



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

COVID-19 May Be Exacerbated by Right-to-Left Interatrial Shunt



To the Editor:

We hypothesize that right-to-left interatrial shunt (RTLIAS), platypnea-orthodeoxia syndrome (POS), and paradoxical embolization may exacerbate coronavirus disease 2019 (COVID-19) in select patients with a patent foramen ovale (PFO).¹ We therefore read the description by Fabre and colleagues² of the clinical course of a 45-year-old woman with COVID-19 and a PFO with great interest. A pulmonary embolism and a thrombus straddling the PFO developed, and she died despite embolectomy and extracorporeal membrane oxygenation.² We suspect that RTLIAS may have contributed to her refractory hypoxia and that the initial improvement with prone positioning raises the possibility of POS.

Positional hypoxia while upright that improves with recumbency is characteristic of POS, a syndrome described in 25% of reported patients with RTLIAS.³ Recognition of POS is important, because simple repositioning can reduce the requirement for respiratory support.³ Because the prevalence of PFO is high (20%-30%),³ the absence of reports describing RTLIAS and POS in patients with COVID-19 suggests that these phenomena are being overlooked. Bubble-contrast echocardiography, a minimally invasive bedside test, can detect interatrial defects and RTLIAS.³

The evidence base to guide management of RTLIAS is limited. Patients with RTLIAS respond poorly to positive end-expiratory pressure, are ventilated longer, and receive more interventions for refractory hypoxia.⁴ Whereas some therapies for refractory hypoxia exacerbate RTLIAS,⁴ repositioning, reducing airway pressures, and medical treatment of pulmonary hypertension (eg, nitric oxide, nitrates, and sildenafil) may reduce or reverse RTLIAS.

In select patients, surgical or percutaneous PFO closure could improve hypoxia, reduce the need for invasive ventilation, and prevent paradoxical embolization. However, acute cor pulmonale develops in some patients after PFO closure. Furthermore, hypoxia may improve spontaneously as the functional trigger for RTLIAS resolves, so closure is not always required.

Studies of COVID-19, PFO, and RTLIAS are urgently required to improve patient outcomes. Such data may be relevant to other pulmonary diseases and could redefine the treatment paradigm of refractory hypoxia.

Rajkumar Rajendram, FRCP

Department of Medicine
King Abdulaziz Medical City
PO Box 22490

Riyadh 11426, Kingdom of Saudi Arabia
email: rajkumarrajendram@doctors.org.uk

G. Abbas Kharal, MD

Department of Neurology
Cleveland Clinic Foundation
Cleveland, Ohio

Rishi Puri, FRACP

Department of Cardiovascular Medicine
Cleveland Clinic Foundation
Cleveland, Ohio

References

1. Rajendram R, Kharal GA, Mahmood N, Puri R, Kharal M. Rethinking the respiratory paradigm of COVID-19: a 'hole' in the argument. *Intensive Care Med.* 2020;46:1496-1497.
2. Fabre O, Rebet O, Carjaliu I, Radutoiu M, Gautier L, Hysi I. Severe acute proximal pulmonary embolism and COVID-19: a word of caution. *Ann Thorac Surg.* 2020;110:e409-e411.
3. Marples IL, Heap MJ, Suvarna SK, Mills GH. Acute right-to-left inter-atrial shunt; an important cause of profound hypoxia. *Br J Anaesth.* 2000;85:921-925.
4. Vavlitou A, Minas G, Zannetos S, Kyprianou T, Tsagourias M, Matamis D. Hemodynamic and respiratory factors that influence the opening of patent foramen ovale in mechanically ventilated patients. *Hippokratia.* 2016;20:209-213.

Right-to-Left Interatrial Shunt in COVID-19 Patients With Pulmonary Embolism



Reply

To the Editor:

We read with great interest the letter from Rajendram and colleagues¹ in response to our previous publication of a young patient presenting with a severe pulmonary embolism as an initial symptom of a coronavirus disease 2019 (COVID-19) infection.² We reported our clinical experience and insisted on the facts that the initial workup showed the patient had a patent foramen ovale with clot into it, which made us choose the surgical treatment rather than an intravenous thrombolytic therapy. After the surgical embolectomy, mechanical ventilation of our patient was difficult, with refractory hypoxemia. Although this was somehow improved by prone positioning, the patient was supported with extracorporeal membrane oxygenation and died of multiorgan failure soon after.

Rajendram and colleagues¹ very interestingly hypothesized that platypnea-orthodeoxia syndrome with a right-to-left interatrial shunt, in relation with the initial patent foramen ovale, might have played a crucial role. We do not think this was possible in our patient because the patent foramen ovale was closed during the cardiac operation with a polypropylene running suture. Moreover, no interatrial shunt was seen in the various echocardiograms done in the postoperative period. In our opinion, improvement of blood gas exchange in prone decubitus was mostly due to the release of posterior atelectasis in an obese patient as in "classic" acute respiratory distress syndrome.³ We think that parenchymal severe inflammatory aggression was per se the main mechanism of lung failure in our patient.

Also, it is important to underline that unlike in the initial period, when we published our article, in the last 3 weeks, almost 65 publications have showed the link and the high frequency between COVID-19 and pulmonary embolism. These proximal or distal thromboses of lung vessels may also present a preponderant factor in the impairment of pulmonary oxygenation in COVID-19 patients.

Olivier Fabre, MD, PhD

Olivier Rebet, MD

Illir Hysi, MD

Department of Cardiac Surgery of Artois
Centre Hospitalier de Lens