

Reviewer #1:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** The authors describe a case of PFO closure with ICE assistance. They have described the case and technique involved in good detail. There are definite advantages to ICE use in PFO closure as highlighted by authors - no need for TEE operator which conserves resources, potentially better imaging evaluation of PFO, ability to perform valsalva maneuver in the absence of anesthesia. This is a technique that should be highlighted in the interventional community.

Response: Thank you very much for your review.

Reviewer #2:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** In this study the authors reported the implantation of a device for the closure of a patent foramen ovale (PFO) in order to prevent a recurrence of stroke by monitoring the procedure with intracardiac echocardiography (ICE). Some criticism has to be manifested. They talk about the PFO as an abnormality certainly causally connected to the stroke and they depicted the procedure to close it as certainly life-saving. Unfortunately the PFO is very weakly connected to embolic events (stroke in particular) in the only prospective longitudinal study reported in the literature [1]. Most of our knowledge regarding the relationship between the PFO and stroke is based on data of association of PFO and stroke in weakly designed studies such as the case control studies. In addition the intervention of closure

is fraught with possible certain complications in the follow-up [2]: thrombus formation on both facets of the umbrella device, most rarely umbrella dislocation and atrial arrhythmias (atrial fibrillation in particular) and some patients refer atypical chest pain after the closure. So the authors should present the case emphasizing the pros and cons of this procedure. The authors say that ICE has got higher potential than transesophageal echocardiography in visualizing right cardiac masses (atrial mixoma and chiari network) and eventually to better visualize the anatomic features of the foramen ovale. They however forgot to mention the higher potential of this approach in visualizing major clinical problems such as lead endocarditis masses and post lead extraction floating masses inside the right atrial chamber the so called “ghosts” [3,4]. That must be added in order to better describe the ICE potential. The intracardiac echocardiographic images are difficult to decipher because of poor quality even for an expert in the field. Since they support the main result of the study, images of better quality should be provided; alternatively a scheme put aside that could explain the details of the specific tomographic view has to be added.

REFERENCES

1. Meissner I, Khandheria BK, Heit JA, Petty GW, Sheps SG, Schwartz GL, et al. Patent foramen ovale: innocent or guilty? Evidence from a prospective population-based study. *J Am Coll Cardiol.* 2006;47(2):440-5.
2. Krumdordf U, Ostermayer S, Billinger K, Trepels T, Zadan E, Horvath K, et al. Incidence and clinical course of thrombus formation on atrial septal defect and patient foramen ovale closure devices in 1,000 consecutive patients. *J Am Coll Cardiol.* 2004;43(2):302-9.
3. Caiati C, Pollice P, Lepera ME, Favale S. Pacemaker Lead Endocarditis Investigated with Intracardiac Echocardiography: Factors Modulating the Size of Vegetations and Larger Vegetation Embolic Risk during Lead Extraction. *Antibiotics (Basel, Switzerland).* 2019;8(4).
4. Caiati C, Luzzi G, Pollice P, Favale S, Lepera ME. A Novel Clinical Perspective on New Masses after Lead Extraction (Ghosts) by Means of Intracardiac Echocardiography. *Journal of clinical medicine.* 2020;9(8).

Response: Thank you very much for your review and we have revised the manuscript according to your comments. We have mentioned that PFO is weakly associated with the embolic events because the only prospective longitudinal study showed negative result. Also, in the discussion, we showed the closure is fraught with possible certain complications including the thrombus formation, atrial arrhythmia and chest pain in the follow-up. We also discussed the pros and cons of this procedure. Besides, we showed the potential of ICE in visualizing major clinical problems such as lead endocarditis masses and post lead extraction floating masses inside the right atrial chamber, with reference added. However, we did not have images with better quality since we just recorded these images during procedure. Thank you very much for your very helpful suggestion, we will get better images in the future practice.

Revision reviewer:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** The paper has been substantially improved.

Response: Thanks for your comments.