Pleural effusions occurring with right heart failure

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Purpose of review

Pleural effusions commonly occur in patients with left heart failure. However, there is increasing evidence that patients with pulmonary hypertension and isolated right heart failure frequently have pleural effusions.

Recent findings

Three recent studies have evaluated the incidence of pleural effusions without an alternate explanation in patients with idiopathic/familial pulmonary arterial hypertension (14%), pulmonary arterial hypertension associated with connective tissue diseases (33%), and portopulmonary hypertension (30%). The majority of patients in all three studies with pleural effusions without an alternate explanation were found to have isolated right heart failure. In these studies, mean right atrial pressures and death during follow-up were significantly higher in patients with pleural effusions and isolated right heart failure compared to patients with no pleural effusions.

Summary

Pleural effusions without an alternate explanation occur commonly in at least three subtypes of pulmonary arterial hypertension. The majority of patients with pleural effusions also have isolated right heart failure that is thought to be responsible for the development of the effusions. Patients presenting with pulmonary hypertension should be evaluated for pleural effusions, and if present, should receive a work-up for right heart failure.

Keywords

pleural effusions, pulmonary arterial hypertension, right heart failure

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Introduction

Pleural effusion is a common clinical condition in patients with heart failure, and it is generally accepted that effusions are due to left heart failure. Two historical studies performed by Wiener-Kronish *et al.* [1,2] led to this idea. The first study of congestive heart failure (CHF) patients demonstrated that mean right atrial pressure (mRAP) was not significantly different in patients with or without pleural effusions. Because the pulmonary wedge pressure (PWP) was significantly higher in patients with effusions, they concluded that the effusions were secondary to left heart failure (LHF). The second study showed an absence of pleural effusions in 27 patients with chronic pulmonary hypertension and chronically elevated mRAP ($mRAP = 11 \pm 2$ mmHg). However, this study was small, not all patients had pulmonary hypertension (only 11 of 27 patients), the criteria for right heart failure (RHF) were questionable, and there was no follow-up. On the basis of these studies, it has been accepted that pulmonary arterial hypertension (PAH) and RHF do not play a role in the development of pleural effusions. However, anecdotal evidence of patients with PAH and pleural effusions without LHF, as well as the results of previous animal studies, have led investigators to re-evaluate the potential role that RHF may play in the development of effusions [3,4].

In the past 2 years, three studies have investigated the incidence of pleural effusions in patients with pulmonary hypertension as well as the incidence of concurrent RHF [5••,6••,7•]. The following is a review of these studies and their findings.

Idiopathic and familial pulmonary arterial hypertension

The first of three studies was performed in patients with idiopathic and familial PAH [5••]. This retrospective study examined the medical records of all patients over an 11-year period at one institution with a diagnosis of idiopathic and familial PAH according to the Dana Point clinical classification of PAH [8]. All patients underwent a complete evaluation to exclude other causes of pulmonary hypertension.

In order to be included in the study, patients were required to have a right heart catheterization (RHC) at

the time of initial diagnosis demonstrating a mean resting pulmonary arterial pressure (mPAP) of greater than 25 mmHg, a PWP of less than 15 mmHg, and the absence of other causes of pulmonary hypertension. Patients with left heart systolic or diastolic failure were excluded as well as patients with pulmonary hypertension associated with any cause other than familial or idiopathic. RHF was defined as present by physical examination (jugular venous distention $>$ 3 cm above the sternal angle, hepatojugular reflux, hepatomegaly, right-sided S3, ascites, anasarca, or worsening lower extremity edema); moderate/severe dilation of the right atrium or ventricle with moderate/severe ventricular dysfunction and a noncollapsing inferior vena cava (IVC) on echocardiography; or mRAP greater than 10 mmHg on RHC.

In regards to imaging, posteroanterior/lateral chest X-rays (CXRs), chest computed tomographies (CTs), thoracic ultrasounds, and autopsy results were reviewed. Effusions on CXRs were semi-quantitated on a 0–5 scale [9]. Thickness of effusions based on the maximum distance between the visceral and parietal pleurae were measured on CTs and ultrasounds. Volume of fluid was recorded for autopsied patients. On the basis of the above, effusions were classified as trace, small, moderate, or massive.

A total of 147 patients met the prespecified inclusion/exclusion criteria and were analyzed. Overall, 31 of 147 patients (21.1%) with idiopathic or familial PAH had pleural effusions. Of these patients, 21 (14%) had pleural effusions with no obvious cause. However, 19 patients (90%) were diagnosed with isolated RHF within 30 days of the effusion being noted. RHF was diagnosed in nine patients by RHC, in four patients by echocardiogram, and in five patients by both studies. One patient was diagnosed by 'obvious evidence of RHF on physical examination'.

The authors reported that the mortality rate during the follow-up period was significantly higher in patients with pleural effusions and RHF compared to patients without effusions (68.4 vs. 27.6%, $P < 0.001$) (Table 1). PWP was normal in both groups indicating the absence of LHF. However, the mRAP was significantly higher in patients with pleural effusions and RHF compared to those without pleural effusions (16.0 vs. 8.8, $P < 0.001$). It is also important to note that of the 19 patients with RHF and pleural effusions, 8 had ascites and 8 had pericardial effusions (including two patients who had both). The authors discard the likelihood of the pleural effusions being secondary to the ascites given that the incidence of pleural effusions from ascites is only 4–10% [10,11], and most are unilateral, right-sided, and large. The majority of effusions from ascites in this study (five of eight) were trace to small in size. The authors do not mention the laterality of these effusions. In regards to the pericardial effusions as the cause of the pleural effusions as opposed to RHF, the authors state that pleural effusions secondary to pericardial disease are usually left unilateral. The pericardial effusions were trace to small in seven of the eight patients and no patients had any evidence of tamponade. Again, the authors do not mention which side the pleural effusions were on in patients with pericardial effusions, but only three of the 19 total effusions were left unilateral. Thoracentesis was performed in five of the 19 patients with pleural effusions and RHF. Four of the five effusions were transudative and one was exudative (total protein ratio of 0.61) which may have converted from a transudate to an exudate due to aggressive diuresis [12•].

Key points

- Three studies have demonstrated a significant incidence (14–33%) of pleural effusions with no alternate explanation in patients with subtypes of pulmonary arterial hypertension.
- The majority of patients with pleural effusions with no alternate explanation in these studies were found to have isolated right heart failure that is now thought to be responsible for the development of the effusions.
- In all three studies, mean right atrial pressures and death during follow-up were significantly higher in patients with pleural effusions and isolated right heart failure compared to patients with no pleural effusions.
- A significant percentage of the patients with pleural effusions and isolated right heart failure had pericardial effusions and ascites of unclear cause but most were presumed to be secondary to right heart failure.
- The belief that pleural effusions are only a result of LHF does not appear to be valid and should be potentially discredited.

Although the study was limited by its retrospective nature, few thoracenteses, and RHC not being performed at the same time as the radiographic imaging, this study clearly demonstrates the high incidence of pleural effusions without obvious cause in idiopathic and familial PAH patients. Furthermore, it impressively demonstrates that 90% (19 of 21) of patients with pleural effusions of unknown cause had isolated RHF. The patients with pleural effusions had significantly higher mRAPs but not mPAPs, suggesting that pulmonary hypertension is associated with effusion development only after it causes RHF.

Mechanism of pleural fluid formation

The patients with pleural effusions and isolated RHF had significantly elevated mRAPs. The authors postulate two

Table 1 Clinical characteristics and laboratory data of idiopathic/familial pulmonary arterial hypertension patients

Variables	Patients without pleural effusions ($n=116$)	RHF patients without pleural effusions ($n=61$)	Patients with pleural effusions due to RHF ($n=19$)	*P* value[a]	*P* value[b]
Age (years)	46.5 ± 13.8	45.4 ± 13.4	52.3 ± 12.0	0.085	0.047
Age at diagnosis (years)	41.7 ± 13.8	41.3 ± 13.4	48.9 ± 12.7	0.035	0.032
Female/male	92/24	47/14	17/2	0.467	0.393
Race				0.193	0.398
White	84 (72.4)	48	17 (89.5)		
African–American	17 (14.7)	8	2 (10.5)		
Other and unknown	15 (12.9)	5	0 (0)		
Median follow-up period (months)	36 (1–146)	36 (1–146)	39 (4–123)	0.945	0.843
Death during follow-up	32 (27.6)	25 (41.0)	13 (68.4)	<0.001	0.037
Duration of diagnosis of IPAH or FPAH to death, months	45 (8–146) ($n=32$)	46 (2–211) ($n=25$)	43 (23–125) ($n=13$)	0.920	0.914
Occurrence of RHF	61 (52.6)	61 (100)	19 (100)	<0.001	/
Occurrence of ascites[c]	11 (9.5)	11 (18.0)	10 (52.6)	<0.001	0.003
Occurrence of pericardial effusions[c]	45 (38.8)	32 (52.5)	15 (78.9)	0.001	0.041
Serum total protein (g/dl)	7.1 ± 0.6	7.1 ± 0.6	7.0 ± 0.6	0.334	0.499
Serum albumin (g/dl)	4.0 ± 0.4	3.9 ± 0.4	3.7 ± 0.5	0.052	0.136
Hemodynamics[d]					
mRAP (mmHg)	8.8 ± 5.5	14.1 ± 5.3	16.0 ± 6.8	<0.001	0.199
RVEDP (mmHg)	12.8 ± 6.6	18.3 ± 6.3	18.6 ± 7.2	0.001	0.838
mPAP (mmHg)	57.0 ± 16.0	62.3 ± 15.6	58.2 ± 6.3	0.737	0.268
PWP (mmHg)	9.9 ± 4.5	12.2 ± 5.0	9.8 ± 4.1	0.933	0.070
CO (l/min)	4.3 ± 1.5	4.1 ± 1.6	4.0 ± 1.3	0.437	0.803
CI (l/min/m^2)	2.3 ± 0.7	2.1 ± 0.7	2.2 ± 0.7	0.366	0.952
PVR (Woods units)	13.1 ± 9.0	15.1 ± 10.7	13.2 ± 5.1	0.935	0.477

Unless otherwise indicated, data are presented as mean ± SD, median (range) or *n* (%). *CI*, cardiac index; *CO*, cardiac output; FPAH, familial pulmonary hypertension; IPAH, idiopathic pulmonary hypertension; mPAP, mean pulmonary arterial pressure; mRAP, mean right atrial pressure; PVR, pulmonary vascular resistance; PWP, pulmonary wedge pressure; RHC, right heart catheterization; RHF, right heart failure; RVEDP, right-ventricular end-diastolic pressure.

[a] The comparison is made between the patients with pleural effusions due to RHF and the patients without pleural effusions.

[b] The comparison is made between the patients with pleural effusions due to RHF and the RHF patients without pleural effusions.

[c] The occurrence of ascites or pericardial effusions was assessed for the entire follow-up period.

[d] For patients without pleural effusions, we used the hemodynamic results from the first RHC that the patient received for the diagnosis; for RHF patients without pleural effusions, we used the hemodynamic results that had the highest RAP at RHC; for patients with pleural effusions, we used the hemodynamic results from the RHC performed most closely to the identification of the pleural effusions.

ways in which elevated mRAP leading to elevated central and systemic venous pressures can contribute to pleural fluid formation. First, elevated venous pressures can mechanically impede parietal pleural lymphatic drainage. This was shown in a study of sheep [3] in which elevations of superior vena cava (SVC) pressures greater than 15 mmHg led to decreased lymphatic drainage and pleural effusions. Second, increased venous pressures can cause increased hydrostatic pressure in bronchial and chest wall veins leading to transudation of fluid into the pleural space. In a study in dogs, balloon obstruction of the SVC and IVC led to formation of pleural effusions by this mechanism [4]. Interestingly, it also led to pericardial effusions suggesting that the elevated mRAP directly induced the pericardial effusions, which may have been the reason why pericardial effusions were seen in the study by Tang *et al.* [5••].

Pulmonary arterial hypertension associated with connective tissue diseases

The second study, of patients with PAH due to connective tissue diseases (CTDs), was a retrospective study on a similar cohort of patients with PAH as the first, but studied patients with CTD over a 13-year study period [6••]. The methodology was similar to the last study with the only difference being that the patients studied were diagnosed as having CTDs by rheumatologists and as having PAH associated with CTD according to the Dana Point classification.

Of the 89 patients that met the prespecified inclusion/exclusion criteria, 51 had scleroderma, 18 had mixed connective tissue disease (MCTD), 26 had systemic lupus erythematosus (SLE), 2 had Sjogren's syndrome, 1 had polymyositis, and 1 had rheumatoid arthritis (RA). Overall, 35 of the 89 patients (39.3%) had pleural effusions. Of these patients, 29 (33%) had effusions with no known cause. Twenty-eight of the 29 patients (96.6%) were diagnosed with isolated RHF. Twenty-five patients were diagnosed with RHF by RHC and/or echocardiography and three patients had 'obvious evidence on physical examination'. Five of the 25 patients diagnosed by RHC and/or echocardiography had the diagnostic study(ies) performed greater than 30 days after the pleural effusion was noted. Data from thoracenteses were available for two patients, both of whom had transudative effusions.

In this study, there was a significantly higher mortality (65.5 vs. 37.0%, $P=0.025$) and presence of RHF (96.6 vs. 59.3%, $P<0.001$) in the group of patients with pleural effusions compared to those without. In regards to

Table 2 Hemodynamics of pulmonary arterial hypertension associated with connective tissue disease patients

Hemodynamics[a]	Patients without pleural effusions ($n=54$)	Patients with pleural effusions ($n=29$)	*P* value
mRAP (mmHg)	8.3 ± 4.0	11.3 ± 5.1	0.004
RVEDP (mmHg)	12.2 ± 5.3	13.0 ± 6.3	0.521
mPAP (mmHg)	45.9 ± 12.1	49.2 ± 10.6	0.226
PWP (mmHg)	8.9 ± 3.9	7.7 ± 4.3	0.193
CO (l/min)	4.4 ± 1.4	3.5 ± 1.1	0.004
CI (l/min/m^2)	2.5 ± 0.7	2.1 ± 0.6	0.011
PVR (Woods units) (interquartile ranges)	8.7 (6.8–12.6)	11.7 (9.2–15.8)	0.016

Unless otherwise indicated, data are presented as mean ± SD or median (interquartile ranges). *CI*, cardiac index; *CO*, cardiac output; mPAP, mean pulmonary arterial pressure; mRAP, mean right atrial pressure; PVR, pulmonary vascular resistance; PWP, pulmonary wedge pressure; RVEDP, right-ventricular end-diastolic pressure.
[a] For patients without pleural effusions, we used the hemodynamic results from the first RHC patients received for the diagnosis; for patients with pleural effusions, we used the hemodynamic results from the RHC performed closest in time to the identification of the pleural effusions.

hemodynamics, the authors demonstrate that patients with pleural effusions had a significantly higher mRAP and pulmonary vascular resistance (PVR) with no difference in mPAP or PWP compared to patients without effusions (Table 2). Essentially, pulmonary hypertension causes chronically elevated right-sided filling pressures leading to RHF and pleural effusions. The lack of difference in mPAP between patients with and without effusions suggests that pulmonary hypertension alone is not responsible for the effusions, but rather the RHF that results from the PH. Both groups had a normal PWP and the patients with effusions had a lower (although nonsignificant) PWP than those without effusions, which excludes LHF as a contributing cause for the effusions.

The biggest critique of this study is the difficulty in excluding the CTD itself as a cause of pleural effusions since pleural involvement is common in SLE, RA, and MCTD. The authors offer the explanation that the incidence of effusions in the three previously stated diseases is 20–50%, whereas in scleroderma, polymyositis, and Sjogren's syndrome it is less than 7%. If the effusions were secondary to the CTD, one would expect to see a larger proportion of effusions in the former three diseases compared to the latter three. However, in this study, 27% of patients with SLE, RA, and MCTD had effusions compared to 40% of patients with scleroderma, polymyositis, and Sjogren's syndrome, suggesting an alternate mechanism.

It is again important to address the high incidence of pericardial effusions and ascites in patients with pleural effusions. The authors explain that pericardial inflammation secondary to CTD itself is unlikely because of the similar percentage of pericardial effusions in this study

Table 3 Demographics and clinical characteristics of portopulmonary hypertension patients

Variables	Patients without pleural effusions ($n=21$)	Patients with pleural effusions ($n=10$)	Patients with pleural effusions and RHF ($n=7$)	*P* value[a]	*P* value[b]
Age at diagnosis of POPH (years)	49.1 ± 10.3	49.7 ± 9.2	45.7 ± 7.1	0.885	0.424
Female/male	8/13	6/4	5/2	0.441	0.198
Cause of portal hypertension				0.002	0.003
Viral hepatitis	17 (81.0)	2 (20.0)	1 (14.3)		
Other liver diseases	4 (19.0)	8 (80.0)	6 (85.7)		
Mean follow-up period (months)	31.1 ± 26.3	23.6 ± 22.4	28.6 ± 25.1	0.445	0.826
Occurrence of RHF	6 (28.6)	7 (70.0)	7 (100)	0.052	0.001
Occurrence of ascites[c]	8 (38.1)	10 (100.0)	7 (100)	0.001	0.007
Occurrence of pericardial effusions[c]	7 (33.3)	4 (40.0)	3 (42.9)	1.000	0.674
Serum BNP (pg/ml)	303.1 ± 318.9 ($n=19$)	804.7 ± 628.5 ($n=9$)	1179.7 ± 353.7	0.009	<0.001
Six-minute walk distances (m)	423.3 ± 72.0	359.0 ± 90.1	347.0 ± 91.9	0.047	0.041
Treatment[d]				0.417	0.371
Receiving prostaglandins	5 (23.8)	4 (40.0)	3 (42.9)		
Not receiving prostaglandins	16 (76.2)	6 (60.0)	4 (57.1)		
Death during follow-up	3 (14.3)	4 (40.0)	4 (57.1)	0.172	0.043
Time from POPH diagnosis to death (months)	54.3 ± 14.7	43.3 ± 37.8	43.3 ± 37.8	0.657	0.657
Serum total protein (g/dl)	7.0 (6.7–7.6)	6.7 (5.7–8.1)	6.5 (4.9–7.9)	0.403	0.257
Serum albumin (g/dl)	3.4 (3.1–3.6)	3.0 (2.4–4.0)	3.4 (2.3–4.3)	0.422	0.979

Unless otherwise indicated, data are presented as mean ± SD, median (interquartile ranges), or as a percentage which is denoted in parentheses. BNP, brain natriuretic peptide; POPH, portopulmonary hypertension; RHF, right heart failure.
[a] The comparison is made between patients with and those without pleural effusions.
[b] The comparison is made between patients without pleural effusions and those with effusions and RHF.
[c] The occurrence of ascites or pericardial effusions was assessed for the entire follow-up period.
[d] The patients listed as having pleural effusions and receiving prostacyclin all developed effusions after initiation of prostacyclin. Patients who developed effusions prior to initiation of prostacyclin were included in the group not receiving prostacyclin.

and the one in idiopathic/heritable PAH patients (72.4 and 78.9%, respectively). As for the ascites, the authors do not offer an explanation for this, but it can be presumed to be similar to the one provided in the study by Tang *et al.* [5••]. They explain that pleural effusions secondary to ascites are usually unilateral, right-sided, and large. However, the majority of effusions in this study were bilateral and trace-to-small, making it less likely that the effusions were secondary to ascites.

The study has significant limitations similar to those of the previous study, but it impressively demonstrates the strong association between PAH associated with CTD, pleural effusions, and RHF. Given the elevated mRAP, PVR, and lower cardiac index (*CI*) in the group of patients with pleural effusions, the cause is likely the RHF that was present in 96.6% of these patients.

Portopulmonary hypertension

The final study was performed in patients with portopulmonary hypertension (POPH) that were given a diagnosis of such after evaluation by a hepatologist and according to the Dana Point classification [7•]. POPH was defined as a mPAP greater than 25 mmHg at rest, PVR greater than 240 dyne/s/cm^5, and a mean PWP or left-ventricular end-diastolic pressure less than 15 mmHg. All patients were required to have clinical or CT evidence of cirrhosis or ultrasound evidence of portal hypertension with absence of other causes of PAH. This retrospective study was performed over a 10-year period and all other methodological aspects of the study are similar to the previous two studies.

A total of 33 patients met the inclusion/exclusion criteria. Overall 12 of the 33 patients (36.4%) had pleural effusions. Of these patients, 10 (30%) had effusions with no obvious cause. Seven of the 10 patients (70%) were diagnosed with isolated RHF within 30 days. Five patients were diagnosed with RHF by both RHC and echocardiography, one patient by RHC only, and one patient by echocardiography only. Data from thoracenteses were available for two patients, both of whom had transudative effusions.

There was a significantly increased mortality (57.1 vs. 14.3%, $P = 0.043$) and mRAP (15.3 vs. 7.9 mmHg, $P = 0.010$) in the group of patients with pleural effusions and RHF compared to those without pleural effusions (Tables 3 and 4). There was no difference in PWPs between the two groups demonstrating the absence of LHF. Of the 33 patients included, the majority (21) had POPH secondary to viral hepatitis. However, a significantly greater percentage of patients with nonviral hepatitis had pleural effusions than those with viral hepatitis (80 vs. 20%, $P = 0.002$). These data suggest that if the study were repeated in a group with similar numbers of hepatitis from all causes, then there would likely be a greater number of pleural effusions, and potentially, RHF. Of great importance is that the occurrence of ascites was significantly higher in the patients with pleural effusions (100 vs. 38.1%, $P = 0.007$). The authors cannot definitively conclude that the pleural effusions in patients with RHF were not secondary to ascites but offer the explanation that effusions secondary to ascites are unilateral right-sided in 67–85% of patients and massive [13–15]. In this study, 40% of effusions were unilateral right-sided and only 30% were massive, suggesting an alternate cause for the majority of effusions. Furthermore, they state that mRAP is usually low (approximately 6 mmHg) in patients with cirrhosis and portal hypertension [16], but the mRAP in patients with pleural effusions was 15.3 mmHg, again suggesting that RHF is the cause. Finally, they report higher serum brain natriuretic peptide levels in the patients with pleural effusions, implicating worse right ventricular function as the cause (patients with LHF were excluded).

Of the three studies, this is the only one that is not completely convincing that the cause of pleural effusions

Table 4 Hemodynamics of portopulmonary hypertension patients

Hemodynamics[a]	Patients without pleural effusions ($n = 21$)	Patients with pleural effusions ($n = 10$)	Patients with pleural effusions and RHF ($n = 7$)	*P* value[b]	*P* value[c]
mRAP (mmHg)	7.9 ± 6.4	11.6 ± 7.2	15.3 ± 4.9	0.158	0.010
RVEDP (mmHg)	9.5 ± 6.1	13.4 ± 6.3	16.1 ± 4.1	0.112	0.013
mPAP (mmHg)	48.2 ± 12.2	58.4 ± 10.6	53.0 ± 7.4	0.972	0.343
PWP, mmHg	8.7 ± 3.8	9.5 ± 4.1	10.7 ± 4.0	0.597	0.242
CO (l/min)	5.3 ± 1.8	5.5 ± 1.5	5.2 ± 1.5	0.717	0.942
CI (l/min/m^2)	2.6 ± 0.7	2.9 ± 0.8	2.8 ± 0.9	0.257	0.511
PVR (Woods units)	8.4 ± 4.7	8.6 ± 3.5	9.9 ± 3.0	0.911	0.433

Unless otherwise indicated, data are presented as mean ± SD or median (interquartile ranges). *CI*, cardiac index; *CO*, cardiac output; mPAP, mean pulmonary arterial pressure; mRAP, mean right atrial pressure; PVR, pulmonary vascular resistance; PWP, pulmonary wedge pressure; RHC, right heart catheterization; RHF, right heart failure; RVEDP, right ventricular end-diastolic pressure.

[a] For patients without pleural effusions, we used the hemodynamic results from the first RHC that patients received for the diagnosis; for patients with pleural effusions, we used the hemodynamic results from the RHC performed closest in time to the identification of the pleural effusions.

[b] The comparison is made between the patients without pleural effusions and the patients with pleural effusions.

[c] The comparison is made between the patients without pleural effusions and those with effusions and RHF.

with no alternate explanation in patients with pulmonary hypertension is RHF. The authors acknowledge that it is possible that some of the pleural effusions may be secondary to ascites, but not the bilateral and trace-to-small effusions. Regardless, this study certainly offers adequate evidence to suggest the possibility that RHF is playing a causal role in a number of pleural effusions in portopulmonary hypertension patients.

Management recommendations

On the basis of the data reviewed, we have made the following management recommendations. All patients with newly diagnosed PAH should undergo a posteroanterior/lateral CXR. Patients with ongoing PAH that develop symptoms or signs of pleural effusion such as dyspnea, dry cough, pleuritic chest pain, decreased breath sounds, or dullness to percussion at the bases should also undergo a posteroanterior/lateral CXR. If a pleural effusion of any size is noted, then patients should undergo diagnostic testing for heart failure if no other obvious cause of the effusion can be identified. If patients undergo thoracentesis for further evaluation of the effusion, pleural fluid should be sent for N-terminal pro-brain natriuretic peptide (pro-BNP) pro-BNP in addition to the usual studies, as this is the best way to identity an exudative pleural effusion secondary to heart failure [12•]. Diagnostic testing for heart failure can include serum BNP or pro-BNP, echocardiography, and/or RHC. If heart failure is identified, either left or right, appropriate medical therapy according to standard guidelines should be instituted given the increased mortality in this group of patients.

Conclusion

To date, three studies have demonstrated a significant incidence (14–33%) of pleural effusions with no alternate explanation in patients with subtypes of PAH. These effusions are now thought to be due to isolated RHF given the significantly higher mRAPs and normal PWPs. The mortality among patients with pleural effusions and RHF was significantly higher compared to PAH patients without pleural effusions, reinforcing that it is imperative that patients be screened for pleural effusions and RHF after the diagnosis of PAH. The majority of pleural effusions are trace-to-small so may not be readily apparent on physical examination.

A significant percentage of patients with pleural effusions and isolated RHF have pericardial effusions and ascites of unclear cause but most are presumed to be secondary to RHF. The pericardial effusions and ascites are predominantly trace-to-small without evidence of causing hemodynamic compromise, so their significance may be minimal.

On the basis of these studies, the belief that pleural effusions are only a result of LHF should be seriously questioned and potentially discredited. Further study needs to be devoted to determine if similar conclusions can be drawn for pleural effusions occurring in other types of pulmonary hypertension.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 292).

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2 Wiener-Kronish JP, Goldstein R, Matthay RA, *et al.* Lack of association of pleural effusion with chronic pulmonary arterial and right atrial hypertension. Chest 1987; 92:967–970.

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5 •• Tang K, Robbins IM, Light RW. Incidence of pleural effusions in idiopathic and familial pulmonary arterial hypertension patients. Chest 2009; 136:688–693.

This is the first study to describe an association between pleural effusions and pulmonary arterial hypertension induced right heart failure. Specifically, the focus is on investigating this relationship in patients with idiopathic and familial pulmonary arterial hypertension.

6 •• Luo Y, Robbins IM, Karatas M, *et al.* Incidence of pleural effusions in patients with pulmonary arterial hypertension associated with connective tissue diseases. Chest 2011 [Epub ahead of print].

This is the first study to document the large incidence of pleural effusions and isolated right heart failure in patients with pulmonary arterial hypertension secondary to connective tissue disease.

7 • Luo Y, Robbins IM, Hemnes AR, *et al.* Incidence of pleural effusions in patients with portopulmonary hypertension. Chest 2010; 138:379A.

This study continues to investigate pleural effusions induced by right heart failure in patients with portopulmonary hypertension. It delves into mechanisms responsible for this process, and discusses the role that ascites and pericardial effusions play in patients with right heart failure.

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