

## Unexplained Hypoxemia in a COVID-19 Patient: Possibility of an Anatomical Intrapulmonary Shunt

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### Abstract

The COVID-19 pandemic has caused an unprecedented number of acute respiratory failure admissions in intensive care units (ICU). These patients are requiring intensive respiratory support including invasive mechanical ventilation. We presented a case of a young male patient who was mechanically ventilated for COVID-19 related acute respiratory distress syndrome (ARDS). The patient while recovering from ARDS developed unexplained hypoxemia on sitting position (orthodeoxia). In saline bubble trans-esophageal echocardiography, microscopic bubbles were seen in the left atrium after a gap of few cardiac cycles suggesting a possibility anatomical intrapulmonary shunt. The patient was managed with supportive medical treatment and weaned from invasive mechanical ventilation.

**Keywords:** Anatomical Intrapulmonary Shunt; COVID-19; Acute Respiratory Distress Syndrome; ARDS; Unexplained Hypoxemia

### Introduction

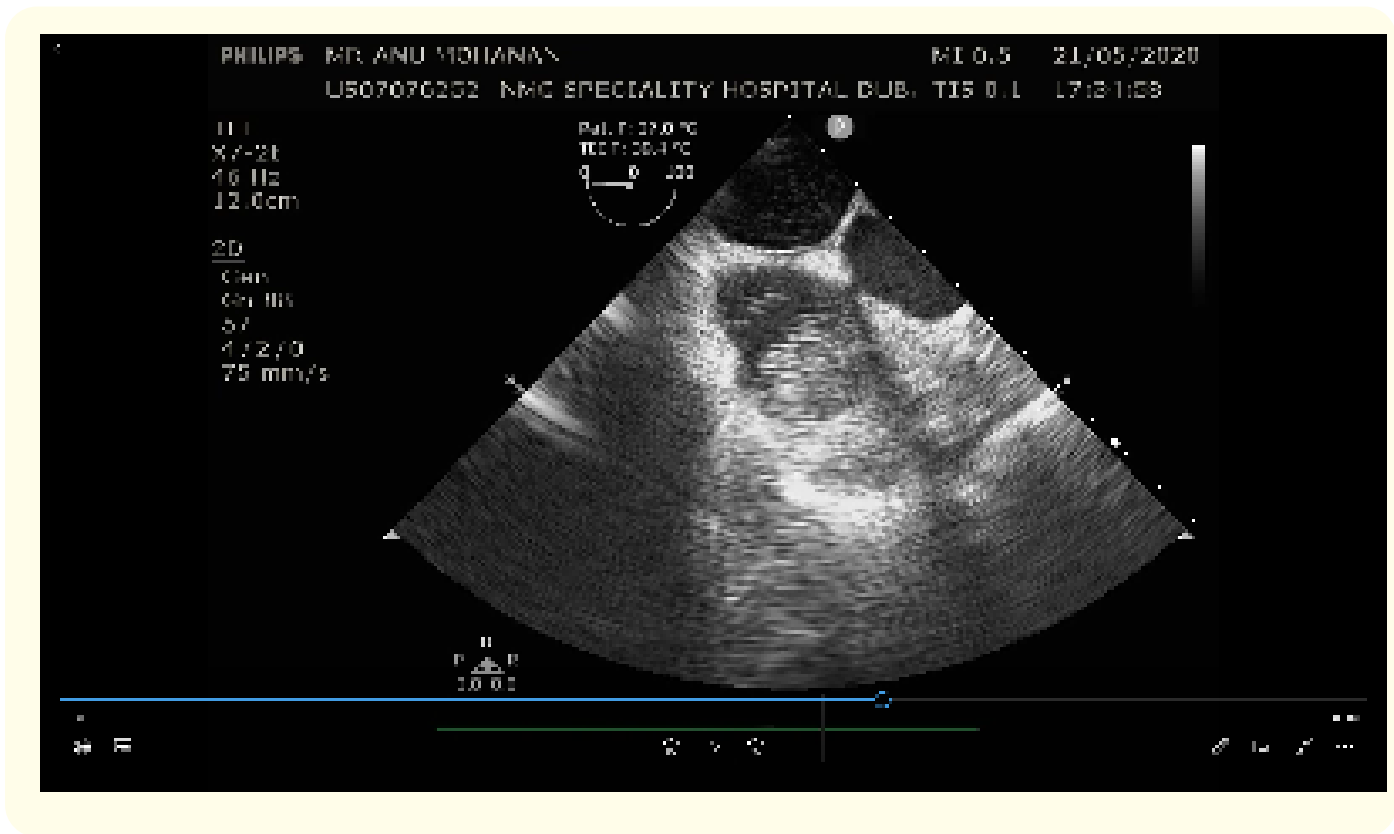
The COVID-19 pandemic has caused unprecedented admissions into intensive care units (ICU) of patients with acute respiratory failure. The acute respiratory distress syndrome (ARDS) is a severe form of pulmonary manifestation of COVID-19 with worse outcomes [1]. We presented a case of a 38-year old male who was mechanically ventilated for severe ARDS due to COVID-19.

While weaning from invasive mechanical ventilation, the patient developed unexplained hypoxemia on changing posture (platypnea-orthodeoxia). Saline contrast trans-esophageal echocardiography (SC-TEE) showed left atrium filling with saline microbubbles after a delay of four cardiac beats.

### Case Report

38-year old male with no previous comorbidities admitted in our hospital with complaints of dry cough for five days, breathlessness and fatigue for two days. On examination his peripheral oxygen saturation (SpO<sub>2</sub>) was 85% on room air, respiratory rate 29/min and chest X-ray showing bilateral peripheral haziness. He was started on oxygen support and nasal swab was tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) by reverse transcriptase polymerase chain reaction (RT-PCR). He was started on hy-

droxychloroquine (HCQ) 400 mg BID for one day followed by 200 mg BID for 10 days and lopinavir/ritonavir 400 mg/100 mg BID for 14 days, enoxaparin 60 mg subcutaneous once daily and intravenous methylprednisolone 40 mg 12 hourly for 10 days. He was tried on awake prone positioning for AHRF without much benefit, was intubated and started on mechanical ventilation as per ARDS-net protocol, lung protective ventilation strategy. In view of moderate ARDS, he was tried for prone ventilation but became further hypoxemic and turned again to supine. After nine days of mechanical ventilation, patient oxygenation and lung compliance started improving and he was given spontaneous breathing trials. The patient became dyspnoeic and SpO<sub>2</sub> dropped to 78% at same oxygen concentration (FiO<sub>2</sub>) as soon he was made from 30° to 75° head up. The trial was deferred for the day. Patient had a similar drop of SpO<sub>2</sub> on the next day while change of position. The possibility of a shunt was considered in view of repeated episodes of platypnea-orthodeoxia. The shunt fraction at 100% FiO<sub>2</sub> was calculated to be 12.9%. Transthoracic echocardiography window was suboptimal for any intracardiac shunt evaluation. SC-TEE was performed bedside to review for any intracardiac or extracardiac shunt. The microbubbles appeared in the left atrium on administration of 10 ml agitated saline mixed with 0.5 ml air through a peripheral vein after a gap of 4-5 cardiac beats from the right atrium (Video). We tried to locate the bubbles in pulmonary veins but left pulmonary veins could not be visualized though, filling seems to be occurring from left side. This explains the platypnea-orthodeoxia was possibly due to an anatomical intrapulmonary shunt. Patient CT pulmonary angiography (CTPA) did not show any anomalous arteriovenous connections in lungs and thoracic cavity. The patient did not have any previous surgical history or any family history of intracardiac shunts. The patient was managed conservatively with tracheostomy, weaned from mechanical ventilation, discharged after two weeks of rehabilitation and decannulation of tracheostomy with SpO<sub>2</sub> 87% on room air in standing position and 94% on lying down. The patient was educated about the condition and need of digital subtraction angiography (DSA) and possible therapeutic embolization (DSA) for possibility of anatomical intrapulmonary shunt.



### Discussion

The pulmonary manifestations are caused by SARS-CoV-2 virus binding to angiotensin converting enzyme 2 (ACE2) receptor over Type II pneumocytes either causing direct cytotoxicity and/or dysregulated host inflammatory response and hyperinflammation [2]. ARDS is severe pulmonary manifestation of COVID-19 requiring invasive mechanical ventilation with higher morbidity and mortality.

ARDS is known to cause physiological intrapulmonary shunting and wide alveolar-arterial gradient. In our patient we noticed hypoxemia with change in posture (orthodeoxia) which was unexplained and cannot be linked to otherwise recovering pulmonary pathology from COVID-19. The patient had no previous chronic illness and no significant surgical or family history.

Silent intrapulmonary shunts in adults are known and can be linked to either pulmonary arteriovenous malformations (PAVM) or anastomoses (PAVA), with later being more common [3]. The lungs can be divided into different zones (also described as West's Zone) depending on relation of pulmonary arterial and venous pressure with alveolar pressure. Ventilation-perfusion (V/Q) matching is best in Zone 2 with alveolar pressure more than venous pressure but less than arterial pressure. The gravitational effect on blood flow to dependent regions is accentuated in the upright posture. In addition, the right ventricular preload reduces on upright posture, and thus reduces blood flow to pulmonary arteries. This results in postural increase of Zone 1 area in lung apices with alveolar pressure exceeding arterial and venous pressure, resulting in ventilation-perfusion (V/Q) mismatching. The lung parenchymal abnormalities like ARDS which have characteristic involvement of lung bases can accentuate this V/Q mismatch and can explain orthodeoxia in this patient. The patient may have an undiagnosed previous intrapulmonary shunt which got manifested due to worsening of V/Q mismatch with COVID-19 related ARDS. The other possible etiology of orthodeoxia like pulmonary embolism and intracardiac shunt were excluded using TEE and CTPA. Cirrhosis which can cause hepatopulmonary shunts excluded with ultrasound abdomen and normal liver function tests.

Saline contrast transthoracic or TEE are non-invasive bedside methods for non-invasive diagnosis of intracardiac or extracardiac shunts. Transthoracic echocardiography in our patient due to the suboptimal window was non-diagnostic. Saline bubble TEE is more than 97% sensitive for detection of intrapulmonary shunts but poor specificity of 49% [4]. Saline bubble TEE can also be used for semi-quantitative grading of the shunt with grade 0 having no bubbles and intense bubbling in grade 3 (>100 bubbles per frame). The grade-3 shunt however, can increase the positive predictive value (PPV) of SC-TEE for detection PAVM of up to 92.5% [5].

This case highlights the importance of echocardiography in evaluation of unexplained hypoxemia in critically ill patients. The diagnosis of a possible anatomical intrapulmonary shunt in this patient along with severe COVID-19 pneumonia related ARDS was made after SC-TEE. The ventilation perfusion mismatch and shunting is known with ARDS but unexplained hypoxemia should be evaluated further to exclude other differential diagnosis.

The extensive bubbling in the left atrium after more than three cardiac beats suggested a possibility of PAVM or PAVA which need further evaluation by DSA.

### Conclusion

In conclusion, unexplained hypoxemia in a critically ill patient should be extensively evaluated. The bedside echocardiography is a useful initial tool for screening of an occult intra cardiac and extracardiac shunts.

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