Association of migraine with patent foramen ovale closure: A systematic review and meta-analysis

Yan-Li Wang a,c,1, Fang-Ze Wang b,1, Yuan Zhang a, Jiwei Jiang a, Ziyan Jia a, Xiangrong Liu c, Jian Wang b,*, Jun Xu a,c,*

a Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
b Department of Cardiology, Weifang People’s Hospital, Weifang Medical University, Weifang, China
c China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

ARTICLE INFO

Keywords:
Migraine
Patent foramen ovale closure
PFO
Right-to-left shunt

ABSTRACT

Background: The potential correlation between patent foramen ovale (PFO) and migraine has been previously reported, but whether PFO closure plays a role in reducing migraine burden has not reached an agreement.

Method: We searched PubMed, Embase, China National Knowledge Infrastructure (CNKI), Wanfang Database, VIP Science Technology Periodical Database and China Biology Medicine Database (CBM) through September 30, 2021 to identify associations between PFO closure and outcome of migraine burden. The control groups consisted of drug treatment or sham procedure.

Result: Three randomized clinical trials (RCT) and 9 case-control studies were eligible for inclusion (1754 participants), of which 7 reported nonrecurrence of migraine, 4 reported reduced migraine-frequency and migraine-days, and 5 reported HIT-6 score and 4 reported MIDAS score. The mean (SD) age of participants was 40.68 (3.81) years and 1340 (76.39%) were women. PFO closure was significantly associated with a reduced risk of migraine-recurrence by 4.47 (95% CI, 2.94 – 6.80; \(I^2 = 12\%\)), frequency of migraine by 0.35 (95% CI, 0.17 – 0.53; \(I^2 = 0\%\)) and monthly migraine days by 0.28 (95% CI, 0.10 – 0.46), and decreased score of HIT-6 (SMD 1.23, 95% CI 0.52 – 1.95, \(I^2 = 93\%)\).

Conclusion: Transcatheter PFO closure is significantly associated with burden reduction of migraine headache.

1. Introduction

Migraine is one of the most prevalent neurological disorders with a one-year prevalence among adults ranged from 6.0% to 14.3% in East Asia, leading to an impaired quality of life and substantial financial cost [1]. Approximately one-third of migraineurs are preceded by aura, the most common visual symptoms, that is a brief episode of neurological dysfunction [2]. Patent foramen ovale (PFO) is a common congenital defect of the heart, causing an interatrial slit-like channel [3]. Several studies have shown that migraine has a close relationship with right-to-left shunt, notably in migraine with aura patients [4–6]. It has been suggested that various factors increasing neuronal excitability are possible mechanisms for this association, including paradoxical emboli, vasoactive substances and neurotransmitters and so on [7–9].

The results of the three main randomized clinical trials (RCT) showed that PFO closure not yet could cure migraine completely, but the frequency of attacks and monthly headache-days could be reduced [10–12]. The effects of transcatheter PFO closure on migraine, therefore, are controversial. Because existing studies are limited by the statistical power with the small sample size of the available datasets and the findings are inconsistent, we performed a systematic review and meta-analysis to detect the impact of PFO closure on migraine.

2. Methods

2.1. Search strategy

This review was prospectively registered on PROSPERO, CRD...
2.2. Selection criteria

We searched PubMed, Embase and China National Knowledge Infrastructure (CNKI), Wanfang Database, VIP Science Technology Periodical Database and China Biology Medicine Database (CBM) for articles published from databases inception until September 30, 2021. The search terms included “patent foramen ovale”, “transcatheter closure”, “right-to-left shunting”, “migraine” and “headache”. The search strategies were designed to identify published reports of clinical trials and case-control studies to evaluate the long-term impact of PFO closure on migraine. According to the eligibility criteria, two researchers (LW and ZW) independently screened the titles and abstracts and then full-text articles against the inclusion and exclusion criteria. Disagreements were resolved by discussion or consultation with a third author (YZ).

Studies were considered eligible if they were randomized clinical trial (RCT), and case-control study, compared with drug treatment or sham procedure, had at least 6 months of follow-up, published in the English or Chinese language and assessed outcomes including migraine-free, the monthly number of migraine attacks, the mean number of migraine days per month, headache impact test-6 (HIT-6) scores and migraine disability assessment survey (MIDAS) scores [13-15]. Literature review, conference abstract and case report, comment, meta-analysis and controlled before-after study were excluded.

2.3. Data extraction and study quality assessment

We extracted the following data using a standardized form: study characteristics (first author, year of publication, country, sample size, and duration of follow-up), baseline characteristics of participants (age, sex), interventions (drug treatment, PFO closure and sham procedure), outcomes and postprocedural therapy. Methodological quality was assessed using the Newcastle-Ottawa Scale (NOS) for non-randomized studies and the Jadad scale for randomized controlled trials (RCTs) [16,17]. A descriptive analysis of each study is shown in Table 1.

2.4. Statistical analysis

For dichotomous outcomes, odds ratios (ORs) and 95% CIs were estimated for each study. For continuous outcomes, the standard mean difference and corresponding 95% CIs were calculated. Both fixed-effects and random-effects model meta-analyses were performed, and in case of substantial heterogeneity, the random-effects model was used. Heterogeneity was tested by Chi-squared test and was quantified by the I² statistic, with I² values>50% suggesting significant heterogeneity. Statistical analyses were performed using the “Metafor” package in R statistical software, version 4.0.3. A 2-side P < 0.05 was considered statistically significant.

3. Results

Figure 1 shows that 1214 potentially relevant articles are retrieved after duplicates removal. After reviewing 77 full-text articles for eligibility, three RCT, one non-randomized concurrent control-trial and eight case-control studies meet the eligibility criteria. In total, 1754 participants were enrolled. The mean (SD) age of participants was 40.68 (3.81) years and 414 participants were men. Table 1 shows the characteristics of the included trials. Trials were performed in the Italy (N = 4),[18-21] China (N = 5),[22-26] England (N = 1) [10] and America (N = 1).[12] and a multicenter trial performed at 20 centers.[11] One trial compared a sham procedure,[10] one trial compared a combination treatment with drug treatment and sham procedure,[12] and other ten trials compared drug treatment.[11,18-28] Seven trials reported on complete cessation of migraine, [10-12,18,19,21,23] four trials reported on frequency of migraine attack and migraine days per month, [10-12,25] five trials reported on HIT-6 score,[10,22-25] and four trials reported on MIDAS score.[10,11,20,21].

3.1. Risk of bias

The funnel plot depicting the potential publication bias between the complete arrest of migraine analyzed as a categorical variable and PFO closure was shown in eFigure 2. To correct the asymmetry of the funnel plot, two additional studies (the hollow circle) were needed. Among the total, three articles found to be moderate quality (NOS score: 6–7; Jadad score: 3–4) and nine were high quality (NOS score > 7; Jadad score > 4).

3.2. PFO closure and migraine-free

Seven trials reported the incidence of complete arrest of migraine. [10-12,18,19,21,23] Compared with medical therapy or sham procedure, PFO closure significantly increased the rate of migraine-free by 4.47 (95% CI, 2.94–6.80). Heterogeneity was low to moderate (I² = 12%, P = 0.33), so the common-effect model was used. (Fig. 1).

3.3. PFO closure with migraine frequency and migraine days

Four trials reported on frequency of migraine attack and migraine days per month. [10-12,25] Compared with the drug therapy group, patients with PFO closure treatment showed a significant reduction in monthly migraine days by 0.28 (95% CI, 0.10–0.46), with low heterogeneity (I² = 0%, P = 0.53). And monthly migraine attacks were statistically decreased by 0.35 (95% CI, 0.17–0.53), with low heterogeneity (I² = 0%, P = 0.61). (Fig. 2).

3.4. PFO closure and change in activities of daily living score

A random-effects model was selected due to the high heterogeneity among the studies (I² = 93%, P < 0.01). HIT-6 score was significantly decreased in the transcatheter closure patient group (SMD 1.23, 95 %CI 0.52–1.95). However, there was no statistically significant difference in MIDAS score between both groups (SMD 0.96, 95 %CI −0.55–2.47). (Fig. 3).

4. Discussion

Migraine, the second leading cause of disability worldwide,[29] is a paroxysmal disease characterized by complex sensory dysfunction and headache, and accompanied by aura in approximately one in four migraine patients.[30] It is possible that many factors are associated with migraine, including menstruation, emotional stress and weather changes, poor sleep and right-to-left shunting and so on.[29,31]. Besides, a large cohort study found that migraine may increase risk of ischemic stroke with an adjusted hazard ratio of 2.26.[32].

A study from part of the Northern Manhattan Study found that there was no significant difference in the prevalence of PFO between subjects with migraine and those without migraine, and no relationship was demonstrated between PFO and self-reported migraine.[33] However, a study that divided migraine into those with and without aura indicated that PFO presence is more prevalent in migraine patients with aura than without aura or controls.[34,35]. Furthermore, several controlled before-and-after studies proved that percutaneous closure of interatrial septal defect could be beneficial to reduce intensity, frequency and duration of migraine.[36–39]. No residual right-to-left shunt is an important factor in reducing the burden of migraine.

Our findings are consistent with these previous meta-analyses that transcatheter closure can significantly improve symptoms of migraine patients on headache duration and frequency.[6,40,41]. And studies providing HIT-6 scores and MIDAS scores were also included in our analysis, which were not involved in previous studies; second, this is the
| Authors, year | Country | Design | Participants | Age, y | male, % | N | Follow-up | Comparator(s) | Outcomes | Postprocedural therapy | Grade |
|--------------|---------|--------|--------------|--------|---------|---|-----------|--------------|----------|-----------------------|-------|
| Anzola, 2006 | Italy   | case-control | patients with migraine and PFO | 40/36 | 5/4, 18.5/14.8 | 50/27 | 12 m | drug treatment | Overall migraine severity score, indicating the frequency, duration, and intensity of the attacks and the occurrence of the aura in the prodromal phase; The difference between baseline and final score | Aspirin 300 mg qd*6m | high |
| Dowson, 2008 | UK      | RCT/(MIST) | patients with migraine and PFO | 44.3/44.6 | 12/11, 16.2/15.1 | 74/73 | 6 m | a sham procedure | Cessation of migraine headache; The Headache Impact test (HIT-6) and the Migraine Disability Assessment (MIDAS) questionnaire; incidence of migraine during the healing phase | Aspirin and clopidogrel 75 mg qd*3m | high |
| Vigna, 2009  | Italy   | case-control | patients with moderate/severe migraine, PFO, large right-to-left shunt, and subclinical brain MRI lesions | 42/43 | 5/3, 9.4/10.3 | 53/29 | 6 m | drug treatment | Frequency and severity of migraine recurrence, >50% decrease in the number of total and disabling attacks | (Aspirin 100 mg + clopidogrel 75 mg) qd*3m + aspirin 100 mg qd*3m | moderate |
| Rigatelli, 2010 | Italy | case-control | patients with migraine and PFO | 40/38.9 | 11/6, 23.9/15 | 40/46 | 6 m, 12 m | drug treatment | MIDAS score; reduction or abolition of migraine and aura with a 4-grade scale: 100% (total resolution), 50% reduction, 25% reduction, or 0% (unchanged). | None | high |
| Biasco, 2014 | Italy   | case-control | patients with migraine and PFO | 46.4/47.1 | 22/17, 24.7/13.3 | 89/128 | 6 m, 12 m | drug treatment | MIDAS; the subjective perceived benefit TCD study | Aspirin 100 mg qd*6m and clopidogrel 75 mg qd*3m | high |
| Mattle, 2016 | Twenty centuries | RCT/(PRIMA) | Migraine with aura patients and PFO | 44.1/42.7 | 8.9/15.17 | 53/54 | 12 m | drug treatment | Reduction in monthly migraine days; the change in the monthly number of migraine with aura days; the number of patients free of migraine attacks; MIDAS | Acetylsalicylic acid 75–100 mg qd*6m and clopidogrel 75 mg qd*3m | high |
| Xing, 2016  | China   | non-randomized clinical trial /(EASTFORM) | severe migraineurs with a right-to-left shunt (RLS) (grade II-IV) | 39/38.3 | 33/33, 26.4/28.4 | 125/116 | 6 m, 12 m | drug treatment | HIT-6 score; the degree of headache impact; The change score | Aspirin 100 mg qd*6m | moderate |
| Tobis, 2017 | USA     | double-blind study/(PREMIUM) | patients with migraine and PFO | 42.8/43.7 | 13/12, 10.6/11.2 | 123/107 | 1, 3, 6, and 12 m | drug treatment with a sham procedure | The responder rate for a 50% reduction from the monthly number of migraine attacks; a significant decrease in the mean number of migraine days per month | None | high |
| Zhang, 2018 | China   | case-control | patients with migraine and PFO | 53/57 | 44.5/47.9 | 119/119 | 1 m, 6 m | drug treatment | Reduction in monthly migraine days; the monthly number of migraine attacks | None | high |
| He, 2019    | China   | retrospective study | patients with migraine and PFO | 37.1/39.2 | 23/29, 25.3/28.7 | 91/101 | 1y, 5y | drug treatment | HIT-6 | None | moderate |
| Tian, 2019  | China   | case-control | patients with migraine and RLS | 38.5/36.5 | 20/17, 35.1/29.8 | 57/57 | 1y | drug treatment | HIT-6 | Aspirin 100 mg qd*6m | high |
| Wang, 2019  | China   | Prospective case-control | patients with migraine and PFO | 39.7/31 | 8/3, 47.1/50 | 17/6 | 6 m | drug treatment | Frequency of migraine attack; monthly migraine days; HIT-6 | Aspirin 100 mg qd*6m | high |
Fig. 1. Associations between complete cessation of migraine and PFO closure.

Fig. 2. Associations of PFO closure with migraine frequency (A) and migraine days (B).

Fig. 3. Associations of PFO closure with change in activities of daily living score. (A: HIT-6 score; B: MIDAS score).
meta-analysis that has included the most relevant literature so far, and publication bias was included in the analysis. We demonstrated that PFO occlusion could reduce headache severity, of the five studies included, only the MIST (Migraine Intervention with STARFlex Technology) trial reported no improvement in severity of headache was realized. The possible reason may be the residual amount of shunt and absence of shunt related to substantial reduction in migraine. \[42\] And there may be a dose-effect relationship between residual shunt and migraine symptoms.\[42,43\] Besides, due to the subjective nature of the HIT-6 questionnaire, HIT-6 scores are heavily influenced by the variability of pain tolerance across individuals.\[23\] The procedure of PFO occlusion is not complicated, and the operation can be performed in less than half an hour, and the patient can be discharged from hospital in 3–4 days. The results of this meta-analysis suggest that the clinical indications for PFO occlusion should be strictly selected, and that the use of foramen ovale occlusion can effectively relieve migraine symptoms, reduce pain of patients and improve their overall quality of life. The possible mechanisms by which patients with PFO are prone to migraine are as follows. First, right-to-left shunt may allow serotonin or other vasoactive substances such as neurotransmitters or endothelin circumventing the lungs, instead of being metabolized by lung monamine oxidase, and directly entering the cerebral circulation.\[9,44\] These may lead to stimulation of trigeminal and cerebrovascular, because large amounts of serotonin exposed to the brain\[45,46\]. Second, subclinical emboli across a PFO may be responsible for migraine, especially for migraine with aura\[7\], paradoxical emboli generated into the occipital area, causing the visual aura and subsequent headache\[47\] paradoxical emboli generated into Furthermore, oral aspirin and clopidogrel reduced the frequency of migraine after transcatheter PFO closure.\[48\].

5. Limitation

There are several limitations of this study. First, due to the retrospective nature of studies, recall bias and reporting bias cannot be entirely ruled out. The second is heterogeneity, especially in case-control studies. Third, further subgroup stratification analysis by aura is not conducted, because of the limited number of published studies. And different studies have used different evaluation index, therefore causing some clinical endpoints are only applicable to the included studies.

6. Conclusion

The collective evidence confirmed that migraine could be effectively improved after transcatheter PFO closure, in particular when patients are at risk for paroxysmal embolism or visual aura. In order to testify the diagnostic values of PFO closure to improve migraine burden, more large samples, multi-center prospective randomized controlled trial are required.

Author contributions

JX, XRL conceived and designed the study. YLW, FZW contributed generation of the manuscript. RZL, JWX helped revise the manuscript. All authors contributed to the editing of the manuscript.

Funding

This study was supported by the National Natural Science Foundation (Grant Numbers 82071187, 81870821, 81471215), The National Key Research and Development Program of China (2021YFC2500103), Beijing Youth Talent Team Support Program (201800021225TD08), National key research and development program (2019YFC01209028) and Beijing Natural Science Foundation grant (L182055).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jchaa.2022.100992.

References

[1] T. Takeushima, Q. Wan, Y. Zhang, M. Komori, S. Stretton, N. Bajana, T. Treuer, K. Ueda, Prevalence, burden, and clinical management of migraine in China, Japan, and South Korea: a comprehensive review of the literature, J. Headache Pain 20 (1) (2019), https://doi.org/10.1186/s11919-016-0162-4.
[2] A. Charles, J.M. Hanno, Migraine aura: new ideas about cause, classification, and clinical significance, Curr. Opin. Neurol. 28 (3) (2015) 255-260.
[3] P.T. Hagen, D.G. Scholtz, W.D. Edwards, Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts, Mayo Clin. Proc. 59 (1) (1984) 17-20.
[4] B. Kheiro, A. Abdalla, M. Osman, et al., Percutaneous Closure of Patent Foramen Ovale in Migraine: A Meta-Analysis of Randomized Clinical Trials, JACC Cardiovascular Interventions 11 (8) (2018) 816-818.
[5] J. Allani, Migraine and Patent Foramen Ovale,Curr. Neurol. Neurosci. Rep. 14 (2) (2014), https://doi.org/10.1007/s11910-013-0452-4.
[6] Y.-L. Shi, J. Lv, X.-T. Han, G.-L. Luo, Migraine and patent foramen ovale closure: a systematic review and meta-analysis, BMC cardiovascular disorders 17 (1) (2017), https://doi.org/10.1186/s12872-017-0644-9.
[7] H.-C. Diener, T. Kurth, D. Dodick, Patent foramen ovale and migraine, Curr. Pain Headache Rep. 11 (3) (2007) 236-240.
[8] M. G. Bossu, Patent foramen ovale and migraine: Evidence for a link? Headache Currents 3 (2) (2006) 44-51.
[9] J.A. Zeller, K. Frahm, R. Baron, et al., Platelet-leukocyte interaction and platelet activation in migraine: a link to ischemic stroke? J. Neurol. Neurosurg. Psychiatry 75 (7) (2004) 984-989.
[10] A. Downow, M.J. Mullen, R. Pearfield, K. Muir, A. Khan, C. Wells, S.L. Lipscombe, T. Rees, J.V. De Giovanni, W.L. Morrison, D. Hildick-Smith, G. Elrington, W. S. Hills, L.S. Malik, A. Rickards, Migraine intervention with STARFlex technology (MIST) trial: A prospective, multicenter, double-blind, sham-controlled trial to evaluate the effectiveness of patent foramen ovale closure with STARFlex septal repair implant to resolve refractory migraine headache, Circulation 117 (11) (2008) 1397-1404.
[11] H.P. Matthe, S. Evers, D. Hildick-Smith, W.J. Becker, H. Baumgartner, J. Chataway, M. Gaweł, H. Gobel, A. Heinez, E. Horlick, I. Malik, S. Ray, A. Zernansky, O. Findling, S. Windecker, B. Meier, Percutaneous closure of patent foramen ovale in migraine with aura, a randomized controlled trial, Eur. Heart J. 37 (26) (2016) 2029-2036.
[12] J.M. Tobis, A. Charles, S.D. Silberstein, S. Sorenson, B. Maini, P.A. Horwitz, J. C. Gurley, Percutaneous Closure of Patent Foramen Ovale in Patients With Migraine: The PREMIUM Trial, J. Am. Coll. Cardiol. 70 (22) (2017) 2766-2774.
[13] W.F. Stewart, R.B. Lipson, K. Solderen, J. Libberman, J. Sawyer, Reliability of the migraine disability assessment score in a population-based sample of headache sufferers, Cephalalgia : Int. J. Headache 19 (2) (1999) 107-114.
[14] WARE J E, JR., BJÖRNER J B, KOSINSKI M. Practical implications of item response theory and computerized adaptive testing: a brief summary of ongoing studies of widely used headache impact scales. Medical care, 2000, 38(9 Suppl): Ii73-82.
[15] M. Kosinski, M.S. Bayliss, J.B. Björner, et al., A six-item short-form survey for measuring headache impact: the HIT-6, Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation 12 (8) (2003) 963-974.
[16] A. Stang, Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses, Eur. J. Epidemiol. 25 (9) (2010) 603-605.
[17] A.R. Jadad, R.A. Moore, D. Carroll, C. Jenkinson, D.J.M. Reynolds, D.J. Gavigan, H.J. McQuay, Assessing the quality of reports of randomized clinical trials: Is blinding necessary? Control. Clin. Trials 17 (1) (1996) 1–12.
[18] G.P. Anzola, G.B. Frisone, E. Morandi, F. Canili, E. Onorato, Shunt-associated migraine responds favorably to atrial septal repair: a case-control study, Stroke 37 (2006) 430-434.
[19] C. Vigna, N. Marchese, V. Inchingolo, G.M. Ginnantempo, M.A. Facelli, P. Di Vesti, M. Impaglialetti, R. Natali, A. Russo, B. Fanelli, F. Loperfido, Improvement of migraine after patent foramen ovale percutaneous closure in patients with subclinical brain lesions: a case-control study, JACC Cardiovascular Interventions 2 (3) (2009) 107-112.
[20] G. Rigatti, F. Dell’Avvocata, F. Ronco, P. Cardiali, M. Giordan, G. Braggion, S. Aggio, M. Chiniaglia, G. Rigatti, J.P. Chen, Primary transcatheter patent foramen ovale closure is effective in improving migraine in patients with high-risk anatomic and functional characteristics for paradoxical embolism, JACC Cardiovascular Interventions 3 (3) (2010) 282-287.
[21] L. Biasco, V. Infantino, F. Orzan, S. Vicentini, C. Rovera, G. Longo, A. Chiniaglia, R. Belli, G. Allahs, F. Gaita, Impact of transcatheter closure of patent foramen ovale in the evolution of migraine and role of residual shunt, J. Cardiol. 64 (5) (2014) 390-394.
[22] Y.-Q. Xing, Y.-Z. Guo, Y.-S. Gao, Z.-N. Guo, P.-P. Niu, Y. Yang, Effectiveness and Safety of Transcatheter Patent Foramen Ovale Closure for Migraine (EASTFORM) Trial, Sci. Rep. 6 (1) (2016), https://doi.org/10.1038/srep30981.

[23] Y.-D. He, X.-L. Yan, C. Qin, P. Zhang, Z.-N. Guo, Y. Yang, Transcatheter Patent Foramen Ovale Closure Is Effective in Alleviating Migraine in a 5-Year Follow-Up, Front. Neurol. 10 (2019), https://doi.org/10.3389/fneur.2019.01224.

[24] D.C. Tian, W. Chen, Q. Tian, et al., Clinical Study of Patent Foramen Ovale Transcatheter Closure on Migraine Patients Combined with Right-to-left Shunt, Neuronal Injury Functional Reconstruction 14 (04) (2019), pp. 173-5+98.

[25] Y.Y. Wang, E.C. Qiu, G.Y. Wang, et al., Relationship between migraine and PFO and characteristic of migraine in PFO patients after PFO closure, Chinese J. Pain Medicine 25 (05) (2019) 344-350.

[26] H.W. Zhang, Q.S. Shen, Observation of interventional occlusion in 238 cases of migraine with patent foramen ovale, Chinese J. Interventional Cardiology 26 (11) (2018) 627-631.

[27] J.L. Mas, B. Guillou, A. Charles-Nelson, et al., Patent foramen ovale occlusion in stroke patients with migraine in the CLOSE trial. The CLOSE-MIG study, European J. Neurology 28 (8) (2021) 2700-2707.

[28] E. Morandi, G.P. Anzola, F. Cavalli, E. Onorato, Migraine: traditional or innovative treatment? A preliminary case-control study, Pediatr. Cardiol. 26 (3) (2005) 231-235.

[29] D.N. Krause, K. Warwinge, K.A. Haanen, L. Edvinsson, Hormonal influences in migraine - interactions of oestrogen, oxytocin and CGRP, Nature reviews Neurology 17 (10) (2021) 621-633.

[30] P.J. Goadsby, P.R. Holland, M. Martin-Oliveira, J. Hoffmann, C. Schankin, S. Akerman, Pathophysiology of Migraine: A Disorder of Sensory Processing, Physiol. Rev. 97 (2) (2017) 553-622.

[31] G.P. Anzola, E. Morandi, F. Cavalli, E. Onorato, Different degrees of right-to-left shunting predict migraine and stroke: data from 420 patients, Neurology 66 (5) (2006) 765-767.

[32] ADELBORG K, SZPLIGETI S K, HOLLAND-BILL I, et al. Migraine and risk of cardiovascular diseases: Danish population based matched cohort study. BMJ (Clinical research ed) 2018, 360 1166.

[33] T. Rundek, M.S.V. Elkind, M.R. Di Tullio, E. Carrera, Z. Jin, R.L. Sacco, M. Homma, Patent foramen ovale and migraine: A cross-sectional study from the Northern Manhattan Study (NOMAS), Circulation 118 (14) (2008) 1419-1424.

[34] J. Domitrz, J. Mieszkowski, A. Kamiński, Relationship between migraine and patent foramen ovale: a study of 121 patients with migraine, Headache 47 (9) (2007) 1311-1318.

[35] F.J. Carod-Artal, et al., Prevalence of patent foramen ovale in migraine patients with and without aura compared with stroke patients. A transcatheter Doppler study, Cephalalgia: International J. Headache 26 (8) (2006) 934-939.

[36] LUERMANS J G, POST M C, TEMMERMAN F, et al. Closure of a patent foramen ovale is associated with a decrease in prevalence of migraine: a prospective observational study. Acta cardiologica, 2008, 63(5): 571-7.

[37] N.W. Shammas, E.J. Dippel, G. Harb, et al., Interatrial septal defect closure for prevention of cerebrovascular accidents: Impact on recurrence and frequency of migraine headaches, J. Invasive Cardiol 19 (6) (2007) 257-266.

[38] M. Reisman, R.D. Christofferson, J. Jesurum, J.V. Olsen, M.P. Spencer, K.A. Krabill, L. Diehl, S. Aurora, W.A. Gray, Migraine headache relief after transcatheter closure of patent foramen ovale, J. Am. Coll. Cardiol. 45 (4) (2005) 493-495.

[39] Q. He, Y. Zhang, F. Wang, C. Li, R. Guo, X. Li, B. Luan, H. Zhao, L. Meng, H. Chen, L. Meng, Impact of right-to-left shunt and transcatheter closure on the clinical features of migraine, Int. J. Neurosci. 130 (3) (2020) 270-275.

[40] A. Elbadawi, K. Barseghian, A. Rezq, N. Binwale, E. Alostaki, A. H. Mohamed, S. Vuyyala, G.O. Ogunbayo, M. Saad, Meta-analysis of randomized trials on percutaneous patent foramen ovale closure for prevention of migraine, Acta Cardiol. 74 (2) (2019) 124-129.

[41] Q.-Q. Zhang, J.-J. Lu, M.-Y. Yan, X.-W. Hu, Y.-R. Qin, D.-P. Wang, J.-H. Jiang, Q. i. Fang, H.-R. Zhao, S. De Vleeschouwer, The Efficacy of Percutaneous Patent Foramen Ovale Closure on Migraine: a Meta-Analysis of Randomized Controlled Trials and Observational Studies, Biomed Res. Int. 2021 (2021) 1-9.

[42] E. Ben-Asha, P. Rengilo-Moreno, R. Al-Bawardy, D. Kolte, R. Cigarroa, L. Cruz-Gonzales, R. Salkhya, S. Elmariah, E. Pomerantsev, L.M. Vaina, MingMing Ning, F. S. Buonanno, J.W. Hung, I. Ingelss, I.F. Palacios, Effect of Residual Interatrial Shunt on Migraine Burden After Transcatheter Closure of Patent Foramen Ovale, JACC Cardiovascular Interventions 13 (3) (2020) 293-302.

[43] M. Schwerzmann, S. Wiher, K. Nedeltchev, H.P. Mattle, A. Wahl, C. Seiler, B. Meier, S. Windecker, Percutaneous closure of patent foramen ovale reduces the frequency of migraine attacks, Neurology 62 (8) (2004) 1399-1401.

[44] M.M. Ning, D. Navarretia, I. Ingelss-Arzajle, et al., How the heart whispers to the brain: Serotonin as neurovascular mediator in patent foramen ovale related stroke, Stroke 42 (3) (2011) e108-e109.

[45] N. Tariq, S.J. Tepper, J.S. Krieger, Patent Foramen Ovale and Migraine: Closing the Debate - A Review, Headache 56 (3) (2016) 462-476.

[46] P. Wilmshurst, S. Nightingale, K.P. Walsh, et al., Clotidigrel reduces migraine with aura after transcatheter closure of persistent foramen ovale and atrial septal defects, Heart (British Cardiac Society) 91 (9) (2005) 1173-1175.