Anesthesia and the patient with pericardial disease

L'anesthésie chez le patient atteint d'une pathologie péricardique

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Abstract

Purpose Pericardial diseases present unique perioperative considerations for the anesthesiologist. The purpose of this review is to provide a summary of the pertinent issues related to the etiology, diagnosis, pathophysiology, and perioperative management of patients presenting for operative treatment of pericardial disease.

Source A selective search of the anesthesia, cardiology, and cardiothoracic surgical literature was carried out with particular emphasis on acute pericarditis, effusion, tamponade, and constrictive pericarditis.

Principal findings The anesthesiologist needs to be well versed in the etiology (i.e., differential diagnosis), pathophysiology, and diagnostic modalities in order to best prepare the patient for surgery. Diagnosis and guidance of management requires a working knowledge of the specific associated

hemodynamic consequences, particularly of the impaired diastolic function that can occur. Echocardiography is essential in the diagnosis and management of these patients.

Conclusions Patients with acute and chronic pericardial diseases often require the need for surgical intervention. Several unique features of acute tamponade and constrictive pericarditis require careful perioperative consideration. With proper preparation and pre-anesthetic optimization, patients with a variety of pericardial diseases can be safely managed before, during, and after their surgical intervention.

Résumé

Objectif Pour l'anesthésiologiste, les pathologies péricardiques s'accompagnent de considérations périopératoires particulières. L'objectif de ce compte-rendu est de résumer certaines des questions pertinentes liées à l'étiologie, au diagnostic, à la physiopathologie et à la prise en charge périopératoire des patients se présentant pour le traitement opératoire d'une pathologie péricardique.

Source Une recherche sélective de la littérature dans les domaines de l'anesthésie, de la cardiologie et de la chirurgie cardiothoracique a été réalisée en se concentrant sur les articles traitant de péricardite aiguë, d'épanchement, de tamponnade et de péricardite constrictive.

Constatations principales L'anesthésiologiste doit bien connaître l'étiologie (c.-à-d. diagnostic différentiel), la physiopathologie et les modalités diagnostiques afin de préparer au mieux son patient à la chirurgie. Le diagnostic et les directives de prise en charge nécessitent une connaissance pratique des conséquences hémodynamiques spécifiques associées, et tout particulièrement de la réduction potentielle de la fonction diastolique. L'échocardiographie est essentielle pour poser un diagnostic chez ces patients et les prendre en charge.

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Conclusion *Les patients atteints de pathologies péricardiques aiguës et chroniques ont souvent besoin d'interventions chirurgicales. Plusieurs caractéristiques uniques de la tamponnade aiguë et de la péricardite constrictive nécessitent un examen périopératoire minutieux. En effectuant une bonne préparation et en optimisant la prise en charge pré-anesthésique, les patients atteints de diverses pathologies péricardiques peuvent être pris en charge en toute sécurité avant, pendant et après leur intervention chirurgicale.*

Patients with a variety of pericardial diseases often present for either invasive diagnostic or therapeutic procedures requiring anesthetic intervention. Whereas information concerning pericardial disease is widely available from various cardiology, anesthesiology, and surgical literature sources, each of these specialties has its own unique perspectives. In this article, the significance of the pertinent pathophysiological considerations is explained along with the corresponding echocardiographic and, where appropriate, surgical perspectives of pericardial disease. In so doing, the purpose of this article is to provide a comprehensive review of the perioperative implications of pericardial disease.

The normal pericardium consists of two tissue layers, namely, a thin smooth visceral layer and a thicker fibrous parietal layer. Between these two layers is the pericardial space which normally contains < 20–25 mL of fluid.¹ Inflammation of the pericardium (i.e., pericarditis) can lead to an excess accumulation of this fluid thereby defining pericardial effusion. The various etiologies of acute pericarditis and effusion are represented in Table 1 and are associated with a wide range of clinical conditions. Their causes can be grouped broadly into infectious, non-infectious, and autoimmune origins. Although non-inflammatory conditions (such as trauma) can also lead to fluid accumulation, acute pericarditis can also result in pericardial effusion. Whether an effusion causes tamponade largely depends on the rate of fluid accumulation. Perioperative management is determined by the overall clinical presentation, with the variable hemodynamic consequences of excessive pericardial fluid accumulation having unique anesthetic considerations.^{2,3}

Patients with a variety of pericardial diseases frequently present for perioperative care. A thorough understanding of the associated pathophysiology and various etiologies of pericardial diseases is required in order to provide optimal anesthetic management. Both acute and chronic conditions occur in the pericardium, each having their own associated clinical concerns. The clinical presentation of pericardial

Table 1 Etiology of pericardial effusion / pericarditis

Infectious
Viral
Bacterial
Tuberculosis
Other
Non-infectious
Traumatic
Penetrating
Non-penetrating
Aortic aneurysm (leaking into pericardial sac)
Post-cardiac surgery
Malignancy
Primary
Metastatic
Acute myocardial infarction
Post-myocardial infarction (Dressler's syndrome)
Renal insufficiency / uremia
Myxedema
Chylopericardium
Post-irradiation
Idiopathic
Autoimmune
Rheumatic fever
Rheumatoid arthritis
Systemic lupus erythematosus
Drug-induced (procainamide)

Adapted from Braunwald⁸⁰ and Oakley⁸¹

effusion is often dependent on other coincident clinical conditions. In particular, pleural effusions can occur due to common inflammatory pathophysiology (Fig. 1). This development can lead to a confusing clinical picture as symptoms common to pericardial effusion, such as dyspnea and orthopnea, can be secondary to the pleural effusion itself or other pulmonary involvement. The therapeutic intervention for pericardial effusion frequently involves concomitant pleural drainage.

Although pericardial tamponade can occur in numerous clinical situations, the post-cardiac surgical patient represents a unique group of patients presenting for pericardial drainage. In the post-cardiac surgery patient, the clinical presentation of tamponade must frequently be differentiated from cardiogenic shock, either from global left ventricular failure or often from isolated right ventricular (RV) failure. In addition, pericardial disruption from the preceding cardiac surgical procedure and the likelihood that the fluid in these postoperative patients is hemorrhagic (often with loculated thrombus) requires special diagnostic consideration. The location and size of effusions as well as

Fig. 1 **A** is a transesophageal echocardiographic (TEE) mid-esophageal four-chamber image demonstrating right atrial collapse (3 arrows) and a moderately large effusion surrounding the right atrium (RA) in a patient following cardiac surgery (LA = left atrium). **B** demonstrates a mid-esophageal descending aorta short-axis view revealing a large left-sided pleural effusion (PE) in the same patient as above (Ao = aorta)

the echocardiographic and hemodynamic consequences are critical to understanding the pathophysiology of pericardial effusion.⁴⁻⁶

Pericardial effusions and tamponade

The clinical presentation of pericardial effusion depends on the speed of accumulation as well as the total volume of pericardial fluid that accumulates.⁷ Spodick outlined the relationship between pericardial stretch induced by this accumulating fluid and the consequent increase in intrapericardial pressure.⁸ In Fig. 2, the intrapericardial pressure curves represent the impact of an accumulating effusion on overall diastolic function. Fluid accumulation that develops slowly allows more time for the parietal pericardium to stretch. Thus, the intrapericardial pressure increases more slowly, and compensatory physiologic mechanisms have time to develop to counter the slowly deteriorating hemodynamic conditions. With rapid fluid accumulation, the limit of the pericardial stretch is reached much earlier with a resultant rapid rise in intrapericardial pressure.

Fig. 2 Pericardial pressure–volume curves are shown in which the volume increases slowly or rapidly over time. In the left-hand panel, rapidly increasing pericardial fluid first reaches the limit of the pericardial reserve volume (the initial flat segment) and then quickly exceeds the limit of parietal pericardial stretch. This causes a steep rise in pressure, which becomes even steeper as smaller increments in fluid cause a disproportionate increase in the pericardial pressure. In the right-hand panel, a slower rate of pericardial filling takes longer to exceed the limit of pericardial stretch because there is more time for the pericardium to stretch and for compensatory mechanisms to become activated. Used with permission from Spodick *et al.*⁸

Cardiac filling is generally dependent on the difference between the intrapericardial and intracardiac pressures. This difference is defined as the myocardial transmural pressure. With an increase in intrapericardial pressure, there is a resultant compression of all cardiac chambers. As the chambers become smaller, cardiac inflow becomes limited, corresponding to a reduction in overall diastolic compliance. This diastolic dysfunction is not due to an intrinsic myocardial effect. Because of the tenuous hemodynamic state, coronary blood flow may also be decreased from the hypotension during tamponade. When equalization of pericardial and cardiac chamber pressures occurs (corresponding to myocardial transmural pressure of zero), it results in near cessation of both cardiac filling and forward blood flow. The consequent hemodynamic collapse can manifest as pulseless electrical activity.

The progression to equalization is dependent on the relative stretch of the pericardium and the rate of fluid accumulation. Often, very large collections of pericardial fluid (in excess of 1 L) can occur if the rate of accumulation is slow (Fig. 3). Equalization is a dynamic process and can fluctuate under the influence of various extracardiac factors, including ventilatory-induced changes in pericardial pressure (discussed further in the text). Activation of the sympathetic nervous system, manifest by tachycardia and peripheral vasoconstriction, occurs in an attempt to maintain blood pressure and cardiac output.

Fig. 3 A transthoracic echocardiographic apical four-chamber view demonstrating a large circumferential pericardial effusion in a patient with advanced lung cancer. Note the imaging depth (26 cm) necessary to picture the entire pericardial space and the heart. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle

Spontaneous (as well as positive pressure) ventilation has significant consequences on myocardial filling with corresponding hemodynamic effects. Normal respiratory variation in cardiac filling occurs due to influences exerted through the transmission of negative intrathoracic pressure (during spontaneous ventilation) on the transmural pressure.⁹⁻¹² Leeman *et al.* demonstrated these changes in groups of healthy volunteers.¹² They demonstrated a small increase in inspiratory blood flow velocity ($< 10\%$) across the tricuspid valve with a corresponding decrease across the mitral valve. This has been a consistent finding in normal patients.^{11,12} Furthermore, normal inspiratory decreases in left ventricular stroke volume (SV) have also been reported.¹²

During inspiration, transmural pressure transiently improves and cardiac filling increases; this then reverts with expiration. With inspiration, the right heart normally increases its filling at the expense of a leftward shift in the interventricular septum. If its compliance is normal, the pericardial space can accommodate most of this shift. This accommodation is incomplete, however, and it is normal for a transient fall in systolic pressure to occur during inspiration. Since the RV diastolic volume increases with inspiration, this is transmitted to the left heart after several cardiac cycles and manifests as an increase in blood pressure following expiration. These two factors combine to produce minimal respiration variation in systolic blood pressure under normal conditions.

Inspiratory changes in SV which manifest as respiratory variation have also been attributed to pleural pressure-induced changes in the capacitance of the pulmonary venous bed. Katz *et al.* concluded that there is some pooling of blood in the pulmonary veins due to the negative pressures occurring during inspiration.¹³ Although this may

be a contributing factor under normal conditions, others attribute it to the competition of the right heart for the relatively fixed total diastolic volume with a resulting reduction in inspiratory left ventricular filling.^{6,7,9,14}

With the development of tamponade, the normal respiratory variations in cardiac filling are greatly exaggerated. As a result of the associated reduction in pericardial compliance, the left heart cannot expand into the constricted pericardial space during inspiration. This causes a pathologic leftward shift of the interventricular septum which impairs both left ventricular filling and flow through the left ventricular outflow tract. Both contribute to the inspiratory reduction in SV which manifests as *pulsus paradoxus* (defined as an inspiratory systolic arterial pressure reduction ≥ 10 mmHg during spontaneous ventilation).¹⁵ Although the decrease in the arterial pulse volume is usually demonstrated by invasive arterial pressure monitoring, it can often be palpated. This palpable decrease in radial pulse was first described by Kussmaul in 1873.¹⁶ The term “total paradox” has been used to describe the total disappearance of the radial or brachial pulse with inspiration.¹⁷ In addition, pulsus paradoxus can also be detected with noninvasive blood pressure measurements using conventional sphygmomanometry. In this case, the pressure is noted when the Korotkoff sounds first become audible during expiration, and it is then differentiated from the pressure when the sounds are continuous during inspiration and expiration, with a difference ≥ 10 mmHg defined as pulsus paradoxus.¹⁷

Although pulsus paradoxus is one of the most sensitive tests for the presence of tamponade,^{18,19} it can be notably absent in certain situations²⁰⁻²² (Table 2). As a result, when present, it is a useful guide towards identifying a potentially high-risk patient, but differences in its sensitivity and specificity present some limitations. Despite significant

Table 2 Conditions where pulsus paradoxus is absent despite tamponade

Aortic insufficiency (severe)
Localized effusion
Severe right ventricular hypertrophy with pulmonary hypertension
Atrial septal defect
Significant (tense) ascites

Table 3 Pulsus paradoxus: differential diagnosis

Pericardial tamponade
Severe chronic obstructive pulmonary disease
Obesity
Congestive heart failure
Asthma
Hypovolemia

hemodynamic compromise, loculated effusions may cause only localized chamber compression (i.e., regional pericardial tamponade). In this situation, limitations in cardiac filling occur independently of respiratory variation, and there may be no pulsus paradoxus present. In severe RV hypertrophy with pulmonary hypertension, severe pre-existing arterial hypertension, tense ascites, atrial septal defects, and severe aortic insufficiency,^{8,23} pulsus paradoxus can also be absent. The specificity of pulsus paradoxus has also been questioned, as it can also occur with severe chronic obstructive pulmonary disease,²⁴ exacerbations of asthma, obesity, congestive heart failure, and significant hypovolemia² (Table 3). Although paradoxical pulse is a regular feature of cardiac tamponade, it is important to note that it is a rare finding in constrictive pericarditis (CP). Indeed, the symptoms are less severe when it does occur, in part because the relatively rigid pericardium of CP reduces the degree to which the intrathoracic respiratory-induced pressure changes are transmitted to the pericardium.

Diagnosis of acute pericarditis and tamponade

The clinical signs and symptoms of pericardial tamponade are well described; dyspnea, particularly when supine (i.e., orthopnea), is one of the most frequent symptoms. This dyspnea is a subjective sensation caused by the increase in left atrial and pulmonary venous pressures which then stimulate juxta-capillary receptors (J-receptors) in the pulmonary alveolar interstitium.^{25,26} Although subjective, the dyspnea-stimulated J-receptors lead to activation of the Hering-Breuer reflex, which results in inspiratory termination before a full inspiration occurs.²⁵ The resulting rapid shallow breathing can significantly impair subsequent oxygenation and ventilation.²⁷

Overall, the clinical presentation of tamponade can be quite non-specific and relies on other diagnostic modalities. The electrocardiogram (ECG) usually demonstrates tachycardia and often has small voltages resulting from the increased distance between the myocardium and the surface ECG electrodes. In addition, the ECG can demonstrate fluctuating changes in amplitude due to swinging of the heart within the pericardium, known as electrical alternans.²⁰ The presence of electrical alternans generally indicates a large effusion.²⁸ Auscultation of the heart may reveal muffled heart sounds as well as a pericardial friction rub. These rubs are classically described as triphasic given that they correspond to atrial systole, ventricular systole, and rapid filling during early diastole. The finding of a pericardial rub needs to be distinguished from that of a pleural rub which usually varies with the respiratory cycle.⁶

In addition to pulsus paradoxus (Table 4), elevated central venous pressure (CVP) and jugular venous

distention are also frequently seen with tamponade. Although the CVP waveform often demonstrates elevated pressures, it should not be relied on for diagnosis. As a result, in the acute management of these patients, any delay in therapy should not be undertaken in order to secure central venous access. Beck's triad, first described in 1935, clinically defined the diagnosis of tamponade as a decrease in arterial blood pressure and an increase in jugular venous pressure (JVP) accompanied by muffled heart sounds.²⁹ This generalized increase in JVP is often confused with a specific inspiratory increase which occurs in the setting of CP and is known as Kussmaul's sign.³⁰

The chest *x-ray* may demonstrate an enlarged cardiac silhouette, with the presence of cardiomegaly indicating an effusion of ≥ 250 mL.⁶ Other radiographic studies, such as computerized tomography (CT) and magnetic resonance imaging (MRI), may also demonstrate pericardial fluid accumulation.

Echocardiography plays a central role in the diagnosis and therapeutic intervention of pericardial effusion.^{28,31-35} Transthoracic (TTE) and transesophageal echocardiographic (TEE) evaluation of the heart and surrounding structures adds critical information regarding the volume and composition of the pericardial fluid as well as the intracardiac blood flow velocities. The quantitative echocardiographic grading of pericardial effusion is accomplished by estimating the distance between the parietal and visceral pericardium. These interpericardial distances, i.e., 0.5 cm, 0.5-2.0 cm, and > 2.0 cm, correspond to mild, moderate, and large effusions, respectively.³⁶ In Fig. 4, a circumferential collection of fluid in the pericardial space is shown, and in Fig. 5, a smaller apical effusion is demonstrated. Localized collections (Fig. 6), frequently loculated and thrombotic in nature, can also result in similar hemodynamic sequelae.

In the post-cardiac surgery patient, differentiating circumferential fluid from localized loculated effusions is particularly important as the pericardial space and mediastinum may contain an abundance of loculated thrombus. In these patients, the absence of a circumferential effusion does not necessarily exclude the diagnosis of a clinically significant effusion or tamponade. After cardiac surgery, the small volumes of pericardial fluid present under usual conditions are not generally seen on echocardiography, with the exception of small collections such as those between the atrium and ascending aorta (i.e., the transverse sinus). Larger collections are considered pathologic and are detected more easily by echocardiography.³⁶

Discriminating between a simple effusion and tamponade can be aided significantly by the accurate interpretation of both two dimensional (2D) echocardiography and Doppler assessments of intracardiac blood flow. In addition to direct chamber compression, increases in pericardial pressure can result in collapse of chamber walls during the

Fig. 4 **A** outlines a transgastric short-axis transesophageal echocardiographic (TEE) image of a moderately large pericardial effusion. Note the circumferential fluid between the epicardium and the pericardium (arrows). **B** is the corresponding transgastric two-chamber view for the same patient

Fig. 5 A transesophageal echocardiographic (TEE) four-chamber view of small effusion near the apex of the heart (arrows). RV = right ventricle; LV = left ventricle

cardiac cycle. As the right atrium generally has the lowest pressure of the cardiac chambers, it is usually the first to collapse (Fig. 1), which is represented by the invagination of the right atrial wall occurring during diastole.³⁷ Indeed, Kronzon *et al.* identified the sensitivity of diastolic atrial collapse more than 25 years ago.³⁸ A similar diastolic collapse of the left atrium or right ventricle (most notable

Fig. 6 A transgastric short-axis transesophageal echocardiographic (TEE) image of a large effusion in a patient three weeks following cardiac surgery. Note the fibrinous strands (arrows) and loculations between the pericardial and epicardial surfaces. RV = right ventricle; LV = left ventricle

Fig. 7 Three-dimensional (3D) full volume acquisition obtained with transesophageal echocardiographic (TEE) demonstrating a moderate pericardial effusion (arrows) surrounding the right atrium (RA) and right ventricle (RV)

at the apex) can also occur. In addition to the 2D images, which may show variable volumes and distribution of the effusion, Doppler assessments of transmitral flow show characteristic patterns in both the spontaneously breathing and positive pressure ventilated patient.^{14,38–40} Three dimensional (3D) echocardiographic imaging (Fig. 7) has also been used to quantify pericardial effusion, although its relative sensitivity and specificity has not been formally compared with 2D imaging.⁴¹

The transmitral flow characteristics (Fig. 8) have been well described,^{11,12} but they can often be a source of confusion, even for the experienced clinician. Part of this confusion is related to the incomplete understanding of the

Fig. 8 A pulsed wave Doppler tracing obtained using transesophageal echocardiography (TEE) showing a mid-esophageal four-chamber view of the transmitral flow in spontaneously breathing patients with pericardial tamponade. Note the reduction in velocities that occur during inspiration, highlighting the echocardiographic correlate of pulsus paradoxus

complexities of normal intracardiac and intrathoracic changes coincident with the respiratory cycle. A thorough understanding of the normal cycles is required before a clinician can integrate the changes that occur with the development of pericardial tamponade. Quantitative assessment of the transvalvular (i.e., tricuspid and mitral) Doppler flow characteristics is central to the echocardiographic description of pericardial tamponade. Respiratory variation in transvalvular flow velocity is a hallmark of the echocardiographic diagnosis of tamponade.⁹ In normal patients, the blood flow velocity across the tricuspid and pulmonary valves usually increases slightly with spontaneous inspiration. Correspondingly, the velocity of the mitral and aortic flow decreases slightly. In tamponade, the blood flow velocity of the tricuspid and pulmonary valves increases sharply (up to 85%) while the transmitral and aortic velocities decrease.¹² The degree to which the transmitral flow decreases to support a diagnosis of tamponade has been variably reported ranging from 25–35%.^{31,42} Two early studies identified the echocardiographic changes seen in tamponade which highlight these respiratory changes.^{11,12} Importantly, TEE assessment in the positive pressure ventilated patient differs significantly, i.e., there are increases in transmitral flow velocity rather than decreases as seen in the spontaneously ventilated patient.

The changes in transvalvular flow during spontaneous ventilation and the physiologic explanations for them are a corollary to the blood pressure changes defined by pulsus paradoxus. That is, with spontaneous inspiration, the transtricuspid flow increases following the increased venous return resulting from the negative intrathoracic pressure. The corresponding decreases (accentuated with tamponade) are

due to the leftward shift of the interventricular septum and possible pooling of blood in the pulmonary venous bed.⁴³

Management of acute pericarditis

The various etiologies of acute pericarditis are outlined in Table 1. Although the vast majority of cases (90%) are idiopathic in origin^{44,45} with the remainder being a scattered assortment of other infectious and non-infectious causes, the treatment options are remarkably similar.⁶ For idiopathic pericarditis, non-steroidal anti-inflammatory drugs (NSAIDs) are considered first-line therapy and successfully treat 85–90% of patients. The NSAIDs used most commonly are indomethacin 75–225 mg·day⁻¹, acetylsalicylic acid (ASA) 2–4 mg·day⁻¹, and ibuprofen 1,600–3,200 mg·day⁻¹.⁶ For the post-myocardial infarction patient where pericarditis can occur in 5–10% of cases, ASA appears to be preferred therapy, as other NSAIDs, at least in experimental settings, have been shown to impair myocardial scar formation^{46–49} and reduce coronary blood flow.⁴⁹ Colchicine 0.6 mg *bid* has also been used alone or in combination with other anti-inflammatory therapies.^{50,51}

For most patients with pericarditis, symptoms usually improve within two weeks, but if persistent, a change in NSAID type or the addition of colchicine may be indicated. Steroids may also be added as secondary therapy, but in studies that have used glucocorticoids as first-line therapy, the incidence of recurrence appears to be greater,^{52–54} making routine steroids inadvisable.^{55,56} The exception is in patients with connective tissue disorders or severe recurrent pericarditis where high-dose steroids may be primarily indicated.⁵⁷

Constrictive pericarditis

Chronic pericarditis can be the late result from any number of acute causes and needs to be differentiated from other clinical entities. Constrictive pericarditis, although relatively uncommon, can occur following infectious (viral, bacterial, or tuberculosis) pericarditis, cardiac surgery, and mediastinal irradiation. Most cases, however, are idiopathic in origin.^{58,59} There is a more complete list of CP etiology in Table 5.

Patients with chronic pericardial constriction may present with a number of signs and symptoms.^{60,61} Tachycardia, though clearly non-specific, is a frequent finding, as the consequent reduction in pericardial compliance in this setting of relatively fixed SV means that increases in tissue oxygen demand can be met only by increases in heart rate.³⁶ Signs of fluid overload range from mild peripheral edema to severe anasarca as well as

Table 4 Sensitivity, specificity, and positive and negative likelihood ratios (LRs) of pulsus paradoxus in the diagnosis of cardiac tamponade

	Pulsus Paradoxus, mmHg	
	>12	>10
Sensitivity, %	98	98
Specificity, %	83	70
LR (95% CI)		
Positive	5.9 (2.4 to 14)	3.3 (1.8 to 6.3)
Negative	0.03 (0 to 0.21)	0.03 (0.01 to 0.24)

CI = confidence interval

*All data from Curtiss *et al.* ($n = 65$)¹⁸Used with permission from Roy *et al.*¹⁷

symptoms related to diminished cardiac output, such as fatigability and dyspnea on exertion. Again, these are non-specific indications and may be similar to RV failure. Physical examination often reveals Kussmaul's sign, an elevated JVP with inspiration.^{16,58} An audible pericardial knock has also been described. Severe constriction can manifest with ascites, pulsatile hepatomegaly, and pleural effusions. These later findings may lead to the misdiagnosis of chronic liver disease. Profound cachexia can also occur in late stages of the disease.

Cardiac investigations and imaging may help with the diagnosis. Electrocardiography demonstrating low voltages and non-specific (but often upward sloping) ST and T wave changes are common.⁶² Patients may also have atrial fibrillation or evidence of atrial changes that may manifest with high voltages, also known as P mitrale. Chest radiography may show a ring of calcification surrounding the heart. Imaging with CT and MRI can be extremely useful in diagnosing CP and in confirming the increased pericardial thickness and calcification. Echocardiography is an essential diagnostic procedure in patients with pericardial constriction, with TEE being particularly sensitive to CP findings.^{63,64}

Several CP findings have been described using echocardiography. These include increased pericardial thickness (with normal pericardium being no more than 1–2 mm in thickness) and an abrupt inspiratory posterior motion of the ventricular septum in diastole, seen with TTE. A less specific finding includes a non-pulsatile dilated inferior vena cava.⁶⁵ Pulsed-wave Doppler also demonstrates characteristic features in CP. The transmitral flow velocity (and in a similar fashion, the transtricuspid RV inflow velocity) demonstrates increased E wave velocities with extremely low A wave velocities, which is consistent with rapid early filling and rapid equalization of left atrium and left ventricle pressures. Changes in the pulmonary vein flows are also consistent with poor atrial filling. As such,

blunting of the S wave velocity with a relatively larger D wave is typically seen along with an exaggerated A wave velocity due to the impaired compliance which then “redirects” flow to the pulmonary vein.³⁶

The “stiff box”⁶⁰ of the calcific pericardium has several predominant physiologic effects which result in some of the features seen in CP. First, the encasing pericardium isolates the heart from the respiratory changes in intra-thoracic pressure. The resulting pressure gradient between the pulmonary veins and the left ventricle (which decreases during inspiration) leads to a reduction in left-sided filling. Thus, small decreases in inspiratory blood pressure can be seen, but pulsus paradoxus is rare. In addition, the fixed constrictive pericardium significantly increases the ventricular interdependence.⁶⁶ In CP, the total blood within the heart changes very little with the respiratory cycle. That is, although the left-sided filling may decrease slightly, the right-sided filling increases due to the inspiratory mediated increases in intra-abdominal pressure that augment venous return (independent of any intrathoracic pressure changes). Lastly, due to the fibrotic constriction, overall diastolic filling is significantly impaired. This results in a relatively fixed SV, making maintenance of cardiac output dependent on increases in heart rate. Thus, tachycardia is a predominant feature of CP.

Although CP can share some of the characteristics of acute pericardial tamponade, its chronic clinical course and diagnostic features generally differentiate it from acute conditions. Features in common include significant diastolic dysfunction with a preserved left ventricular ejection fraction. Both conditions manifest with equally elevated CVP, pulmonary venous pressures, ventricular diastolic pressures, and pulmonary hypertension. In addition, though not always reliably, CVP signs of CP can be differentiated from tamponade by the clinical finding of a “square-root” sign. This is represented on the CVP tracing as a plateau following the Y descent (Fig. 9). However, tachycardia, a frequent finding in both conditions, can make it difficult to discern a discrete plateau (Fig. 10).

Physiologically, the differentiation of CP from tamponade results from the variable ventricular interdependence seen in the two conditions.⁶⁶ Constrictive pericarditis is characterized by an exaggerated ventricular interdependence.⁶⁰ There is considerably more dynamic respiratory fluctuation seen in tamponade than CP, thus making pulsus paradoxus unusual in CP. In some respects, despite the elevated intrapericardial pressures of tamponade, there is still some buffering effect of the left heart on the right. This also explains why Kussmaul's sign of an inspiratory increase in CVP is seen only in CP.⁶⁷ Here, the inspiratory increase in preload, which in CP is mediated by an increase in intra-abdominal pressure (as opposed to reductions in intrapleural pressure which are not transmitted to the heart encased in a

Fig. 9 Hemodynamic changes of constrictive pericarditis as demonstrated from increase pressure monitoring of right atrium (RA) and right ventricle (RV) pressures. Intraoperative hemodynamic tracings before (A) and after (B) pericardiectomy. Before pericardiectomy (A), the diastolic RV tracing demonstrates a “square root” sign (↓), whereas the CVP shows “M” configuration with a plateau after the “y” descent (↓). The RV end-diastolic pressure is 20 mmHg. These features disappeared after pericardiectomy (B), and the RV end-diastolic pressure decreased to 12 mmHg. ECG = electrocardiogram; RVP = right ventricular pressure; PA = pulmonary artery pressure; CVP = central venous pressure. Modified from Skubas *et al.* with permission.⁶⁵

calcific shell), cannot be accommodated by the fixed pericardium of CP.

Constrictive pericarditis vs restrictive cardiomyopathy

Although a relatively uncommon diagnostic dilemma, the differentiation between CP and restrictive cardiomyopathy (RC) can cause confusion. A review of the etiology of RC is presented in Table 6.⁶⁸ Many features considered characteristic of CP may also be present in patients with RC.

Fig. 10 Note the loss of right ventricular pressure/central venous pressure plateau when the R-R interval is diminished (i.e., tachycardia). From Morshedi-Meibodi A, *et al.*, with permission.⁶⁹

Table 5 Etiology of constrictive pericarditis

Etiology	Frequency %
Idiopathic or viral	33-46
Post cardiac surgery	18-37
Post mediastinal radiation therapy (e.g., Hodgkin's disease or breast cancer)	9-13
Miscellaneous	8-36
Post-infectious (tuberculosis or purulent pericarditis)	
Trauma	
Asbestosis	
Systemic lupus erythematosus	
Rheumatoid arthritis	

Based on Bertog *et al.*⁵⁹ and Ling *et al.*⁵⁸

However, distinct differences can be found on physical exam, ECG, and echocardiography. The various features that differentiate CP from RC are presented in Table 7.

An important pathophysiologic feature of CP is dissociation of intrathoracic from intracardiac pressure coupled with the increased ventricular interdependence, features not manifest in RC.⁶⁹ Doppler echocardiography can be used to demonstrate this. Mitral inflow velocity variation of > 10% (but commonly $\geq 25\%$) is suggestive of CP.⁶⁵ In CP, E wave velocity is normal (or elevated), indicating preserved elastic recoil, even when the respiratory variation in transmitral E wave is blunted or absent. However, the E wave is reduced in RC as a result of intrinsic myocardial disease. In addition, increased respiratory variation in the mitral inflow E wave velocities differentiates CP from RC where minimal respiratory variation is seen. Mitral annular tissue Doppler can also assist in the differentiation of CP

Table 6 Etiology of restrictive cardiomyopathy

Infiltrative disorders
Amyloidosis
Hemosiderosis
Sarcoidosis
Endomyocardial fibroelastosis
Scleroderma
Radiotherapy
Idiopathic

from RC. Typically, the E' velocity is $< 8 \text{ cm}\cdot\text{sec}^{-1}$ in RC and $> 8 \text{ cm}\cdot\text{sec}^{-1}$ in CP.

Surgical considerations

A variety of approaches have been described to address surgical therapy of pericardial effusion. These include needle pericardiocentesis, percutaneous catheter drainage and balloon pericardiotomy, pericardioperitoneal shunt, subxiphoid pericardial window, and pericardial window through either anterolateral thoracotomy or thoracoscopy.⁷⁰ Needle pericardiocentesis, ideally performed using echocardiographic guidance, can also be used to obtain fluid for diagnostic purposes. The optimal drainage procedure for non-constrictive effusions is unclear and varies according to operator preference and familiarity. The choice of drainage procedure is also partly dependent on the etiology of the effusion and the overall clinical condition of the patient.

The most common surgical approaches involve either subxiphoid access to the pericardial space or a direct intrathoracic technique via either thoracotomy or video-assisted thoracoscopy (VATS). Compared with the subxiphoid window, the advantage of the thoracotomy or VATS approach is that it allows for the creation of a pleuropericardial window. This facilitates continued drainage from the pericardial space into the adjoining pleural space and the avoidance of tamponade recurrence while the effusive process dissipates.⁷¹ Long-term control of the effusive pericardium appears to be better with an intrathoracic approach where a communication between the pericardium and the pleura can remain to allow continuous drainage into the pleural space.⁷² Whereas this approach may not always address the primary reason for the fluid collection itself, it does prevent the development of an ongoing pericardial effusion and decreases the risk of recurrent tamponade. Any subsequent pleural accumulation, if significant, can be dealt with via simple tube thoracostomy.

Surgery for CP is quite different from that for pericardial effusion, varying in both surgical approach and perioperative risks. In contrast to pericardial effusion, CP is best treated with pericardiectomy (pericardial stripping) through a sternotomy in order to allow a more thorough removal of a large portion of the constricting pericardium. Regardless of the approach used, surgery for effusion is technically more straightforward, and complications arising from the procedure are uncommon. Significant bleeding is also unusual, but its occurrence always demands a contingency plan. In addition, ventricular function is not usually affected by the effusion or the procedure itself so the postoperative course is usually smooth.

Table 7 Features differentiating constrictive pericarditis from cardiac restrictive cardiomyopathy

Clinical feature	Constrictive pericarditis	Restrictive cardiomyopathy
Early diastolic sound	Frequent	Occasional
Late diastolic sound	Rare	Frequent
Atrial enlargement	Mild or absent	Marked
Atrioventricular or intraventricular conduction defect	Rare	Frequent
QRS Voltage	Normal or low	Normal or high
Pulsus paradoxus	Frequent, but usually mild	Rare
Pericardium	Thickened	Normal
Left ventricular hypertrophy	Unusual	Frequent
Mitral or tricuspid regurgitation	Rare	Frequent
Transmitral E wave velocity	Normal (or elevated)	Reduced
Transmitral flow velocity variation	Common: exhalation $>$ inspiration ($\geq 25\%$)	Rare
Pulmonary venous flow velocities	Respiratory variation ($\geq 25\%$); S:D > 1	Little respiratory variation S:D < 1
Mitral annular velocities	$E' > 8 \text{ cm}\cdot\text{sec}^{-1}$	$E' < 8 \text{ cm}\cdot\text{sec}^{-1}$
CVP	No Respiratory Variation	Normal Respiratory Variation

S = systolic; D = diastolic; CVP = central venous pressure

Adapted from Whittington *et al.*³⁶ and Morshedi-Meibodi *et al.*⁶⁹

In contrast, pericardial stripping for CP is a more technically demanding procedure and poses a significant risk of acute and persistent bleeding from injury to the myocardium and the epicardial vessels. The operation carries significantly more morbidity as it is usually carried out through a sternotomy with the occasional need for cardiopulmonary bypass. The postoperative course can be unpredictable as, unlike pericardial drainage, the myocardium can be variably affected by the underlying disease process. There is often a prolonged period of persistent constrictive physiology which manifests in continued patient symptoms and cardiopulmonary instability.

Following surgical resection for CP, the diastolic filling patterns can remain abnormal in a significant number of patients.⁷³⁻⁷⁵ Indeed, Senni *et al.* reported diastolic follow-up in 58 patients following pericardiotomy for CP.⁷⁶ Early (within 14 days of surgery) Doppler follow-up demonstrated persistent diastolic abnormalities in up to 60% of these patients. Later follow-up (more than three months postoperatively) demonstrated persistent diastolic abnormalities in 40% of the original patients. Furthermore, those with abnormal Doppler findings were more likely to be symptomatic. Indeed, although most patients were asymptomatic in the month following surgery, more than 80% of patients who had abnormal findings continued to have dyspnea (New York Heart Association classes II-IV).⁷⁶

Anesthetic considerations

A number of clinical parameters need to be integrated during the development of an anesthetic plan for the patient with pericardial disease, particularly those requiring drainage of acute pericardial effusion. The acuity of presentation and the patient's signs and symptoms play a crucial role in determining the anesthetic management strategy. In addition to incorporating the patient's hemodynamic profile into the anesthetic approach, the choice of surgical approach has its own nuances to consider. Importantly, the perioperative management requires a multi-disciplinary approach based on clear communication of the intraoperative plan amongst the entire team involved.

The anesthetic plan requires careful consideration of the preoperative assessment and investigations, anesthesia (including induction, maintenance, and emergence), and the immediate postoperative period. A focused history and physical examination should be completed in order to illicit the etiology of the pericardial effusion (and its possible concomitant conditions) as well as the severity of any hemodynamic compromise. Ideally, a thorough and complete preoperative evaluation should be undertaken,

although the time required to do this must be balanced by the overall condition of the patient. Frequently, there is limited time for an extensive evaluation as the urgency of the situation often dictates rapid intervention. In a patient with known pericarditis or effusion, an evaluation for the presence of tamponade should be foremost as the preoperative evaluation proceeds. Symptoms to identify and explore include tachypnea, dyspnea, orthopnea, lightheadedness, and chest pain/pressure. Physical examination should include an evaluation of vital signs and an assessment of any respiratory compromise, including the presence of decreased oxygen saturation and adequacy of air entry on chest auscultation. Tachycardia, hypotension, pulsus paradoxus, and jugular venous distension should be noted, and auscultation of the heart should focus on the presence of any pericardial rubs or muffling of the heart sounds.

The extent of preoperative investigations is dependent on the stability of the patient and the urgency of surgery. Laboratory investigations should focus on hematologic (hemoglobin and platelet count), coagulation (international normalized ratio), and biochemical analysis, including electrolytes and creatinine level (to assess renal function). If conditions allow, a chest *x-ray*, CT scan, or MRI can be useful; however, an echocardiogram can be essential in making the correct diagnosis of pericardial effusion with or without tamponade.

In addition to the use of routine monitors, preoperative invasive arterial blood pressure monitoring is essential. Although useful, establishing central venous access is clearly optional and should not delay urgent pericardial decompression in severely compromised patients. However, in the absence of a specific central venous cannula, the risk of significant bleeding does necessitate that large-bore peripheral venous access should be established. Preparation for anesthetic induction should include the availability of adequate resuscitation fluids (including cross-matched blood) as well as the ready access to vasopressors (e.g., phenylephrine or norepinephrine) and inotropic agents (epinephrine). A defibrillator should also be readily available due to the possibility of a malignant dysrhythmia occurring with the subsequent manipulation of the pericardium and heart.

The various anesthetic management strategies to consider in the patient undergoing pericardial drainage procedures are summarized in the algorithm in Fig. 11. The patient presenting with significant signs and symptoms of compromise, such as dyspnea in the recumbent position or overt pulsus paradoxus, should be handled with extreme caution. If the patient is nearing hemodynamic collapse, an awake subxiphoid percutaneous drainage approach is warranted to relieve the immediate compromise. This can be followed by addressing the effusion afterwards in a

Fig. 11 Management strategies for patients with varying severity of pericardial effusion / tamponade. In the absence of overt cardiogenic shock, management of pericardial effusion drainage relies on the determination of its hemodynamic significance. When no tamponade is present, a conventional intravenous induction can proceed. If there is significant tamponade, consideration can be given to the potential for an inhalational induction, unless specific contraindications exist.

(#) Conditions that might preclude inhalational induction include significant aspiration risk, significant obesity, severe orthopnea, or an uncooperative patient. If positive pressure ventilation is well tolerated without worsening of the hemodynamic state, conventional intubation can proceed with the use of paralytic agents. The need for vasoactive therapy should be anticipated regardless of the technique chosen

more definitive manner. However, if the patient is uncooperative and combative, anesthesia may have to be induced with contingencies made for a possible cardiac arrest and the need for emergency open drainage. The asymptomatic and cooperative patient who demonstrates no hemodynamic consequence can be managed more conventionally and with considerably more preparation and time. However, the majority of patients lie between these two clinical extremes.

Several anesthetic approaches can be utilized for patients presenting for a drainage procedure.^{2,3,77} Local anesthesia with supplemental sedation may be used for needle pericardiocentesis and even for subxiphoid windows (in more heavily sedated patients). The use of ketamine may allow for the maintenance of spontaneous ventilation. Otherwise, general anesthesia is required, ideally with concomitant endotracheal intubation. The hemodynamic goals for patients requiring general anesthesia should include maintaining (and usually augmenting)⁷⁸ preload. Other important goals include the maintenance of afterload, contractility, and heart rate (optimally in sinus rhythm

to facilitate ventricular filling with an atrial “kick” in patients with acute diastolic dysfunction).

Airway and ventilatory management requires careful attention. Positive pressure ventilation should be avoided as much as possible, and if and when required, it should be instituted cautiously with the minimal inspiration pressure required to provide adequate minute ventilation. The combination of positive pressure ventilation that decreases venous return as well as vasodilation and direct myocardial depression from the anesthetic agents themselves can result in significant hemodynamic deterioration. When conditions allow, an inhalational induction technique may be ideal and should aim to minimize coughing and straining while maintaining spontaneous ventilation. The use of sevoflurane for inhalational induction offers many advantages, particularly as it is less pungent than isoflurane and desflurane and is thus better tolerated by those under mask anesthesia. Premedication with any agents that can depress respiration should be avoided as these can prolong induction by reducing minute ventilation. Care should be taken to ensure a deep level of anesthesia before any manipulation of the

airway is attempted. Invariably, hypotension from vasodilation occurs and can be treated with a continuous vasopressor infusion as the inhalational induction continues.

Intravenous induction of anesthesia can be accomplished safely in patients who are hemodynamically stable (without evidence of tamponade). However, if an intravenous induction is planned in patients not considered candidates for inhalational induction (Fig. 11), consideration should be given to positioning the patient to allow for surgical preparation and draping. If the hemodynamics deteriorate during induction, this will facilitate proceeding with the operation expeditiously once the patient is anesthetized and the airway secured after intubation. This preparation for immediate surgical intervention can also be prudent during inhalational induction, with careful attention during induction not to allow noxious stimuli to the patient that may lead to coughing and/or apnea.

Once the airway is instrumented, the choice of endotracheal tube is partly dependent on the surgical technique utilized. The subxiphoid approach can be accomplished without the need for lung isolation and one-lung ventilation (OLV); however, OLV is usually required for thoracotomy and VATS approaches. In the unstable patient, the additional time it takes to place a double-lumen tube may be problematic. It may be more expeditious to position a single-lumen endotracheal tube and subsequently place an endobronchial blocker.⁷⁹ One limitation in patients who cannot tolerate OLV is the difficulty in accomplishing the direct intrathoracic approach. In this population, the subxiphoid approach may be a better operative choice.

Anesthesia maintenance can be accomplished with various combinations of volatile inhalational agents; intravenous opioids, propofol, and ketamine have all been used successfully. The potential for a breach of the pleural space and the possibility of preoperative hypoxemia should preclude the use of nitrous oxide. Short- or intermediate-acting muscle relaxants may be utilized if necessary but ideally only when the patient has been shown to tolerate positive pressure ventilation. Continuous intravenous infusions of vasopressor or inotropic agents may be required to maintain hemodynamic stability, but they should be considered temporizing measures with their own adverse consequences due to excessive vasoconstriction which may restrict overall cardiac output.

Longer-acting opioids (i.e., morphine or hydromorphone) can be used prior to emergence from anesthesia for postoperative analgesia. Consideration should also be given to either local anesthetic infiltration of the wound or the performance of intraoperative regional nerve blocks (i.e., intercostal nerve blocks) by the surgeon. Decisions regarding extubation at the conclusion of the procedure should depend on the patient's cardiovascular and respiratory status. Similarly, the need for continued intensive

postoperative monitoring is dependent on the overall status of the patient. Patients may require a variable period of continuous monitoring in a postanesthesia care unit or an intensive care unit setting.

Summary

Acute and chronic pericardial diseases often require patients to present with the need for surgical intervention. The anesthesiologist needs to be well versed in the etiology (i.e., differential diagnosis), pathophysiology, and diagnostic modalities in order to best prepare the patient for surgery. Several unique features of acute tamponade and CP require careful perioperative consideration. With proper preparation, the patient presenting with pericardial disease can be optimally and safely maintained.

Multiple choice questions

- Constrictive pericarditis can be associated with all of the following EXCEPT:
 - Prominent pulsus paradoxus
 - Calcific pericardial findings on chest computed tomography
 - Increased interventricular dependence
 - Tuberculosis
- In pericardial tamponade, cardiac output is enhanced by which of the following?
 - Fluid administration
 - Milrinone administration
 - Positive pressure ventilation
 - All of the above
- Which of the following is seen in the spontaneously ventilating patient with pericardial tamponade?
 - An increase in heart rate and blood pressure during inspiration
 - A decrease in heart rate and blood pressure during expiration
 - An increase in heart rate and blood pressure during expiration
 - A decrease in heart rate and blood pressure during inspiration
- Initial therapy for post-myocardial infarction pericarditis includes:
 - Prednisone
 - Acetaminophen
 - Indomethacin
 - Acetylsalicylic acid
- Conditions where pulsus paradoxus is absent despite significant pericardial tamponade include all of the following EXCEPT:

- a) Tricuspid regurgitation
- b) Aortic insufficiency
- c) Atrial septal defect
- d) Right ventricular hypertrophy

For the correct responses to these multiple choice questions, refer to the electronic supplementary material for this article.

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