urgent surgical management regardless of the score should be considered in case of a type A aortic dissection, ventricular free wall rupture, severe chest trauma or iatrogenic hemopericardium that cannot be controlled percutaneously.

Step 1 Etiology		Step 2 Clinical presentation		Step 3 Imaging	
Malignancy	2	Dyspnea/Tachypnea	1	Cardiomegaly on X-ray	1
Tuberculosis	2	Orthopnea and no rales	3	Electrical alternans on ECG	0.5
Recent radiotherapy	1	Hypotension	0.5	Microvoltages on ECG	1
Recent viral infection	1	Progressive sinus tachycardia	1	Circumferential effusion (> 2 cm in diastole)	3
Recurrent effusion, previous puncture	1	Oliguria	1	Moderate effusion (1–2 cm)	1
Chronic renal failure	1	Pulsus paradoxus > 10 mmHg	2	Small effusion (< 1 cm), no trauma	−1
Immunodeficiency	1	Pericardial chest pain	0.5	Right atrial collapse > 1/3 of cardiac cycle	1
Hypo/hyperthyroidism	−1	Pericardial friction rub	0.5	Inferior vena cava > 2.5 cm, < 50% inspiratory collapse	1.5
Systemic autoimmune disease	−1	Rapid worsening of symptoms	2	Right ventricular collapse	1.5
		Slow evolution	−1	Left atrial collapse	2
				Mitral/tricuspid respiratory flow variations	1
				Swinging heart	1

the effusion are indications for a pericardiocentesis regardless of the extent of effusion, but this is much less clear when the effusion causes few symptoms and the source of the effusion is more or less established. The European Society of Cardiology's Working Group on Myocardial and Pericardial diseases issued a helpful position statement to guide the physician in the triage of cardiac effusion and tamponade [21]. The authors developed an unvalidated tool that combines the (likely) etiology, clinical presentation and imaging parameters into a three-step score (Table 2). A score of 6 and above indicates that an urgent pericardiocentesis is required, at least after ruling out contraindications, while a score below 6 suggests that the procedure can be postponed or planned electively. The authors specifically highlight four clinical pericardial effusion scenarios that are obviously exempted from the score, however: type A dissection, ventricular rupture after myocardial infarction, chest trauma, which all often require an immediate surgical intervention, and an iatrogenic hemopericardium.

Procedural considerations

There are only a few conventional ways to remove excess pericardial fluid and a percutaneous pericardiocentesis is by far the most straightforward and virtually always the fastest technique. It is a very safe technique if performed by an experienced operator in a patient without contraindications for a percutaneous procedure. Ideally, a basic laboratory panel including an INR and a platelet count should be performed before the procedure, as an INR above 1.5 and a platelet count below 50,000 are considered to be relative contraindications for a pericardiocentesis [22]. Anticoagulation is also a relative contraindication for a pericardiocentesis [22]. Still, an urgent pericardial drainage might be unavoidable in acutely or chronically anticoagulated patients during or just after an electrophysiological or coronary intervention. In addition, a low platelet count is common in pericardiocentesis patients who have an underlying malignancy, especially when being treated with chemotherapy [23]. A prophylactic platelet transfusion is rarely needed and even often unproductive before a pericardial puncture in these patients, however, even with a platelet count below 20,000 p/mL [23–25]. Still, it is advisable to carefully use a echocardiography- and fluoroscopy guided parasternal or apical approach for such patients, although in experienced hands a subxiphoidal approach appears to be safe as well [24].

In the past decades, access to the pericardial sac has become much safer because of the systematic use of imaging modalities to guide the procedure. It is mandatory to obtain a good interpretation of the extent and localization of the effusion before the procedure, although emergency pericardial punctures sometimes simply cannot wait. Imaging will also identify other factors that directly influence the mode and localization of the puncture, such as intrapericardial masses or adhesions. In contemporary tertiary practices, patients with pericardial disease will often undergo advanced multimodality cardiac imaging, including cardiac magnetic resonance imaging, CT scan and positron emission tomography, which may all assist in deciding if, when and how a pericardial drainage should be carried out [26–28]. Most often, however, a routine echocardiography is the fastest and most accessible tool to visualize the effusion, followed by fluoroscopy guiding the position and trajectory of the needle during the procedure itself. A typical example is shown in Fig. 2.

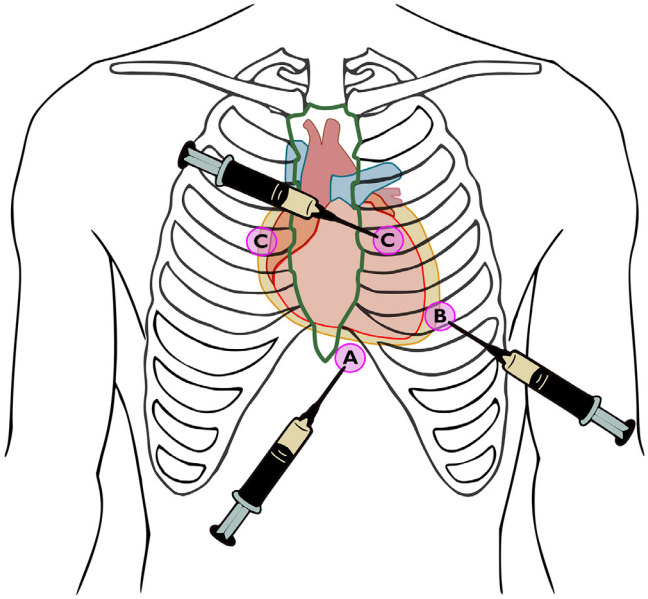

Fig. 1. Entry ports (circles, A = subxiphoidal, B = apical, C = parasternal) and direction of needle trajectory in standard pericardiocentesis approaches.

Several puncture sites are possible, but the standard subxiphoidal, parasternal or apical approaches are most commonly used (Figs. 1 and 3). The choice of the anatomical location for the puncture depends on the extent and localization of the pericardial fluid, patient anatomy, as well as on the expertise of the cardiologist. Most often, the puncture should be directed towards the most extensive fluid accumulation, which might also be affected by the position of the patient. Care should be taken to avoid puncturing intercostal and internal mammary arteries, as well as liver and lungs. After successfully accessing the pericardial sac, a J-tip wire is advanced and exchanged for an indwelling pigtail catheter. The need for prolonged drainage beyond the initial fluid removal after a pericardiocentesis depends on the etiology of the effusion and

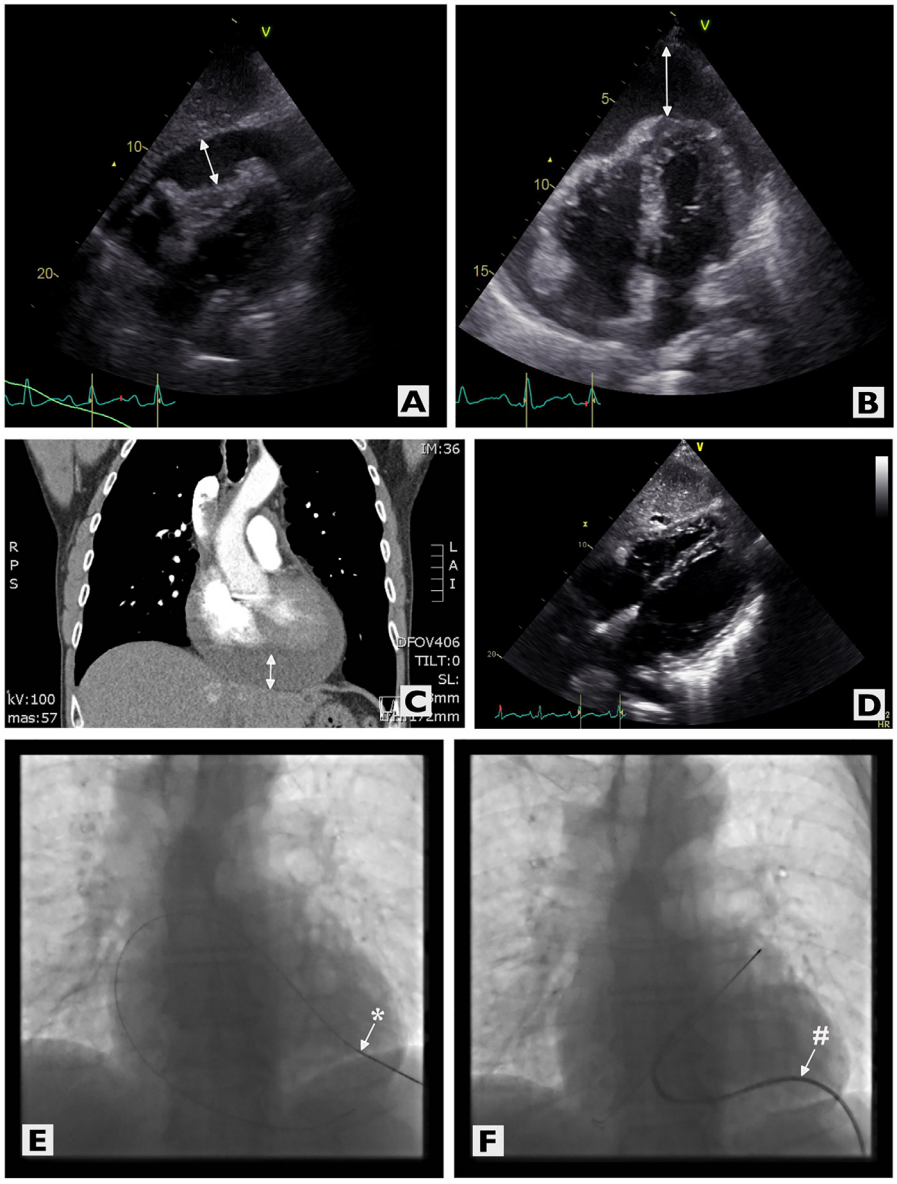

Fig. 2. Imaging of a pericardial effusion and pericardiocentesis in a 62-year old male patient with a metastasized pulmonary adenocarcinoma. Panels A, B and C demonstrate the effusion (double-headed arrow) on transthoracic echocardiography (subxiphoidal (A) and apical (B) views) and CT (C). Panels E and F show fluoroscopic images during the pericardiocentesis; panel E shows the needle tip (*) puncturing the pericardium while a guide wire is advanced in the pericardial space, and panel F shows advancement of a pig tail catheter (#). Panel D is an echocardiographic subxiphoidal view after complete drainage three days after the pericardiocentesis. The effusion was hemorrhagic and contained malignant cells on pathological examination.

the reason for pericardiocentesis, the clinical evolution and the rate of fluid drainage. In most cases, however, the risk of recurrence can be halved by leaving a pigtail catheter in place for at least one to two days, and is recommended for the majority of cases. The catheter can usually be removed as soon as it produces less than 30–50 mL/day.

In some cases, a surgical drainage might be preferred over a percutaneous approach, for instance when an ongoing pericardial hemorrhage needs to be managed early after cardiac surgery. Still, most post-cardiac surgery or malignancy-related pericardial effusions can be effectively managed percutaneously. A surgical drainage can also become unavoidable in recurrent cases, after a failed attempt at a percutaneous drainage, or when echocardiographic features suggest that a percutaneous puncture might not be safe or feasible. This might be in case of posterior located effusions, or excessive pericardial adhesions and a loculated aspect, or a clearly clotted hemopericardium [29]. Regardless of the reason for a pericardial drainage, reinterventions because of re-accumulation are less frequent after a surgical intervention. Alternatives to surgery for posteriorly located effusions include a transesophageal, transpleural or transbronchial pericardial puncture, but there is only anecdotal evidence on the safety of such approaches [30,31]. Alternatively, posteriorly located effusions can also be effectively reached via a more caudal transhepatic trajectory [32].

Ultrasound-guided approach

Echocardiography has revolutionized pericardiocentesis procedures, and over the past decades it has become a truly indispensable tool. Before the advent of routine cardiac ultrasound, a pericardiocentesis was performed blindly or under fluoroscopic guidance. In experienced hands, echocardiography-guided pericardial drainage has proven to be a very effective procedure, with

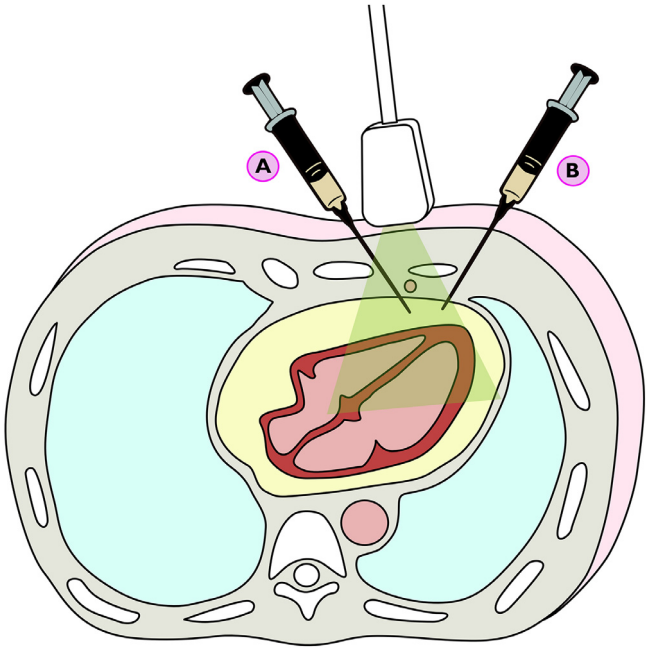

Fig. 3. Transverse view of two anterior puncture approaches with ultrasound guidance (circles, A = medial to lateral, B = lateral to medial). With a medio-lateral approach, care needs to be taken to avoid puncturing the internal mammary artery.

few complications. A large series from the Mayo Clinic's covering procedures from 1979 to 2000 reported overall major and minor complication rates of only 1.2% and 3.5%, respectively [10]. Usually, a quick echocardiographic assessment of the localization and the safest needle puncture approach right before the procedure suffices. Much more than fluoroscopy, echocardiography indeed enables the operator to assess the nature and localization of the effusion, the presence of adhesions, and intrapericardial masses versus pericardial fat.

Osman and colleagues describe a variant of the parasternal puncture technique, using a medial to lateral oblique needle trajectory under continuous in-plane ultrasound monitoring [33]. The advantage of using a high-frequency linear ultrasound probe when puncturing from a parasternal entry is that it allows visualization and avoidance of the left internal mammary artery (Fig. 3). There are several additional techniques or tricks that can be used to enhance the efficacy and hence safety of an ultrasound-guided pericardial puncture. One simple but effective and safe way to ensure pericardial localization while puncturing is to inject agitated saline through the needle. A more elaborate but very safe approach uses continuous real-time echocardiography monitoring throughout the procedure, using a bracket mounted on the ultrasound probe [34].

Fluoroscopy-guided approach

Like cardiac ultrasound, fluoroscopy has made performing a pericardiocentesis much safer and more effective than a blind puncture. In contemporary practice, fluoroscopy is largely used to guide the needle advancement, after establishing the extent of the effusion and ideal needle trajectory via echocardiography. Using a lateral fluoroscopic view, the operator can safely advance the needle tip with the guidance of the epicardial halo sign as a kind of 'no-go zone' [35]. The epicardial halo phenomenon is a distinct radiographic line bordering the heart; although its origins are not well understood, its intensity clearly correlates with the extent of pericardial fluid [35]. In our view, although certainly not always necessary, the addition of fluoroscopy to cardiac ultrasound helps avoid myocardial puncture or laceration. It might also be an alternative imaging technique when ultrasound is not possible, as for instance in patients with mediastinal emphysema. In addition, a correct placement of the tip of the needle in the pericardial space can be verified with a small amount of contrast, before advancing a guidewire. This can be especially helpful when blood is aspirated, avoiding the advancement of the guidewire into a ventricle or great vessel.

CT-based approach

Echocardiography often suffices to assess the necessity of a pericardiocentesis and to gauge the procedural requirements and risk. Sometimes additional imaging techniques are required to safely access the pericardial space, or to better assess the nature of the effusion and pericardial disease during the workup of a patient with a large pericardial effusion, however. A computed tomography (CT) improves the diagnostic yield of a traditional workup of clinical assessment, cardiac ultrasound, inflammatory markers and pericardial fluid cytology, especially in patients with a malignancy [36]. In addition, CT can be useful in guiding the pericardiocentesis itself. Like cardiac ultrasound, a CT-guided pericardial drainage appears to be safe and effective in experienced hands [37–39]. As it requires repeated scans while advancing both the anesthesia and puncture needles to the pericardium, the technique takes longer and is clearly more elaborate than the standard echo-guided puncture. With the help of a disposable grid with 1 cm^2 radiopaque lines, however, it is especially worth considering in case of (very) small or posteriorly located effusions, as well as with loculated effusions and when there is reduced echogenicity [40].

Invasive hemodynamic monitoring

Invasive hemodynamic monitoring is not routinely required during a pericardiocentesis [22], but is used in some institutions to rule out effusive-constrictive pericarditis. In effusive-constrictive pericarditis, features of reduced pericardial compliance and hemodynamically significant pericardial fluid are simultaneously present [41]. Typically, atrial pressure remains elevated and symptoms then persist after evacuating the pericardial effusion in these patients. Although the diagnosis of concomitant constrictive pericardial disease in patients undergoing pericardiocentesis can be made non-invasively using multimodality imaging, at least in experienced hands, a cardiac catheterization is strictly indicated when imaging does not provide a definite diagnosis of constriction [22,42].

Diagnostic steps

Pericardial fluid samples are usually sent to the laboratory for further analyses, unless the etiology is crystal clear such as in iatrogenic effusions. Standard tests to determine whether serous fluid is an exsudate or a transudate, including protein, glucose, cell count, LDH, are rarely informative, however, as most pericardial effusions appear to be exsudates [43,44]. Still, a low glucose level can be useful for early diagnosis of bacterial pericarditis. Additional samples should nevertheless be sent for (myco)bacterial and fungal culture or PCR testing, as well as cytology (see further). To complete the work-up of pericardiocentesis patients, a complete blood count and chemistry should be done, including a renal and thyroid function. In selected patients, tumor markers, serology and tests to rule out systemic autoinflammatory diseases might also be helpful.

Complications

In the modern era of echocardiography-guided pericardiocentesis, complication rates are low, but it can still be a high-risk procedure in inexperienced hands (Table 3). Mortality directly related

Table 3
Complications of a pericardiocentesis.

Cardiac complications
Free wall laceration and myocardial perforation
Coronary puncture
Bacterial pericarditis
Arrhythmias and cardiac arrest
Vagal reaction and bradycardia
Pneumopericardium
Decompression syndrome and congestive heart failure
Non-cardiac complications
Pneumothorax
Hemothorax - Internal mammary artery laceration
Hepatic or intraabdominal bleeding
Diaphragmatic laceration and phrenic nerve injury

to the pericardiocentesis itself is very rare, while in-hospital death (about 15%) is largely related to the underlying disease process [13]. The most feared and life-threatening direct complication of a pericardial drainage procedure is myocardial free wall laceration or coronary puncture, occurring in less than 1% of procedures [13]. The risk of such complications should be kept to a minimum by performing the procedure under echocardiographic guidance, even when done urgently. As such a bleeding sometimes only becomes symptomatic a few hours after the pericardiocentesis, high-risk patients such as after an iatrogenic hemopericardium might need at least a few hours of close monitoring.

Even in urgent pericardial drainage procedures in the catheterization lab or emergency room, care needs to be taken to maintain strict aseptic conditions during the puncture and catheter insertion, to avoid bacterial infections. Prophylactic antibiotic use is not recommended, however [22]. Ideally, blood pressure and electrocardiographic monitoring is always performed during a pericardial puncture. Arrhythmias including atrial fibrillation, are relatively common in pericardiocentesis patients. Atrial or ventricular arrhythmias are triggered by the puncture needle or the pericardial dwelling catheter, particularly in patients with enhanced susceptibility due to the underlying pericardial disease. Patients can also become vagal while puncturing the pericardium, especially in the absence of adequate local anesthesia, and develop a severe bradycardia. This might exacerbate the hemodynamic impact of the pericardial effusion and requires prompt atropine administration in addition to a fast fluid challenge.

Pericardiocentesis is an essential skill for cardiologists and emergency care specialists, and therefore it is important that the physician performing the procedure is skilled in emergency pericardial drainage and is aware of the potential complications associated with it. A minimum of 5 supervised procedures during training have been recommended [21]. Although a pericardial drainage is not rare, it might be uncommon enough for trainees to only be able to acquire experience in just a handful of procedures. A cheap home-made teaching model for ultrasound-guided pericardiocentesis, using two balloons and a fiber supplement, has been successfully developed as a proxy for pericardiocentesis, but physicians in training should nevertheless be exposed to as many real-life procedures as possible under expert supervision [45].

Complex invasive cardiac procedures are often performed under full anticoagulation or antiplatelet therapy, adding to the risk of an urgent pericardial drainage in case of an iatrogenic cardiac tamponade [4]. Drainage of acute effusions related to cardiac procedures was indeed found to be associated with a 2.4-times higher risk of complications and a 27% higher risk of in-hospital mortality in a contemporary large Chinese pericardiocentesis series [13]. This is likely related to the antithrombotic therapies, but also to the additional challenge of correctly locating a small hemorrhagic pericardial fluid collection, indistinguishable from circulating blood, in urgent circumstances.

When a patient deteriorates after initial improvement after a pericardiocentesis, a pericardial decompression syndrome needs to be ruled out. Pericardial decompression syndrome is a rare complication, resulting in a paradoxical acute global cardiac failure and pulmonary edema after pericardial drainage. Its occurrence is probably underreported, and might occur in up to 5% of all pericardiocentesis cases, especially after rapid drainage of a large volume. The pathophysiology of acute myocardial dysfunction following pericardial drainage is poorly understood and is probably multifactorial, related to relative changes in right versus left ventricular hemodynamics [46] and coronary flow, as well as changes in sympathetic drive [47]. As a consequence, the management of decompression-related cardiac failure is mainly supportive. It is thought to be largely preventable by limiting the initial volume drained to 1000 mL, and removing the remaining fluid more slowly via an indwelling catheter.

Hemodynamic deterioration following initial improvement after pericardial drainage can also by caused by a pneumopericardium. Sudden negative intrapericardial pressure, e.g. while drawing a deep breath or excessive coughing, can cause air to be sucked in and trapped in the pericardial space, both during open needle access during the pericardiocentesis or after the procedure when the drainage system is not well connected. A small amount of air is harmless, but large amounts can cause a tension pneumopericardium and hemodynamic instability and need to be managed immediately. It is important to rule out an iatrogenic tension pneumopericardium in a patient who remains or becomes hemodynamically unstable despite a successful pericardial drainage, in which case an emergency echocardiography will show an obscured heart, and a fluoroscopy will reveal the presence of intrapericardial air. Other causes of hemodynamic instability after a pericardiocentesis include a pneumothorax or an excessive bleeding from an inadvertent liver or intercostal artery puncture and also need to be ruled out immediately using additional imaging.

Outcome after pericardiocentesis

Both short and long-term outcome of patients undergoing a pericardiocentesis largely depend on the etiology of the effusion [48]. Recurrences after a pericardiocentesis are rather frequent, certainly when no pericardial drain is left in place for at least 24–48 h after the pericardiocentesis [49]. Registries suggest that recurrences affect 1 out of every 4 patient after a pericardiocentesis [29,50]. Often, a new pericardiocentesis is then unavoidable. In other cases, especially in cancer patients, a more permanent surgical intervention or an extended catheter drainage can be necessary. In addition, in asymptomatic patients with a pericardial effusion initially managed non-invasively, it remains important to monitor the extent of the effusion over time and plan an intervention when symptoms arise or the effusion progresses [21,51]. Although some patients with a pericardial effusion often initially have features of constriction on imaging after pericardiocentesis, this rarely progresses to serious symptomatic constriction requiring surgery [42].

Life expectancy after a pericardiocentesis for a post-viral infection or idiopathic effusion is excellent, but can be bleak in other etiologies [48]. We recently reported on the outcome of our consecutive pericardiocentesis patients over the span of a decade, with a median follow-up of 26 months [9]. Unsurprisingly, patients with malignant pericardial effusion had a significantly worse long-term prognosis compared to patients with another (or no definite) diagnosis (hazard ratio 3.3, 95% CI 2.4–4.6). After two years, about 80% of patients with an underlying malignancy had died. Similar very poor survival rates in cancer patients were reported in another contemporary cardiac tamponade cohort [23,52]. Patients with an iatrogenic effusion also have a poorer outcome in the years fol-

lowing the pericardiocentesis, reflecting a higher risk due to their comorbidities rather than excessive immediate risk associated with the procedure itself.

Pericardiocentesis in malignancy

Although there are geographical differences in the etiology of pericardial effusions requiring pericardiocentesis, malignancy is universally one of the most frequent causes. Cancer-related pericardial effusions are especially frequent in tertiary hospitals with a large oncology practice. A significant pericardial effusion can affect the outcome of cancer patients, in the form of a life-threatening acute tamponade but also as a first or additional metastatic site. Early detection and expedite work-up of a pericardial effusion can therefore have a significant impact on the management of cancer patients.

Several pathophysiological mechanisms can contribute to a cancer-related pericardial effusion. The effusion is frequently either due to metastatic or direct invasion of a non-cardiac tumor, often resulting in a hemopericardium, but also secondary to mediastinal lymph node involvement or even paraneoplastic [53]. Furthermore, effusions can also be caused by or be the result of specific cancer treatments, such as mediastinal radiation, certain chemotherapeutic agents or opportunistic infections in immunocompromised patients receiving chemotherapy, as well as post-operatively in patients who underwent thoracic surgery. Primary solid tumors of the pericardium, including malignant mesotheliomas and synovial sarcomas, are very rare, and herald a poor prognosis [54].

The diagnosis or exclusion of cancer-related pericardial involvement in malignancy is to large extent established by pericardial cytology. The sensitivity of pericardial fluid cytology ranges from 67% to 92%, depending on the 'gold' standard used per study [55–57] Most often, a specific interpretation of the cytology can be made, i.e. samples appear either benign or malign while an "atypical cells" labeling is uncommon [57]. Assessment of tumor markers in pericardial fluid can help distinguishing malignant from nonmalignant effusions, especially in sanguineous samples with negative cytology, although the cut-off values of these markers remain controversial [58].

Known cancer patients undergoing pericardiocentesis often have a benign cytologic interpretation of their pericardial fluid [57]. Vice versa, up to 90% of patients with a pericardial fluid sample cytology positive for malignancy have previously known cancer, however [56,57]. In a contemporary cohort of consecutive pericardiocentesis patients, positive cytology was found in a quarter of all patients and more than half of the cancer patients [9]. Importantly, more than 10% of pericardiocentesis patients had a new diagnosis of cancer or had a first metastatic site of an already diagnosed cancer. In this study, outcome was equally deplorable regardless of the presence of cancer cells in pericardial fluid samples [9]. In a similar cohort, lung cancer but not breast cancer patients did have a significantly shorter survival with a positive compared to a negative pericardial cytology [23]. In any case, and given the relatively high rate of new diagnoses of malignancy in patients undergoing pericardiocentesis and the clear consequences for treatment and survival, a systematic cytological analysis of pericardial fluid in the absence of a clear-cut alternative clinical diagnosis is simply mandatory [9].

When the etiology of an effusion remains unclear, a pericardial biopsy is sometimes considered to establish the underlying disease in selected cases [22]. Given the pathophysiology of pericardial effusions in cancer, however, it might be more likely to detect malignant cells in fluid samples rather than in a random surgical pericardial biopsy. A direct comparison between pericardial fluid cytology and a pericardial biopsy showed an excellent concordance (88%) [56]. However, cytology appeared to be much more sensitive in detecting pericardial malignancy: 92% versus only 55% for pericardial biopsy. Hence, a pericardial biopsy is rarely necessary, at least not in the initial work-up of the patient with an unexplained pericardial effusion. Still, a concomitant biopsy at the time of pericardiocentesis can increase the sensitivity of detecting malignancy in patients with low-volume effusion [56]. Visually targeted samples taken during pericardioscopy do not appear to improve the diagnostic yield of pericardial biopsies [59]. A biopsy via a minimal invasive surgical procedure might also be preferred in patients with a substantial intrapericardial solid mass.

Malignant effusions tend to relapse. A surgical approach via a pericardial window has long been considered as the most definite way to treat malignant effusions. In one contemporary retrospective study in cancer patients, a surgical pericardiotomy indeed led to a significantly lower risk of relapse versus a percutaneous drainage [60]. On the other hand, the placement of a pericardial catheter allows local administration of sclerotherapy or chemotherapy [61,62]. Several small studies have indeed shown that intrapericardial administration of such agents can prevent relapses, but side effects including fever are fairly common, and sometimes quite severe [63]. In practice, most malignant effusions are treatable percutaneously provided that a catheter is left in place for at least a few days, and a surgical approach can be mostly reserved for relapses or percutaneously inaccessible effusions. In advanced or terminal cancer patients, a percutaneous balloon pericardiotomy can be considered as a less invasive alternative to a surgical pericardial window, although repeat interventions still remain frequent after such a procedure [64]. In the end, it is important to realize that the patient's prognosis is largely determined by the underlying malignancy, which is often in an advanced stage when causing a pericardial effusion [65].

Conclusions

Given the pace of progress made in advanced invasive cardiac therapies and cancer therapies, it is likely that the need for pericardiocentesis procedures will only continue to grow in the foreseeable future, especially in tertiary centers. Fortunately, with the help of several procedural improvements over the past decades, echocardiography and fluoroscopy-guided percutaneous pericardiocentesis has become the standard intervention for evacuating large pericardial effusions, as well as an essential tool in the diagnostic work-up of an unexplained pericardial effusion. When performed by skilled physicians assisted by appropriate imaging it is indeed a very safe procedure, and provided that an indwelling catheter is placed, it is also very effective with an acceptable risk of recurrences. Although some dedicated techniques to safely access the pericardium, even when no or very little fluid is present, have been around for over 20 years, such devices have not yet been adopted in daily practice outside a handful of highly specialized centers. The next frontiers in pericardial effusions management are more likely to be better prevention by safer coronary and electrophysiology interventional techniques in the first place, as well as earlier detection of pericardial involvement and earlier and targeted therapies in cancer-related effusions. Ideally, these frontiers should be pushed with the help of randomized clinical trials.

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