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## Worsening Hypoxemia in the Face of Increasing PEEP: A Case of Large Pulmonary Embolism in the Setting of Intracardiac Shunt

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Conflict of interest:** None declared

**Patient:** Male, 40  
**Final Diagnosis:** Patent foramen ovale  
**Symptoms:** Dyspnea exertional • hemoptysis • shortness of breath  
**Medication:** —  
**Clinical Procedure:** Airway pressure release ventilation  
**Specialty:** Critical Care Medicine

**Objective:** Rare co-existence of disease or pathology  
**Background:** Patent foramen ovale (PFO) are common, normally resulting in a left-to-right shunt or no net shunting. Pulmonary embolism (PE) can cause sustained increased pulmonary vascular resistance (PVR) and right atrial pressure. Increasing positive end-expiratory pressure (PEEP) improves oxygenation at the expense of increasing intrathoracic pressures (ITP). Airway pressure release ventilation (APRV) decreases shunt fraction, improves ventilation/perfusion (V/Q) matching, increases cardiac output, and decreases right atrial pressure by facilitating low airway pressure.

**Case Report:** A 40-year-old man presented with dyspnea and hemoptysis. Oxygen saturation (SaO<sub>2</sub>) 80% on room air with Aa gradient of 633 mmHg. Post-intubation SaO<sub>2</sub> dropped to 71% on assist control, FiO<sub>2</sub> 100%, and PEEP of 5 cmH<sub>2</sub>O. Successive PEEP dropped SaO<sub>2</sub> to 60–70% and blood pressure plummeted. APRV was initiated with improvement in SaO<sub>2</sub> to 95% and improvement in blood pressure. Hemiparesis developed and CT head showed infarction. CT pulmonary angiogram found a large pulmonary embolism. Transthoracic echocardiogram detected right-to-left intracardiac shunt, with large PFO.

**Conclusions:** There should be suspicion for a PFO when severe hypoxemia paradoxically worsens in response to increasing airway pressures. Concomitant venous and arterial thromboemboli should prompt evaluation for intracardiac shunt. Patients with PFO and hypoxemia should be evaluated for causes of sustained right-to-left pressure gradient, such as PE. Management should aim to decrease PVR and optimize V/Q matching by treating the inciting incident (e.g., thrombolytics in PE) and by minimizing ITP. APRV can minimize PVR and maximize V/Q ratios and should be considered in treating patients similar to the one whose case is presented here.

**MeSH Keywords:** Continuous Positive Airway Pressure • Embolism, Paradoxical • Foramen Ovale, Patent • Hemodynamics • Pulmonary Embolism • Ventilation-Perfusion Ratio

**Full-text PDF:** <http://www.amjcaserep.com/abstract/index/idArt/898521>



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## Background

Patent foramen ovale (PFO) is a common finding in many individuals, normally resulting in a left-to-right shunt or no net shunt. Pulmonary embolism (PE) can cause a sustained increased pulmonary vascular resistance (PVR) and right atrial pressure (RAP). Positive end-expiratory pressure (PEEP) has been shown to improve oxygenation by recruiting atelectatic airways, but it does so at the expense of increasing intrathoracic pressures (ITP).

Airway pressure release ventilation (APRV), albeit an unconventionally used ventilator mode, improves oxygenation by maximizing ventilation/perfusion (V/Q) matching and decreasing shunt fraction. APRV has also been shown to increase cardiac output and decrease RAP by allowing lower peak and mean airway pressures when compared to standard ventilator modes.

## Case Report

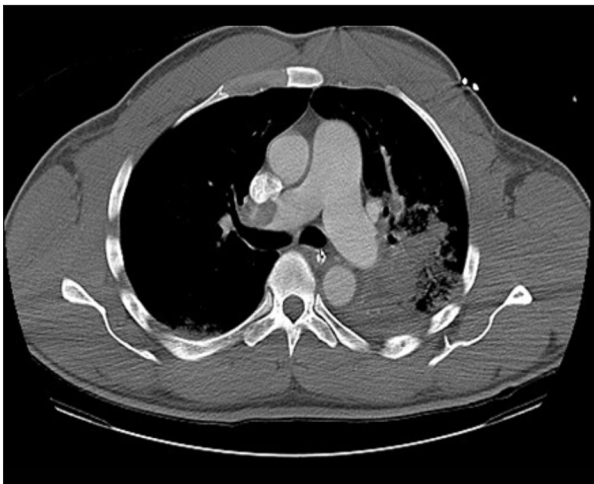
A 40-year-old man without prior medical history presented with 3 days of progressively worsening dyspnea at rest, cough productive of yellow sputum, subjective fever, cough, and 2 days of hemoptysis estimated to be approximately 100 mL per day. He denied chest pain, orthopnea, paroxysmal nocturnal dyspnea, chills, night sweats, weight loss/gain, sick contacts, travel, recent immobilization, leg swelling, or pain. Vital signs on presentation to the ER were: temperature 37.8°C (100°F), blood pressure (BP) 152/93 mmHG, pulse 113 beats per minute, and respiratory rate 21 breaths per minute. Oxygen saturation (SaO<sub>2</sub>) was initially 80% on room air and 88–92% on a 100% nonrebreather mask, with occasional desaturations with movement. Results of a physical exam were remarkable for rales in the left mid-lung field, and decreased breath sounds at the left lung base. Breathing was non-labored without accessory muscle use, and he spoke in full sentences. No wheezing,

rhonchi, JVD, peripheral edema, leg swelling/pain, abdominal distension, or tenderness were appreciated. The patient had intact mental status.

Aa gradient was calculated to be 633 mmHg (Table 1). Chest Xray showed “nearcomplete opacification of the left lower lobe, pneumonia, and/or atelectasis, as well as effusion.” The patient was intubated, with improvement in the appearance of his chest Xray. Vital signs postintubation showed BP of 199/99 and pulse of 124, but his SaO<sub>2</sub> dropped further to 71% on assist control with FiO<sub>2</sub> 100% and a PEEP of 5 cmH<sub>2</sub>O. With successive PEEP, SaO<sub>2</sub> dropped to 60–70% and BP decreased to 81/39. Due to hemodynamic compromise, APRV ventilation was initiated, with improvement of SaO<sub>2</sub> to 95% and improvement in BP. A CT pulmonary angiogram (CTPA) was ordered to evaluate the pulmonary vasculature as well as the lung parenchyma, which was not done immediately primarily due to hemodynamic instability and elevated serum creatinine. In the meantime, bedside lower-extremity venous duplex was performed showing “extensive near occlusive or occlusive deep venous thrombus (DVT) within the left popliteal vein.” While the venous duplex was being performed, it was noted that the patient was not moving his right side and examination revealed right-sided hemiparesis. He was emergently taken for CT of the head, as well as CTPA. The CT head showed extensive acute left middle cerebral artery territory infarct with associated significant left frontotemporal and parietal brain edema, and mild left-to-right midline shift. CTPA showed pulmonary embolism with moderate-to-severe clot burden, right heart strain with flattening of interventricular septum, and enlargement of the right-sided chambers and main pulmonary artery (Figures 1, 2). Transthoracic echocardiogram demonstrated an atrial septal aneurysm with a significant right-to-left intracardiac shunt, suggestive of a wide patent foramen ovale, and possible right ventricular enlargement with moderate right atrial enlargement (Figure 3, Video 1).

**Table 1.** Standard laboratory assessment. Relevant findings include elevated creatinine, leukocytosis, and significant hypoxemia while on 100% FiO<sub>2</sub>.

Chemistry						
Sodium	Potassium	Chloride	Bicarbonate	BUN	Creatinine	Glucose
137 mmol/L	4.3 mmol/L	104 mmol/L	25 mmol/L	16 mg/dL	1.5 mg/dL	106 mg/dL
CBC						
White blood cell		Hemoglobin		Hematocrit		Platelet
13.6 K/uL		16 g/dL		45.2%		180 K/uL
Arterial blood gas on 100% non-rebreather						
pH		PCO <sub>2</sub>		PaO <sub>2</sub>		Bicarbonate
7.44 mmHg		34 mmHg		56 mmHg		25 mmHg



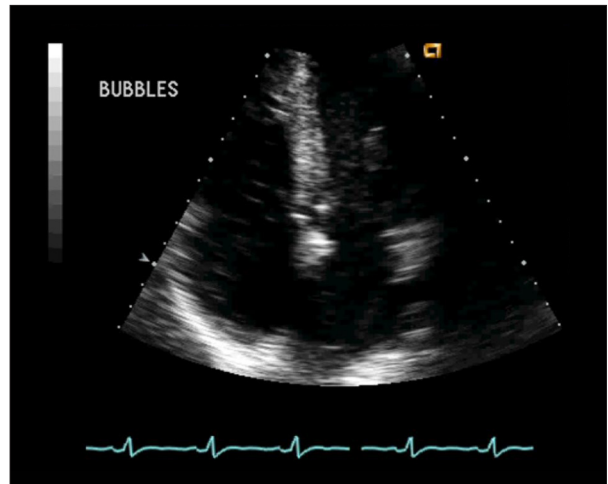
**Figure 1.** CT pulmonary angiography demonstrating a large embolus lodged in the right main pulmonary artery with dilation of the pulmonary trunk. Also seen is bilateral parenchymal airspace disease, likely representing atelectasis and/or pneumonia.



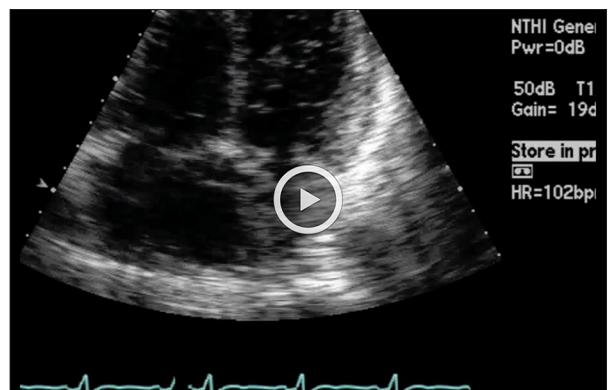
**Figure 2.** CT pulmonary angiography with evidence of right ventricular and right atrial enlargement, interventricular septal flattening, and bilateral parenchymal airspace disease, likely representing atelectasis and/or pneumonia.

## Discussion

The patient presented with refractory hypoxemia that was resistant to, and in fact was progressively worsened by, higher positive pressure. Moreover, the patient developed arterial embolism (stroke) associated with venous thrombosis (DVT and PE), signifying possible paradoxical embolism. Both the presence of refractory hypoxemia, especially when worsening with increasing PEEP, as well as coexistence of venous and arterial thromboembolic disease should raise suspicion for intracardiac anatomical shunt and a pressure gradient that favors right-to-left shunting.



**Figure 3.** Transthoracic echocardiogram with bubble study in the apical 4-chamber view demonstrating a large PFO, as well as right atrial and right ventricular enlargement.



**Video 1.** Transthoracic echocardiogram with bubble study in the apical 4-chamber view. Large PFO is demonstrated by immediate passage of bubbles from the right side of the heart (viewer's left) to the left side of the heart (viewer's right).

PEEP, through recruitment of unused respiratory units, leads to an increase in lung volume at which a patient breathes, i.e., an increase in functional residual capacity (FRC); this increases oxygenation [1]. This increase in FRC within the confined volume of the thorax (and to some extent the abdomen) in turn causes increased ITP, as well as increased pericardial, myocardial, and pulmonary vascular transmural pressures. In doing so, RAP will increase, as will PVR at higher levels of PEEP [1]. PE is also shown to increase PVR and right ventricular afterload, leading to an increase in RAP. Increased RAP decreases systemic venous return, dropping both left ventricular preload and cardiac output [1].

A PFO is a communication between the right atrium and left atrium. PFO was found in 25–30% of individuals in both an autopsy study and in a community-based transesophageal

echocardiography study [2,3]. PFOs are normally a hemodynamically insignificant defect, as left atrial pressure largely outweighs RAP, normally resulting in a left-to-right shunt or no net shunt. But, as seen in our patient, a large PE can cause a sustained increase in PVR and RAP, which is enough to shift this shunt in the opposite direction. This relatively large anatomic pressure gradient can result in the shunting of blood to the left side of the heart without contacting the pulmonary vascular bed, causing profound hypoxemia. Additionally, increased right-sided pressure can further facilitate the transit of venous emboli to the arterial circulation, and may predispose a patient to further embolic injury, as seen in this case.

Classically, echocardiography with bubble study or contrast has been the confirmatory study of choice for PFOs and atrial septal defects. More recently, transcranial Doppler has become a validated method for detecting right-to-left shunts, as well as their degree of severity. Transesophageal echocardiography is now thought by many to underestimate the severity of shunts, especially in sedated and intubated patients [4]. Transcranial Doppler can grade shunt severity more accurately than echocardiogram by quantifying microbubble detection [5]. For these reasons, transcranial Doppler would be appropriate to evaluate a patient such as the one discussed in this report.

Lack of improvement in oxygenation despite increase in PEEP should raise suspicion for intracardiac shunt [6]. A similar finding has been documented in patients with acute respiratory distress syndrome (which can also increase PVR) who have PFOs [7]. This results in the bypass of blood to the left side of the heart without contacting the pulmonary vascular bed, causing profound hypoxemia. Adding positive pressure in an attempt to improve oxygenation can in fact further increase PVR and RAP. This can increase right-to-left shunt through the PFO, resulting in paradoxical hypoxemia [6,7]. As mentioned earlier, transcranial Doppler can accurately quantify the severity of a right-to-left shunt. The use of transcranial Doppler in patients with PFO on APRV may demonstrate the effect of this ventilator mode on intracardiac shunts.

In addition to precipitating right-to-left shunt, our patient's PE itself contributed to his hypoxemia by causing a significant V/Q mismatch in the form of physiologic dead space. Moreover, the presence of large PE in our patient resulted in a dramatic

reduction in systemic blood pressure in response to increasing levels of PEEP owing to a decrease in left ventricular preload and cardiac output [1].

APRV was used in our patient, which likely resulted in positive effects on both oxygenation and hemodynamics. APRV improves oxygenation by maximizing V/Q matching through recruitment of collapsed respiratory units with adequate perfusion, decreasing shunt fraction [8–10]. APRV is also known to improve hemodynamics by allowing lower peak and mean airway pressures [6,7,11–13]. This resulted in increased cardiac output and decreased RAP, decreasing our patient's right-to-left shunt and maintaining a higher BP.

## Conclusions

In patients with severe and refractory hypoxemia, especially when associated with a paradoxical worsening of oxygenation in response to elevated airway pressures, there should be a suspicion for shunts such as PFO. Similarly, patients with concomitant venous and arterial thromboembolic disease should be evaluated for paradoxical embolism via intracardiac shunt. While a transient right-to-left gradient is sufficient to cause a paradoxical embolism in the absence of a net right-to-left shunting, patients with profound hypoxemia should be evaluated for etiologies that result in sustained net right-to-left pressure gradient, such as PE. This requires the clinician to have a high index of suspicion for anatomic shunts, especially when routine chest radiography shows little or no pathology to explain the degree of hypoxemia.

Management should be aimed toward decreasing PVR and optimizing V/Q matching by both treating the inciting incident (e.g., thrombolytic therapy in PE) and by minimizing the effects of mechanical ventilation on ITP. Ventilator modes such as APRV can work to minimize both PVR and maximize V/Q ratios and should be considered in treating patients similar to the one in this report.

The use of transcranial Doppler in patients with intracardiac shunts on APRV may confirm our hypothesis that low-pressure ventilator modes are beneficial in reducing right-to-left shunts.

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