

The importance of detection and percutaneous closure of patent foramen ovale during the coronavirus disease 2019 pandemic

To the editor Hospitals are currently trying to curtail elective services to reduce risk posed to patients and medical staff while increasing hospital capacity to treat patients with coronavirus disease 2019 (COVID-19). We therefore read with great interest the guidance on the performance of echocardiography by Gackowski et al,¹ which was published in the April issue of *Kardiologia Polska (Kardiol Pol, Polish Heart Journal)*.

We agree that echocardiography must be problem-oriented and should focus on identification of important abnormalities.¹ During the pandemic, as ever, echocardiography should only be performed if it affects the management. In this context, the guidance on the management of valvular and structural heart disease² is also relevant. These recommendations suggest that closure of patent foramen ovale (PFO) should be deferred during the pandemic.²

As a consequence of these 2 guideline documents, physicians and sonographers may feel that screening for PFO is unnecessary during the COVID-19 pandemic. This may be counterproductive, because patients with PFO may be at high risk of adverse outcomes from COVID-19. Prevention of recurrence after PFO-related stroke is the only indication for PFO closure currently supported by high-quality randomized data.³ Another important indication is the treatment of hypoxia due to right-to-left interatrial shunt.³

Acute respiratory distress syndrome that occurs with COVID-19 is unusual.⁴ In some patients with COVID-19, hypoxia and the shunt may be greater than expected for the degree of lung injury seen on imaging.⁴ The etiology of right-to-left shunt in COVID-19 is likely multifactorial. Whereas intrapulmonary shunt (IPS) is inevitable, COVID-19 may trigger right-to-left interatrial shunt in selected patients with an interatrial defect (eg, PFO).⁴ In these patients,

right-to-left interatrial shunt may exacerbate hypoxia and worsen COVID-19.

Approximately 25% of the reported cases of acute right-to-left intracardiac shunt are associated with platypnea-orthodeoxia syndrome.³ This remarkable clinical phenomenon is associated with dyspnea and hypoxia when taking the upright position, which resolve on recumbency. Although the disease is rare, its recognition is important, as simply lying the patient flat may rapidly alleviate hypoxia. However, keeping the patient flat is not a feasible long-term solution. Determining the anatomical substrate of right-to-left intracardiac shunt and platypnea-orthodeoxia syndrome is required to choose the most appropriate management strategy.

We therefore recommend clinicians to consider screening for an interatrial defect with bubble-contrast echocardiography if: 1) platypnea orthodeoxia is detected; 2) the patient is more hypoxic than expected for the degree of lung injury identified; 3) hypoxemia does not significantly improve with supplemental oxygen; and 4) there is a significant drop in the $\text{PaO}_2/\text{FiO}_2$ ratio.

There are no data from randomized controlled trials to guide the management of patients with extrapulmonary shunt. Indeed, the standard approach to the management of refractory hypoxia, which aims to reduce IPS, can exacerbate acute right-to-left interatrial shunt and may, in fact, worsen hypoxia.⁴ Thus, improving outcomes of these unusually hypoxic patients requires treatment of the whole shunt (ie, IPS + EPS) by balancing the effects of any interventions on both IPS and extrapulmonary shunt.

Furthermore, the incidence of venous thromboembolism, stroke, and systemic arterial embolization is high in patients with COVID-19.⁵ Some of these thromboembolic phenomena may be due to paradoxical embolism via PFO.

We hypothesize that, in selected high-risk patients with COVID-19, percutaneous closure of PFO could markedly improve hypoxia, reduce the need for invasive ventilation, and help to prevent paradoxical embolism. We therefore suggest that screening for PFO with bubble-contrast echocardiography and percutaneous closure of PFO should be continued during the COVID-19 pandemic.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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HOW TO CITE Rajendram R, Kharal GA, Mahmood N, et al. The importance of detection and percutaneous closure of patent foramen ovale during the coronavirus disease 2019 pandemic. *Kardiol Pol.* 2020; 78: 614-615. doi:10.33963/KP.15456

REFERENCES

- 1 Gackowski A, Lipczyńska M, Lipiec P, Szymański P. Echocardiography during the coronavirus disease 2019 (COVID-19) pandemic: expert opinion of the Working Group on Echocardiography of the Polish Cardiac Society. *Kardiol Pol.* 2020; 78: 357-363.
- 2 Płońska-Gościński E, Suwalski P, Bartuś S, et al. Management of valvular and structural heart diseases during the coronavirus disease 2019 pandemic: an expert opinion of the Working Group on Valvular Heart Diseases, the Working Group on Cardiac Surgery, and the Association of Cardiovascular Interventions of the Polish Cardiac Society. *Kardiol Pol.* 2020; 78: 498-507.
- 3 Collado FMS, Poulin MF, Murphy JJ, et al. Patent foramen ovale closure for stroke prevention and other disorders. *J Am Heart Assoc.* 2018; 7: 1-22.
- 4 Rajendram R, Kharal GA, Mahmood N, et al. Rethinking the respiratory paradigm of COVID-19: a "hole" in the argument. *Intensive Care Med.* 2020 Jun 2. [Epub ahead of print].
- 5 Klok FA, Kruijff MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb. Res.* 2020 Apr 10. [Epub ahead of print].

Authors' reply We would like to thank Rajendram et al¹ for their interest in our coronavirus disease 2019 (COVID-19) echocardiographic guidelines in the context of screening for patent foramen ovale (PFO) in patients with COVID-19.² However, we disagree with the hypothesis that screening for PFO with bubble-contrast echocardiography and percutaneous closure of PFO should be continued during the COVID-19 pandemic.¹

Rajendram et al¹ stated that, in selected high-risk patients with COVID-19, percutaneous closure of PFO could markedly improve hypoxia, reduce the need for invasive ventilation, and help to prevent paradoxical embolism. In our opinion, whereas the right-to-left shunt through PFO may, to some extent, contribute to hypoxia, it is certainly not the actual cause of the patient's grave clinical status in acute respiratory distress syndrome (ARDS) induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Evidence concerning the prognostic significance of the presence of PFO in ARDS is equivocal.³ A right-to-left shunt may be even protective against right ventricular dysfunction in acute ARDS-associated cor pulmonale.⁴ Its closure may therefore potentially lead to deterioration of the right ventricular function. Overall, there is no unequivocal evidence coming from well-designed clinical trials, which would demonstrate that PFO closure favorably affects prognosis in patients with severe hypoxia due to ARDS. In patients with severe, resistant hypoxia, veno-venous extracorporeal membrane oxygenation (V-V ECMO) may be considered. The presence of an interatrial shunt may, in fact, be beneficial in V-V ECMO.⁵

As far as secondary stroke prevention by PFO closure is concerned, it has to be kept in mind that the annual risk of stroke due to PFO is low compared with other stroke mechanisms. Therefore, PFO should not be considered a cause of stroke until a thorough workup has excluded alternative mechanisms. Such workup should be postponed in patients with active COVID-19.

In summary, we argue against PFO screening in patients with COVID-19. In our opinion, the "less is more" approach is fully justified both on clinical grounds and to protect medical personnel from the unnecessary risk of SARS-CoV-2 infection.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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HOW TO CITE Szymański P, Lipczyńska M, Lipiec P, Gackowski A. The importance of detection and percutaneous closure of patent foramen ovale during the coronavirus disease 2019 pandemic. Authors' reply. *Kardiol Pol.* 2020; 78: 615. doi:10.33963/KP.15457

REFERENCES

- 1 Rajendram R, Kharal GA, Mahmood N, et al. The importance of detection and percutaneous closure of patent foramen oval during the coronavirus disease 2019 pandemic. *Kardiol Pol.* 2020; 78: 614-615.
- 2 Gackowski A, Lipczyńska M, Lipiec P, Szymański P. Echocardiography during the coronavirus disease 2019 (COVID-19) pandemic: expert opinion of the Working Group on Echocardiography of the Polish Cardiac Society. *Kardiol Pol.* 2020; 78: 357-363.
- 3 Lhéritier G, Legras A, Caille A, et al. Prevalence and prognostic value of acute cor pulmonale and patent foramen ovale in ventilated patients with early acute respiratory distress syndrome: a multicenter study. *Intensive Care Med.* 2013; 39: 1734-1742.
- 4 Legras A, Caille A, Begot E, et al; ARCO and CRICS network (2015). Acute respiratory distress syndrome (ARDS)-associated acute cor pulmonale and patent foramen ovale: a multicenter noninvasive hemodynamic study. *Crit Care.* 2015; 19: 174.
- 5 Julliard W, Niles SD, Maloney JD. Venovenous extracorporeal membrane oxygenation in patients with atrial septal defects. *Perfusion.* 2015; 30: 400-402.

Authors' reply Thank you for publishing the comment of Rajendram et al¹ referring to the recently published scientific statement² regarding the diagnostic workup of patent foramen ovale (PFO) during the coronavirus disease 2019 (COVID-19) pandemic. The recommendation of possible deferral of elective diagnostic workup aimed at screening for PFO, which is a preventive procedure affecting long-term prognosis after cardiogenic embolism, was indeed accepted by the Polish experts, in line with the European guidelines.³ Transesophageal echocardiography, as part of diagnostic workup for PFO in particular, is a complex, aerosol-generating procedure with a predictable impact on echocardiography laboratory services in the era of COVID-19.

We acknowledge the comment on a possible rare scenario of platypnea-orthodeoxia as a consequence of PFO. However, this condition is truly rare in non-COVID patients (a review by Colado et al⁴ mentions a prevalence of 2.5% in the PFO population, and not 25%, which is in line with our own observations), although proper diagnosis is valuable in individual cases of chronic, uncontrolled hypoxia. This means that, for most patients with PFO, a clinical benefit will “classically” stem from abated paradoxical embolism. Interestingly, strokes are not abundant during the pandemic.⁵ Even though a suspicion of PFO can be made using computed tomography or magnetic resonance imaging data, the critical diagnostic step involves transesophageal echocardiographic study with a positional maneuver, which can be a critical limiting factor in the sickest patients including those with COVID-19, especially when ventilated. Importantly, extracardiac shunting is an alternative explanation beyond the common diagnosis of PFO. Importantly, transthoracic echocardiography is routinely suggested in all COVID-19 patients with aggravating hypoxia.³

We deeply regret that the referenced publication by Rajendram et al remains to be published in *Intensive Care Medicine*, as we were unable to reach it when preparing this response. It is true that right ventricular overload or failure, which were identified as negative prognostic factors in

patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), may lead to interatrial shunt reversal and worsening of hypoxia merely by inversion of the pressure gradient between the atria. This mechanism is arguably more likely than position-related shunting typical for platypnea-orthodeoxia. At the same time, the right-to-left shunt unloads the right atrium and is likely to decrease right atrial pressure, potentially reducing systemic venous congestion. Experience in treating patients with pulmonary hypertension indicates that sealing interatrial communication does not improve their clinical outcomes and, inversely, septostomy or implantation of an atrial flow regulator⁶ remains an option for the sickest patients without an intracardiac shunt. Therefore, PFO closure during the COVID-19 pandemic cannot be routinely recommended, and the clinical benefit proposed by Rajendram et al¹ remains hypothetical—even if hypoxia could be alleviated.

We acknowledge the pathophysiological insights included in the letter and, indeed, agree that restrictions in diagnostic procedures must be lifted as early as the COVID-19-related healthcare overload decreases—according to local resources and delivery of services. We have actually proposed the statement on identifying urgent indications for structural heart interventions, which might be represented not only by patients with PFO at high risk of recurrent stroke but also the subsets of candidates for transcatheter aortic valve implantation or MitraClip procedures. However, benefits and risks (including device-related thrombosis) must be carefully weighed considering that the procoagulant state appears to be a major pathophysiological component of COVID-19.⁶ We also believe that continuation or suspension of specific lines of diagnostic workup has to be strongly linked with the local influence of the COVID-19 epidemic upon the healthcare system rather than the fact of a pandemic itself.² Considering the fact that high-quality medicine requires an individualized approach and high-level diagnostic inquisitiveness, we appreciate refreshing the still uncommonly diagnosed platypnea-orthodeoxia syndrome to the readers of *Kardiologia Polska* (*Kardiol Pol*, *Polish Heart Journal*).

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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HOW TO CITE Kasprzak JD, Płońska-Gościński E, Bartuś S, et al. The importance of detection and percutaneous closure of patent foramen ovale during the coronavirus disease 2019 pandemic. Authors' reply. *Kardiol Pol.* 2020; 78: 616-617. doi:10.33963/KP.15458

REFERENCES

- 1 Rajendram R, Kharal GA, Mahmood N, et al. The importance of detection and percutaneous closure of patent foramen oval during the coronavirus disease 2019 pandemic. *Kardiol Pol.* 2020; 78: 614-615.
- 2 Płońska-Gościński E, Suwalski P, Bartuś S, et al. Management of valvular and structural heart disease during the COVID-19 pandemic: an expert opinion of the Working Group on Valvular Heart Diseases, the Working Group on Cardiac Surgery, and the Association of Cardiovascular Interventions of the Polish Cardiac Society. *Kardiol Pol.* 2020; 78: 498-507.
- 3 European Society of Cardiology. ESC Guidance for the diagnosis and management of CV disease during the COVID-19 pandemic. <https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance?hit=home&urlorig=/vgn-ext-templating/>. Accessed June 14, 2020.
- 4 Collado FMS, Poulin MF, Murphy JJ, et al. Patent foramen ovale closure for stroke prevention and other disorders. *J Am Heart Assoc.* 2018; 7: 1-22.
- 5 Yaghi S, Ishida K, Torres J, et al. SARS2-CoV-2 and stroke in a New York health-care system. *Stroke.* 2020 May 20. [Epub ahead of print].
- 6 Janus M, Sławek-Szmyt S, Araszkiewicz A, et al. Atrial flow regulator as a bridge to lung transplant in a young patient with drug-resistant idiopathic pulmonary arterial hypertension. *Kardiol Pol.* 2020; 78: 461-462.