Author’s response to reviews

Title: Patent Foramen Ovale Closure by using Transesophageal Echocardiography for Cryptogenic Stroke: Single center experience in 132 consecutive patients

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Author’s response to reviews:

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “Patent Foramen Ovale Closure with only use of transesophageal echocardiography (TEE) for Cryptogenic Stroke: Single center experience in 132 consecutive patients”. These comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made corrections which we hope meet with approval. The responds to the reviewers’ comments are as follows:

Reviewer 1
Good research work with excellent result without any major complications. Certainly it has advantages over doing under fluoroscopy.
Re: Thank you very much for your comments and appreciation of our article.

Reviewer 2
1- Revise throughly the English editing, both grammar and spelling
Re: Thank you very much for your suggestion. In order to improve the English editing of the article, we have sent the manuscript to a language editing company. To confirm that language editing has been performed, we have sent the certificate as the response to the peer review comments.
2- Clarify how you have managed 4 patients with moderate and large RLS demonstrated by the c-TTE at 12 months of follow-up.
Re: Thank you very much for your comments. This is a very good suggestion. We have already revised the article, added the subsequent management for 4 patients with moderate and large RLS demonstrated by the c-TTE at 12 months of follow-up in the discussion section. The possibility of pulmonary vascular malformations in the four (3.1%) patients with a moderate-to-large residual RLS at 12 months of follow-up was ruled out by computed tomographic pulmonary angiography. The four patients were asked to take aspirin (3–5mg/kg body weight) orally to prevent the recurrence of CS and to undergo a review c-TTE with Valsalva maneuver annually. If residual RLS drops to a small shunt, the aspirin treatment can be discontinued. If residual RLS does not reduce and neurology embolism event recurs, then secondary percutaneous intervention or surgical closure is recommended. Your suggestion improved our article. Thank you!
Reviewer 3
This paper gives a clear description of a useful technique. The English is reasonable but would benefit from editing by a native speaker. For instance on P11 L53 the authors state that they disinfected the "perineum" I believe they mean "groin" although I could be misinterpreting their approach to the atrial septum.
Re: Thank you very much for your comments. I really appreciate your suggestions. To improve the article for details, we have sent the manuscript to a native language editing company. Certainly on P11 L53 the "perineum" was replaced by "groin" based on your suggestion. Your suggestion made our article more reasonable. Thank you!

Reviewer 4
The authors reported outcomes of percutaneous PFO closure guided by TEE. The guidance of TEE to close PFO is interesting but recurrence rate is high in follow up period. I assume that the difficulty to place device in PFO guided by TEE contributes to the high rate of residual shunt.
Re: Thanks very much for taking your time to review our manuscript. Your comments have given us important tips. We reviewed the patients’ data and found that the patient with a large residual RLS, as demonstrated by the c-TTE at 12 months of follow-up, was the one who had received transseptal puncture during the closure procedure. Other patients with residual RLS at 12 months of follow-up were not the ones with irregularly shaped PFOs that were difficult to be passed by the multipurpose catheter. And our experience is that PFO closure guided by TEE is no more difficult to be performed than the traditional closure guided by X-ray. Inspired by your point of view, we once again fully discussed the possible causes of the high rate of residual shunt.

1. We assumed that the application of transseptal puncture may have contributed to the large residual shunt. Transseptal puncture technique may be an effective option for facilitating device closure after the failure of conventional approach, but an increased incidence of residual shunt was observed with this technique
2. The high incidence of residual shunt in the follow-up period of this study may be due to the use of c-TTE for assessing RLS. In some other trials c-TTE was used for follow-up. TEE is a semi-traumatic and painful examination for patients, and completing Valsalva maneuver successfully during the process was difficult for some of them. Thus, the residual shunt may have been underestimated.
3. In most studies Amplatzer PFO occluder were widely used and gained good result. While Cardi-O-fix PFO occluder as a domestic PFO device made in China were used in our study. Comparative studies between Cardi-O-fix PFO occluder and other type of occluders have been rarely conducted. Perhaps the lack of effectiveness of the device was also a factor affecting the high rate of residual shunt.
4. Pulmonary arteriovenous malformations, venous abnormalities may coexist with PFO, which may contribute to persistently positive results on bubble testing after PFO closure.
We have already revised the article, added some contents in our discussion section. Thank you again for your comments and hope to get your acceptance.