Pericardial effusion in pulmonary arterial hypertension

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Abstract: Pulmonary arterial hypertension (PAH) is a serious condition that can lead to right heart failure and death. Pericardial effusion in PAH is associated with significant morbidity and mortality, and its pathogenesis is complex and poorly understood. There are few data on the prevalence of pericardial effusion in PAH, and more importantly, the management of pericardial effusion is controversial. Current literature abounds with case reports, case series, and retrospective studies that have limited value for assessing this association. Hence, we summarize the available evidence on this ominous association and identify areas for future research.

Keywords: pulmonary hypertension, pericardial effusion, pericardial tamponade.

Pulm Circ 2013;3(3):467–477. DOI: 10.1086/674302.

INTRODUCTION

Pulmonary hypertension (PH) is a serious condition that can lead to right heart failure and death.[1] The Fourth World Symposium on PH categorized PH into 5 groups.[2] Group I includes patients with pulmonary arterial hypertension (PAH). PAH is defined as a mean pulmonary arterial pressure ≥25 mmHg at rest associated with a pulmonary artery occlusion pressure ≤15 mmHg and pulmonary vascular resistance ≥3 Wood units.[1,2] Group I can be further subdivided into idiopathic PAH (IPAH) or PAH associated with other medical conditions, such as connective tissue disorders, HIV infection, congenital left-to-right shunts, or liver disease.[2]

PAH continues to be an area of cardinal interest to clinicians because of its association with significant morbidity and mortality.[3] Accurate assessment of the prognosis of the disease has proven to be difficult; nevertheless, investigators have identified factors associated with poor prognosis, such as older age, male sex, rapid progression of disease, low functional capacity, elevated plasma brain natriuretic peptide levels, high right atrial pressure, and low cardiac index.[3-5] The echocardiographic factors that adversely affect prognosis in PAH are right ventricular dysfunction and the presence of pericardial effusion.[6-8] Data from the Registry to Evaluate Early and Long-Term PAH Disease Management showed that pericardial effusion worsens the prognosis in patients with PAH.[3] In this registry, the presence of pericardial effusion was associated with a higher mortality, with a hazard ratio (HR) of 2.02 (95% confidence interval [CI], 1.61–2.54).[3] Moderate-to-severe and severe pericardial effusions were associated with mortality

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Submitted January 2013; Accepted June 2013; Electronically published November 22 2013.

with an HR of 2.9 (95% CI, 1.91–4.29) and 3.4 (95% CI, 1.42–8.28), respectively. Interestingly, on multivariate analysis, the presence of pericardial effusion remained significantly associated with poor survival, with an HR of 1.35 (95% CI, 1.06–1.72; $P = 0.014$). Pericardial effusions were evaluated in the parasternal long- and short-axis views and were graded as absent, trace (systolic and diastolic separation of pericardial layers), small (separation <1 cm), moderate (separation ≥1 cm but <2 cm), and large (separation ≥2 cm).[9]

Eysmann et al.[9] prospectively correlated a variety of echocardiographic and hemodynamic parameters with outcomes for 26 patients with IPAH. In these patients, the severity of pericardial effusion was independently associated with mortality. Raymond et al.[10] found that pericardial effusion in patients with IPAH was significantly associated with death (HR, 3.89 [95% CI, 1.49–10.14]). Data from the Chinese registry also showed that patients with pericardial effusion had significantly shorter survival than did those without it.[11] In this registry, patients with PAH with pericardial effusion had 1- and 3-year survival rates of 85% and 68%, respectively; the survival rates for those without pericardial effusion were 93% and 74%, respectively.

Furthermore, a recent Canadian study[12] demonstrated a worse survival among patients with PAH who developed pericardial effusion. In patients without pericardial effusion, the 1-, 3-, and 5-year survival rates were 94%, 80%, and 64%, respectively. Patients with a small pericardial effusion had a similar survival to those without effusion (1-, 3-, and 5-year survival rates of 98%, 73%, and 70%, respectively). Conversely, patients with PAH who had moderate to large pericardial effusion had a significantly higher mortality (1-, 3-, and 5-year survival rates of 80%, 20%, and 0%, respectively).[12]

Despite the negative impact on the prognosis, little information is known on the prevalence, etiology, hemodynamic consequences, and management of pericardial effusion in patients with PAH. The literature abounds with case reports, case series, and retrospective studies that, in isolation, have limited usefulness for assessing this association. This prompted us to summarize the available evidence and identify areas for future research.

PREVALENCE OF PERICARDIAL EFFUSION IN PAH

The prevalence of pericardial effusion varies depending on the type and severity of PAH studied (Table 1). The Chinese PAH registry noted that patients with PAH associated with connective tissue diseases had a higher prevalence of pericardial effusion than did individuals with IPAH (21% vs. 13%).[11] Fijalkowska et al.[13] described a higher prevalence of pericardial effusion in patients with PH (mostly IPAH) who died than in those who remained alive during follow-up (56% vs. 15%). A Canadian study reported the incidence and prevalence of pericardial effusion among 154 patients with PAH.[12] During the initial assessment, the authors found a prevalence of 29%, and over a 2-year follow-up period, they found an incidence of 44.1%.

PATHOGENESIS OF PERICARDIAL EFFUSION IN PH

It is not well understood why pericardial effusion develops in some patients with PAH. In general, pericardial effusion is associated with the severity of right ventricular failure.[6,8] Indeed, among all the usual hemodynamic measurements obtained during right heart catheterization in patients with PAH, mean right atrial pressure correlates best with the size of the pericardial effusion.[6] One of the leading hypotheses suggests that there is impaired fluid reabsorption of pericardial fluid via the venous or lymphatic channels draining into the right atrium. Therefore, a high right atrial pressure compromises the pericardial fluid drainage, which results in its accumulation (Fig. 1).[6,10,14] In support of this hypothesis, investigators demonstrated that, when both systemic and pulmonary venous hypertension were artificially induced in a dog model, a significant amount of pericardial effusion accumulated.[15] Systemic and pulmonary venous hypertension was produced by inflating balloon catheters in the vena cava and left atrium, respectively. The amount of pericardial effusion did not increase by raising the systemic or pulmonary venous pressure independently, which likely reflects a lower right atrial pressure in the systemic venous hypertension group (3.3 mmHg) than in the combined venous hypertension group (13.1 mmHg). Interestingly, there was no significant difference in

Table 1. Studies describing the prevalence of pericardial effusion in pulmonary arterial hypertension (PAH)

Study	Prevalence of pericardial effusion, proportion (%) of cases	Type of PH, proportion (%) of cases	PH-specific treatment, %
Benza et al.[3]	532/2,105 (25)	IPAH: 1,262/2,716 (47); CTD PAH: 648/2,716 (24); other: 806/2,716 (30)	PA: 42; ERA: 47; PDE-5 I: 50
Hinderliter et al.[6]	43/79 (54)	IPAH: (100)	PA alone: 50; PA plus conventional therapy: 50
Batal et al.[8]	11/72 (15)	IPAH: 4/58 (8); CTD PAH: 7/14 (54)	PA: 20 (8 of 47 cases)
Zhang et al.[11]	45/276 (16)	IPAH: 23/173 (13); CTD PAH: 22/103 (21)	PDE-5 I (IPAH): 79; PA (IPAH): 2; PDE-5 I (CTD PAH): 74; PA (CTD PAH): 1
Eysmann et al.[9]	17/26 (65)	IPAH: (100)	Survivors: CCB in 100; nonsurvivors: CCB in 42
Raymond et al.[10]	42/79 (53)	IPAH: (100)	PA alone: 50; PA plus conventional therapy: 50
Hemnes et al.[45]	6/6 (100)	IPAH: 3/6 (50); CTD PAH: 1/6 (17); other: 2/6 (33)	PA: 67 (4 of 6 cases)
Shimony et al.[12]	81/154 (53)	IPAH: 44/154 (29); CTD PAH: 29/154 (19); other: 8/154 (5)	PA: 42; ERA: 61; PDE-5 I: 28
Park et al.[37]	27/41 (28)	CTEPH: 25/41 (61); PPH: 2/41 (5)	NA
Bossone et al.[38]	8/51 (15.7)	PPH	NA

Note: Hinderliter et al.[6] and Raymond et al.[10] are 2 studies involving the same cohort of the patients. CCB: calcium channel blocker; CHD PAH: congenital heart disease–associated PAH; CTD PAH: connective tissue disease–associated PAH; CTEPH: chronic thromboembolic PH; ERA: endothelin receptor antagonist; IPAH: idiopathic PAH; NA, not available; other: includes HIV-associated PAH, porto-pulmonary PAH, drugs/toxins-related PAH, and familial PAH; PA: prostacyclin analog; PDE-5 I: phosphodiesterase-5 inhibitor; PH, pulmonary hypertension; PPH: primary pulmonary hypertension (term formerly used to refer to IPAH).

pericardial fluid accumulation between pulmonary and systemic venous hypertension; however, when both systemic and pulmonary venous pressure were increased, the amount of pericardial fluid was greater than expected as a result of a higher right atrial pressure that limited the drainage of pericardial veins into the right atrium.[15]

On the other hand, inflammatory conditions, such as systemic lupus erythematosus and scleroderma, can independently affect the pericardium and lead to pericardial effusion. In fact, a higher prevalence of pericardial effusion was reported by Fisher et al.[16] among patients with PAH who had scleroderma than among patients with IPAH (HR, 2.83 [95% CI, 1.34–5.98]).

HEMODYNAMIC EFFECT OF PERICARDIAL EFFUSION AND TAMPONADE

The filling of cardiac chambers is dependent on the pericardial sac volume. The accumulation of fluid in the pericardial cavity raises the intrapericardial pressure, hence reducing the compliance of the cardiac chambers. In general, when the fluid in the pericardium accumulates slowly, it does not pose an immediate threat, but it may compromise the intracardiac chamber filling at a later stage.[17] The development of

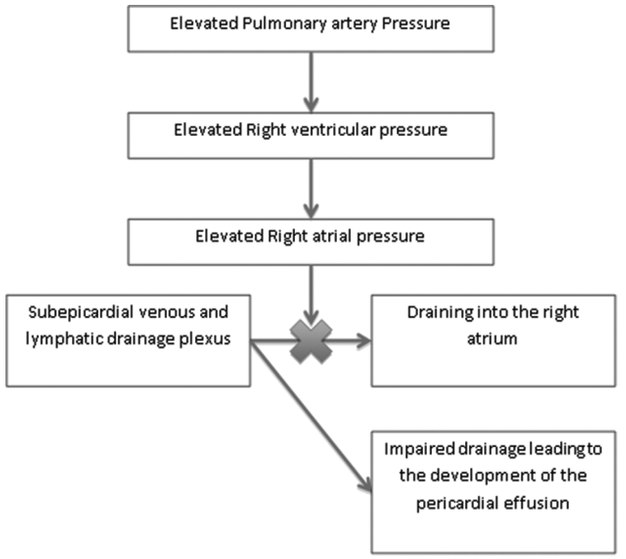

Figure 1. Mechanisms for the development of the pericardial effusion in patients with pulmonary arterial hypertension. A color version of this figure is available in the online edition.

the tamponade depends on the amount of fluid and the rate at which fluid accumulates in the pericardium.

Typically, the intrapericardial pressure (normal value, –3 to –6 mmHg) is lower than the filling pressures of the cardiac chambers; therefore, it does not affect the preload. However, an ample amount of fluid may increase the intrapericardial pressure to a level above the ventricular diastolic pressure.[18] In this case, the elevated pericardial pressure impairs the intracardiac filling, and cardiac tamponade ensues. In cardiac tamponade, the pericardial cavity behaves like a fifth cardiac chamber, reducing the space within the pericardium and thus the capacity of the atria and ventricles to expand appropriately during diastole.[17] In fact, the actual cardiac chamber–filling pressure is the gradient between the intracardiac and intrapericardial pressures. As a result, higher intrapericardial pressure translates into higher diastolic intracardiac pressures to preserve ventricular inflows.[19] In addition, the mean diastolic pressures equalize across cardiac chambers, and ventricular interdependence becomes exaggerated. Equalization of the diastolic pressure in the cardiac chambers is a hallmark sign of cardiac tamponade.[17] Thus, when the volume in a cardiac chamber increases, there must be an equal decrease in other chambers to compensate for it. Because the total pericardial sac volume is fixed by the pressurized effusion, the increase in the right ventricular preload during inspiration is accompanied by a decrease in the left ventricular volume and cardiac output that is manifested as an accentuated pulsus paradoxus. As a result, in tamponade, left heart filling occurs preferentially during expiration when the preload of the right ventricle is less. The ultimate hemodynamic consequence of tamponade is a decrease in cardiac output, with the most extreme manifestation being refractory shock. The mechanisms described above are affected in the presence of PH.

CARDIAC TAMPONADE IN THE PRESENCE OF PULMONARY HYPERTENSION

Uncontrolled PAH eventually leads to right ventricular failure with elevation of right atrial pressure and, in some cases, the development of pericardial effusion.[1,6] When pericardial effusion develops, it further compromises the cardiac hemodynamics. Pericardial effusion worsens the paradoxical interventricular septal motion characterized by displacement of the interventricular septum into the left ventricle during inspiration.[20,21] This interventricular asynchrony impairs the preload of the left ventricle and leads to further decreases in cardiac output.

Limited evidence suggests that patients with right heart failure and circumferential pericardial effusion can develop atypical cardiac tamponade, characterized by isolated left ventricle compression. Cardiac tamponade is unique in PH because right atrial and ventricular diastolic collapse, pulsus paradoxus, and hypotension are usually absent.[22-24] The lack of right ventricular diastolic collapse is attributable to the elevated right-sided pressures that are higher than the pericardial pressure. When the increased intrapericardial pressure exceeds the left ventricular diastolic pressure, there is left atrial and/or ventricular diastolic collapse (Table 2).[25-32] Thus, PAH can conceal the classic presentation of cardiac tamponade.[23,24] The absence of pulsus paradoxus is explained by the incapacity of the noncompliant right ventricle to alter its filling volumes in response to the respiratory cycle.[17] Hypotension may be absent in

Table 2. Left ventricular diastolic collapse in patients with pulmonary hypertension (PH) and pericardial effusion

Authors	RVSP or sPAP, mmHg	Hypotension/pulsus paradoxus	Etiology of PH
Frey et al.[25]	110	Absent/absent	IPAH
Lee et al.[26]	60	Absent/15 mmHg	Scleroderma
Brodyn et al.[27]	60	Absent/absent	Scleroderma
Davies et al.[28]	78	Present/not reported	Mitral stenosis
D'Cruz et al.[29]	75	Absent/absent	HIV-related PH
Gollapudi et al.[30]	94	Absent/absent	Undifferentiated CTD
Dunne et al.[31]	87	Not reported	Scleroderma
Garg and Moorthy[32]	150	Present/18 mmHg	RHD

Note: CTD: connective tissue disease; IPAH: idiopathic pulmonary arterial hypertension; RHD: rheumatic heart disease; RVSP: right ventricular systolic pressure; sPAP: systolic pulmonary artery pressure.

some of these patients because of a compensatory increase in systemic vascular resistance.

CLINICAL EVALUATION

A detailed history and physical examination is essential to evaluate the patients with PAH. The NIH registry found dyspnea as the presenting symptoms in 98% of patients with IPAH at the time of enrollment.[5] Fatigue was seen in 73% of the patients, whereas chest pain was observed in 47%. Other symptoms included syncope in 36% of the patients, edema in 37%, and palpitations in 33%.

No single clinical sign is accurate in indicating the presence of pericardial effusion. The finding of tachycardia, distant or muffled heart sounds, worsening jugular vein distention, and hypotension, accompanied by paradoxical pulse (a drop in systolic blood pressure by >10 mmHg during inspiration) may indicate a large pericardial effusion or cardiac tamponade. Beck's triad consists of hypotension, jugular-venous distension, and muffled heart sounds.[33] However, these signs have not been validated in the presence of PH, and most of them are seen in patients with PH who have advanced disease even in the absence of pericardial effusion. The 6-minute walk test assesses the functional capacity of patients with PAH. Hinderliter et al.[21] showed an inverse relationship between pericardial effusion size and distance walked on 6-minute walk test in patients with PAH. More importantly, worsening of clinical symptoms and/or a decrease in functional capacity in the absence of a clear reason could be attributable to development or worsening of pericardial effusion. Table 3 summarizes the clinical presentation of patients with pericardial effusion or cardiac tamponade.

IMAGING STUDIES

Radiological work-up usually begins with a plain chest radiograph. The presence of pericardial effusion can usually be ascertained by reviewing previous studies (Fig. 2). The suspicion raised by chest radiography should be confirmed by echocardiography, which is the preferred diagnostic method to detect pericardial effusion.[34-36]

In a small cohort of patients with PH, Park et al.[37] affirmed the importance of echocardiography in diagnosing pericardial effusion. The authors retrospectively studied whether patients with PH had pericardial effusion by echocardiography (59 patients had PH associated with chronic thromboembolic disease, and 7 had IPAH). Of these, 22 patients had mild and 5 patients had moderate pericardial effusion. Importantly, the authors noticed higher right atrial pressures in patients with pericardial effusion than in those without. Bossone et al.[38] found pericardial effusion on echocardiographic examination in 8 (15.7%) of the patients with significant right-sided chamber dilatation and reduced right ventricular systolic function. Similarly, Hinderliter et al.[21] found that pericardial effusion was common and that its size was

Table 3. Clinical features in pericardial effusion with or without pulmonary hypertension (PH) and cardiac tamponade

Clinical feature	Pericardial effusion without PH	Pericardial effusion with PH	Cardiac tamponade
Etiology	Left heart disease, CTD, infections	PAH, CTD	Malignancies, trauma, aortic dissection, postsurgery or MI, iatrogenic causes
History	Orthopnea, PND, DOE, disease specific	DOE, syncope, fatigue disease specific	Dyspnea, syncope
Physical examination	No specific signs, may hear (S3, S4, gallop) if secondary to LHD, muffled HS or pericardial rub if due to inflammation	Physical examination findings associated with PAH[a]	Findings similar to pericardial effusion without PH plus hypotension and Beck's triad
Electrocardiogram	Tachycardia, electrical alternans, low-voltage complexes	Findings suggestive of PH[b]	Tachycardia, electrical alternans, low-voltage complexes
Chest radiograph	Normal or enlarged cardiac silhouette	Findings suggestive of PH[c]	Normal or enlarged cardiac silhouette, double lucency sign on lateral radiographs
Echocardiography	Pericardial effusion >50 mL, respiratory variation of the mitral and tricuspid valve is less than 20%–25%	Findings suggestive of PH[d]	Diastolic RA/RV collapse, respiratory variation of the mitral and tricuspid valve is increased, ventricular interdependence
Cardiac catheterization	No specific findings until tamponade physiology ensues	Elevated RA, RV, and PA pressures	Equilibration of intracardiac diastolic pressures, inspiratory increase in right-sided pressures, and reduction in left-sided pressures that are responsible for the pulsus paradoxus

Note: CTD: Connective tissue disorder; DOE: dyspnea on exertion; HS: heart sound; LHD: left heart disease; MI, myocardial infarction; PA: pulmonary artery; PAH: pulmonary arterial hypertension; PND, paroxysmal nocturnal dyspnea; RA: right atrium; RV: right ventricle; RVH: right ventricular hypertrophy.

[a] Augmentation of right sided murmurs with inspiration, diastolic murmur (pulmonary regurgitation, jugular venous distension, loud P2, muffled HS, RV heave), systolic murmur (tricuspid regurgitation).

[b] RVH, right axis deviation, an R/S wave ratio >1 in V1, right bundle branch block, P pulmonale.

[c] Enlarged PA, RA dilatation, normal or enlarged cardiac silhouette.

[d] Elevated pulmonary artery systolic pressure estimated by echocardiography, paradoxical bulging of the interventricular septum into the left ventricle (LV), RVH. Diastolic RA/RV collapse may not be present in patients with PAH. Isolated LV collapse may be seen.

inversely associated with cardiac index and directly related to right atrial size and pressure in patients with IPAH.

Echocardiography is also the gold standard for diagnosis of cardiac tamponade, and the typical findings include right atrial and/or right ventricular diastolic collapse, marked (>40%) respiratory variation in the transmitral Doppler flow velocity, and inferior vena cava plethora (Fig. 3).[39,40] However, in the presence of PH, these signs are less sensitive and specific.[23] In a blinded prospective study, Plotnick et al.[23] found that the echocardiographic clues to predict cardiac tamponade were less accurate in the setting of PH. In patients without PH, the predictive accuracies of right atrial collapse, right ventricular diastolic collapse, transmitral Doppler flow velocity variation, and inferior vena cava plethora were 75%, 80%, 90%, and 95%, respectively. However, the accuracy de-

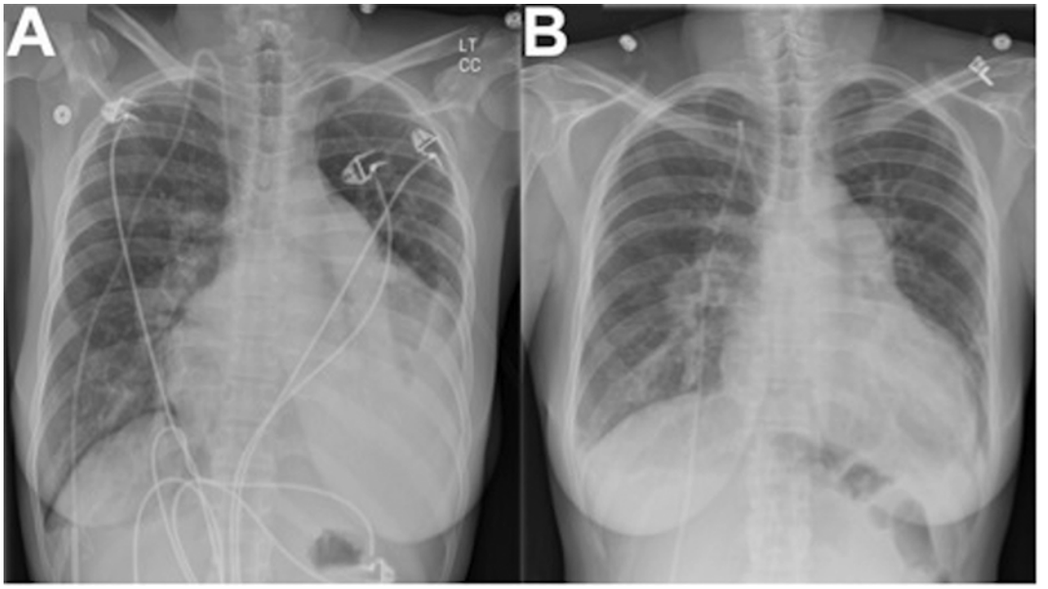

Figure 2. Chest radiographs for a patient with pulmonary arterial hypertension with a large pericardial effusion (*A*) that resolved after pericardial drainage of 900 mL of pericardial fluid (*B*). Both radiographs reveal cardiomegaly and enlargement of the pulmonary arteries.

creased in patients with PH to 67%, 58%, 58%, and 83%, respectively. In patients with PH, inferior vena cava plethora was found to have the best predictive accuracy, whereas right ventricular diastolic collapse and transmitral Doppler flow velocity variation had the least predictive value. Similarly, clinical and echocardiographic signs could not confirm the presence of cardiac tamponade in porto-PH and patients with HIV-associated PH.[41,42]

Baque-Juston et al.[43] evaluated patients with PAH with computed tomography and found that pericardial abnormalities, such as anterior pericardial recess

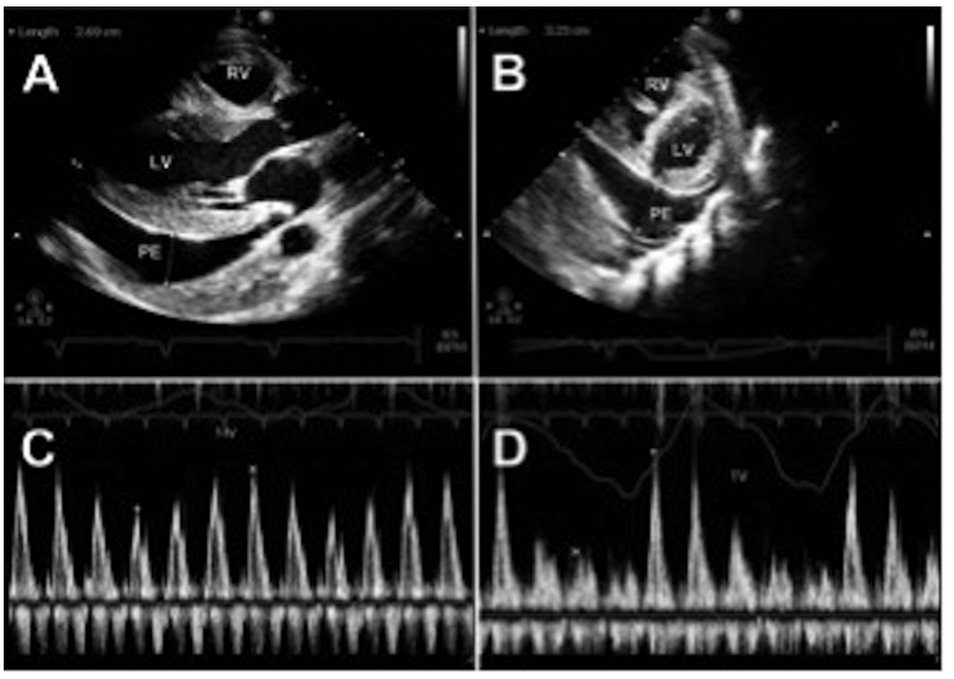

Figure 3. Pericardial tamponade in a patient with heritable pulmonary arterial hypertension. *A*, Parasternal long axis view showing pericardial effusion measured at 2.7 cm. *B*, Parasternal short axis view revealing a large pericardial effusion measured at 3.2 cm and a mildly dilated right ventricle (RV). *C* and *D* show mitral and tricuspid Doppler flow, respectively, with marked respiratory variation (62% across the tricuspic valve and 36% across the mitral valve). LV: left ventricle; MV: mitral valve; PE: pericardial effusion; TV: tricuspid valve.

thickening or effusion, are more frequently seen in patients with severe PAH. In cardiac tamponade, right heart catheterization shows equalization of the diastolic pressures across all chambers without respiratory variation.[44] In addition, there is a characteristic elevation of right atrial pressure between 10 and 30 mmHg with a prominent x wave and a small or absent y wave.

MANAGEMENT

Management of pericardial effusion in the setting of PAH continues to be controversial, mainly because of the limited data.[25,27,31,45-49] In 2004, the European executive summary on the diagnosis and management of pericardial diseases suggested that small pericardial effusions should not be drained in patients with PAH.[50] Cardiac tamponade remained a clear indication for drainage. In addition, they also suggested the drainage of large pericardial effusions (>2 cm). They reported controversy as to whether to drain moderate pericardial effusions (1–2 cm), which may be beneficial in symptomatic patients with potentially treatable comorbidities. Hemnes et al.,[45] in a case series of 6 patients with PAH with large pericardial effusions (tamponade physiology in 5 of them), reported poor outcomes with pericardial drainage. All 5 patients with cardiac tamponade died within 1 year, and 1 patient died within an hour of drainage. The patient without tamponade survived the pericardiocentesis and lived for more than 5 years. Similarly, Krikorian and Hancock[46] and Nafsi et al.[47] reported deaths in their patients with PH after pericardiocentesis. Krikorian and Hancock[46] summarized their data on 123 pericardiocentesis performed for a variety of conditions and reported only 2 deaths in their cohort. One of the deaths occurred in a patient with PAH with suspected cardiac tamponade. Nafsi et al.[47] described the death of a patient with PH with large pericardial effusion (without tamponade) after the drainage of 1,200 mL of pericardial fluid. Brodyn et al.[27] reported symptomatic improvement with medical management of pericardial effusions. Frey et al.[25] described a patient with PH with cardiac tamponade who improved after pericardiocentesis.

Preliminary data, reported in the form of an abstract, showed favorable outcomes with pericardiocentesis.[49] Of 577 patients with PAH, 150 (26%) had pericardial effusions. Of these, 128 had small effusions, and 22 had moderate or large effusions; 14 had findings suggestive of cardiac tamponade requiring pericardiocentesis. Of the 14 patients with hemodynamic instability, 12 had PAH associated with collagen vascular diseases. Survival was 100% at 48 hours after pericardiocentesis, with clinical improvement in 13 patients. The median survivals for patients with PAH with no pericardial effusion, mild pericardial effusion, and moderate pericardial effusion were 69, 36, and 12 months ($P < 0.001$), respectively. The authors concluded that pericardiocentesis could be performed safely in a monitored inpatient setting.

Dunne et al.[31] described 4 patients with scleroderma, elevated right ventricular systolic pressure, and large pericardial effusions. Three of the 4 patients had evidence of tamponade on echocardiographic examination. Of these, 2 patients died of right heart failure after pericardiocentesis. In addition, 1 patient experienced a hemodynamic collapse after the procedure but was immediately managed with sildenafil, epoprostenol therapy, and diuretics.

The mechanism for death immediately after removal of pericardial fluid in certain patients with PH remains unclear. Hemnes et al.[45] postulated that removal of the pericardial effusion leads to the enlargement of the right ventricle cavity, which further pushes the interventricular septum, compressing the left ventricle and leading to hypotension and death. A reduction in coronary blood flow during diastole in a hypertrophic right ventricle can also cause right ventricular ischemia with hemodynamic deterioration. Alternatively, it is possible that these patients have advanced forms of PH with severe right ventricular failure that could lead to a premature death, even if the pericardial tamponade is treated. Death immediately after procedure in cardiac tamponade should not be an expected phenomenon, because there is evidence to suggest that the removal of small quantities of pericardial fluid in the setting of cardiac tamponade results in rapid clinical improvement.[51] Careful selection of cases to undergo drainage and close hemodynamic monitoring of patients both during and after the procedure is essential.

The use of PAH-specific therapy in the management of pericardial effusion in patients with PAH has led to another debate. A controlled, randomized,

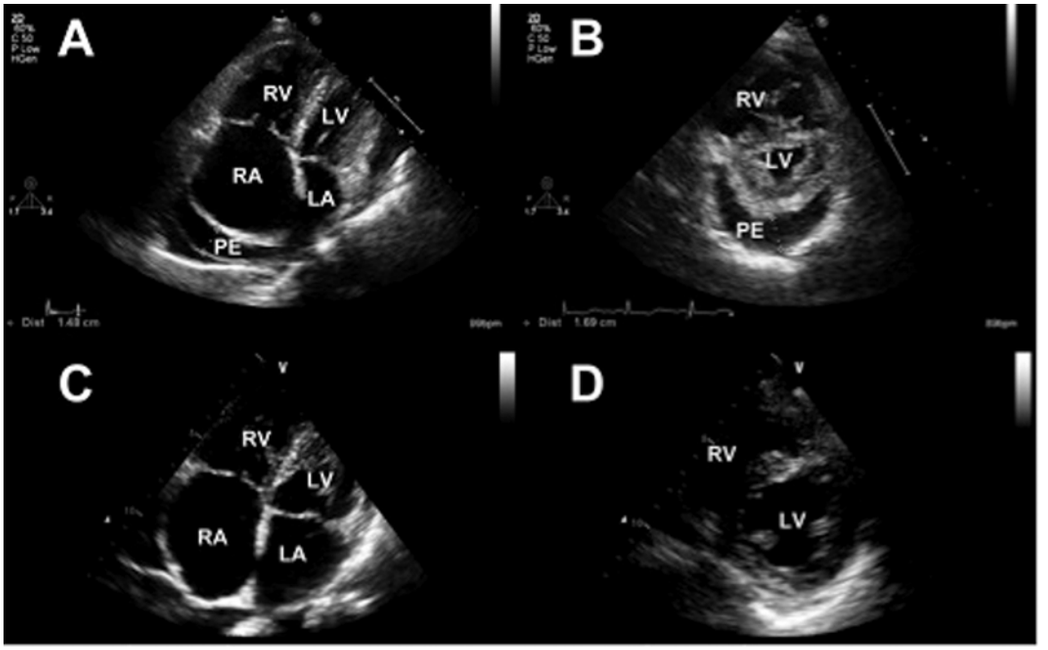

Figure 4. Echocardiographic images showing resolution of pericardial effusion in a patient with pulmonary arterial hypertension before epoprostenol therapy (*A* and *B*) and after a year of epoprostenol therapy (*C* and *D*). LA: left atrium; LV: left ventricle; PE: pericardial effusion; RA: right atrium; RV: right ventricle. A color version of this figure is available in the online edition.

multicenter trial involving patients with PAH evaluated the size of the pericardial effusion before and after 16 weeks of bosentan treatment.[48] The authors reported an improvement in the pericardial effusion scores in treated patients compared with placebo (Fig. 4). Other authors have also reported that PAH specific may be useful in chronic pericardial effusions.[31] Additional research is needed to determine the best treatment for the different degrees of pericardial effusion in patients with PAH who are hemodynamically stable.

CONCLUSION

The presence of pericardial effusion in patients with PAH is an indicator of right heart failure associated with poor outcome. Worsening of symptoms of right heart failure should raise the suspicion for this ominous association. Early detection of pericardial effusion in PAH is accomplished by a high index of suspicion together with echocardiography. Based on the current evidence, small pericardial effusions can be managed medically, but the treatment of larger pericardial effusion remains controversial. Early and aggressive treatment of large pericardial effusions may be helpful after weighing risks and benefits of pericardiocentesis.

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Source of support: ART is supported by CTSA KL2 (grant RR024990) from the National Center for Research Resources, a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research.

Conflict of interest: None declared.