

Protocol

Closure Devices for Patent Foramen Ovale and Atrial Septal Defects

(20209)

Medical Benefit		Effective Date: 10/01/19	Next Review Date: 07/21
Preauthorization	No	Review Dates: 05/09, 05/10, 05/11, 05/12, 05/13, 05/14, 01/15, 11/15, 11/16, 11/17, 07/18, 07/19, 07/20	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With patent foramen ovale and cryptogenic stroke	Interventions of interest are: • Patent foramen ovale closure with a trans-catheter device	Comparators of interest are: • Medical management	Relevant outcomes include: • Overall survival • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With patent foramen ovale and migraine	Interventions of interest are: • Patent foramen ovale closure with a trans-catheter device	Comparators of interest are: • Medical management	Relevant outcomes include: • Symptoms • Quality of life • Medication use • Treatment-related mortality • Treatment-related morbidity
Individuals: • With patent foramen ovale and conditions associated with patent foramen ovale other than cryptogenic stroke or migraine	Interventions of interest are: • Patent foramen ovale closure with a trans-catheter device	Comparators of interest are: • Usual care	Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: • With atrial septal defect and evidence of left-to-right shunt or right ventricular overload	Interventions of interest are: • Atrial septal defect closure with a trans-catheter device	Comparators of interest are: • Surgical atrial septal defect repair	Relevant outcomes include: • Symptoms • Change in disease status • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

Patent foramen ovale (PFO) and atrial septal defects (ASDs) are relatively common congenital heart defects that can be associated with a range of symptoms. PFOs may be asymptomatic but have been associated with higher rates of cryptogenic stroke. PFOs have also been investigated for a variety of other conditions, such as a migraine. Depending on their size, ASDs may lead to left-to-right shunting and signs and symptoms of pulmonary overload. Repair of ASDs is indicated for patients with a significant degree of left-to-right shunting. Transcatheter closure devices have been developed to repair PFO and ASDs. These devices are alternatives to open surgical

repair for ASDs or treatment with antiplatelet and/or anticoagulant medications in patients with cryptogenic stroke and PFO.

SUMMARY OF EVIDENCE

For individuals who have PFO and cryptogenic stroke who receive PFO closure with a transcatheter device, the evidence includes multiple randomized controlled trials (RCTs) comparing device-based PFO closure with medical therapy, systematic reviews, meta-analyses, and observational studies. Relevant outcomes are symptoms, change in disease status, overall survival, morbid events, and treatment-related morbidity and mortality. The RCTs comparing PFO closure with medical management have suggested that PFO closure is more effective than medical therapy in reducing event rates. Although these results were not statistically significant by intention-to-treat analyses in the first three trials [i.e., Evaluation of the STARFlex Septal Closure System in Patients with a Stroke and/or Transient Ischemic Attack due to Presumed Paradoxical Embolism through a Patent Foramen Ovale (CLOSURE), Amplatzer PFO Occluder with Medical Treatment in Patients with Cryptogenic Embolism (PC-Trial), and Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment (RESPECT; initial study)], they were statistically significant in later trials [i.e., RESPECT (extended follow-up), Reduction in the Use of Corticosteroids in Exacerbated COPD (REDUCE), and Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence (CLOSE)]. Use of appropriate patient selection criteria to eliminate other causes of cryptogenic stroke in RESPECT, REDUCE, and CLOSE trials contributed to findings of the superiority of PFO closure compared with medical management. Of note, higher rates of atrial fibrillation were reported in a few of the individual trials and in the meta-analysis that incorporated evidence from RESPECT, REDUCE, and CLOSE trials. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

RCTs of PFO closure and multiple observational studies reporting on the association between PFO and migraine. Relevant outcomes are symptoms, quality of life, medication use, and treatment-related morbidity and mortality. The available sham-controlled randomized trial did not demonstrate significant improvements in migraine symptoms after PFO closure. A second RCT with blinded endpoint evaluation did not demonstrate reductions in migraine days after PFO closure but likely was underpowered. Nonrandomized studies have shown highly variable rates of migraine reduction after PFO closure. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have PFO and conditions associated with PFO other than cryptogenic stroke or migraine (e.g., platypnea-orthodeoxia syndrome, myocardial infarction with normal coronary arteries, decompression illness, high-altitude pulmonary edema, obstructive sleep apnea) who receive PFO closure with a transcatheter device, the evidence includes small case series and case reports. Relevant outcomes are symptoms, change in disease status, morbid events, and treatment-related morbidity and mortality. The body of evidence only consists of small case series and case reports. Comparative studies are needed to evaluate outcomes in similar patient groups treated with and without PFO closure. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have ASD and evidence of left-to-right shunt or right ventricular overload who receive ASD closure with a transcatheter device, the evidence includes nonrandomized comparative studies and single-arm studies. Relevant outcomes are symptoms, change in disease status, and treatment-related morbidity and mortality. The available nonrandomized comparative studies and single-arm case series have shown rates of closure using transcatheter-based devices approaching the high success rates of surgery, which are supported by meta-analyses of these studies. The percutaneous approach has a low complication rate and avoids the morbidity and complications of open surgery. If the percutaneous approach is unsuccessful, ASD closure can be achieved using surgery. Because of the benefits of percutaneous closure over open surgery, it can be determined that trans-

catheter ASD closure improves outcomes in patients with an indication for ASD closure. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

POLICY

The percutaneous transcatheter closure of a patent foramen ovale using a device that has been approved by the U.S. Food and Drug Administration for that purpose may be considered **medically necessary** to reduce the risk of recurrent ischemic stroke if the patient meets all of the following:

- Between 18 and 60 years of age
- Diagnosed with patent foramen ovale with a right-to-left interatrial shunt confirmed by echocardiography with at least one of the following characteristics:
 - PFO with large shunt, defined as >30 microbubbles in the left atrium within three cardiac cycles, after opacification of the right atrium
 - PFO associated with atrial septal aneurysm on transesophageal examination: septum primum excursion >10 mm
- Documented history of cryptogenic ischemic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude any other identifiable cause of stroke, including large vessel atherosclerotic disease and small vessel occlusive disease

AND none of the following are present:

- Uncontrolled vascular risk factors, including uncontrolled diabetes or uncontrolled hypertension
- Other sources of right-to-left shunts, including an atrial septal defect and/or fenestrated septum
- Active endocarditis or other untreated infections
- Inferior vena cava filter.

Transcatheter closure of secundum atrial septal defects may be considered **medically necessary** when using a device that has been approved by the U.S. Food and Drug Administration for that purpose and used according to the labeled indications including:

- Patients with echocardiographic evidence of ostium secundum atrial septal defect;

AND either of the following

- Clinical evidence of right ventricular volume overload (i.e., 1.5:1 degree of left-to-right shunt or right ventricular enlargement); OR
- Clinical evidence of paradoxical embolism.

Transcatheter closure of secundum atrial septal defects is considered **investigational** for all other indications not meeting criteria outlined above.

POLICY GUIDELINES

Two devices approved by the U.S. Food and Drug Administration (FDA) for patent foramen ovale closure and ASD closure are currently marketed: the Amplatzer™ Septal Occluder and the GORE CARDIOFORM Septal Occluder. The GORE HELEX Septal Occluder has been discontinued.

BACKGROUND

PATENT FORAMEN OVALE

The foramen ovale, a component of fetal cardiovascular circulation, consists of a communication between the right and left atrium that functions as a vascular bypass of the uninflated lungs. The ductus arteriosus is another feature of the fetal cardiovascular circulation, consisting of a connection between the pulmonary artery and the distal aorta. Before birth, the foramen ovale is held open by the large flow of blood into the left atrium from the inferior vena cava. Over the course of months after birth, an increase in left atrial pressure and a decrease in right atrial pressure result in permanent closure of the foramen ovale in most individuals. However, a patent foramen ovale (PFO) is a common finding in 25% of asymptomatic adults.¹ In some epidemiologic studies, PFO has been associated with cryptogenic stroke, defined as an ischemic stroke occurring in the absence of potential cardiac, pulmonary, vascular, or neurologic sources. Studies have also shown an association between PFO and migraine headache.

ATRIAL SEPTAL DEFECTS

Unlike PFO, which represents the postnatal persistence of normal fetal cardiovascular physiology, atrial septal defects (ASDs) represent an abnormality in the development of the heart that results in free communication between the atria. ASDs are categorized by their anatomy. Ostium secundum describes defects located midseptally and are typically near the fossa ovalis. Ostium primum defects lie immediately adjacent to the atrioventricular valves and are within the spectrum of atrioventricular septal defects. Primum defects occur commonly in patients with Down syndrome. Sinus venous defects occur high in the atrial septum and are frequently associated with anomalies of the pulmonary veins.

Ostium secundum ASDs are the third most common form of congenital heart disorder and among the most common congenital cardiac malformations in adults, accounting for 30% to 40% of these patients older than age 40 years. The ASD often goes unnoticed for decades because the physical signs are subtle and the clinical sequelae are mild. However, virtually all patients who survive into their sixth decade are symptomatic; fewer than 50% of patients survive beyond age 40 to 50 years due to heart failure or pulmonary hypertension related to the left-to-right shunt. Symptoms related to ASD depend on the size of the defect and the relative diastolic filling properties of the left and right ventricles. Reduced left ventricular compliance, and mitral stenosis will increase left-to-right shunting across the defect. Conditions that reduce right ventricular compliance and tricuspid stenosis will reduce left-to-right shunting or cause a right-to-left shunt. Symptoms of an ASD include exercise intolerance and dyspnea, atrial fibrillation, and less commonly, signs of right heart failure. Patients with ASDs are also at risk for paradoxical emboli.

Treatment of Atrial Septal Defects

Repair of ASDs is recommended for those with a pulmonary-to-systemic flow ratio ($Q_p:Q_s$) exceeding 1.5:1.0. Despite the success of surgical repair, there has been interest in developing a transcatheter-based approach to ASD repair to avoid the risks and morbidity of open heart surgery. A variety of devices have been researched. Technical challenges include minimizing the size of the device so that smaller catheters can be used, developing techniques to center the device properly across the ASD, and ensuring that the device can be easily retrieved or repositioned, if necessary.

Individuals with ASDs and a history of cryptogenic stroke are typically treated with antiplatelet agents, given an absence of evidence that systemic anticoagulation is associated with outcome improvements.

Transcatheter Closure Devices

Transcatheter PFO and ASD occluders consist of a single or paired wire mesh discs covered or filled with polyester or polymer fabric that are placed over the septal defect. Over time, the occlusion system is epithelialized. ASD occluder devices consist of flexible mesh discs delivered via catheter to cover the ASD.

REGULATORY STATUS**PATENT FORAMEN OVALE CLOSURE DEVICES**

The U.S. Food and Drug Administration (FDA) has approved three devices for ASD closure through the premarket approval process or a premarket approval supplement: the Amplatzer Septal Occluder, the GORE HELEX Septal Occluder (discontinued), and the GORE CARDIOFORM Septal Occluder (see Table 1). FDA product code: MLV.

In 2002, two transcatheter devices were cleared for marketing by the FDA through a humanitarian device exemption as treatment for patients with cryptogenic stroke and PFO: the CardioSEAL® Septal Occlusion System (NMT Medical; device no longer commercially available) and the Amplatzer® PFO Occluder (Amplatzer, now St. Jude Medical). Following the limited FDA approval, use of PFO closure devices increased by more than 50-fold, well in excess of the 4,000 per year threshold intended under the humanitarian device exemption,² prompting the FDA to withdraw the humanitarian device exemption approval for these devices in 2007. The Amplatzer PFO Occluder was approved through the premarket approval process in 2016.

In March 2018, the FDA granted an expanded indication to the Gore Cardioform Septal Occluder to include closure of PFO to reduce the risk of recurrent stroke (see Table 1). The new indication was based on results of the REDUCE pivotal clinical trial.³

Table 1. Patent Foramen Ovale Closure Devices Approved by the U.S. Food and Drug Administration

Device	Manufacturer	PMA Approval Date	Indications
Amplatzer™ PFO Occluder	St. Jude Medical	Nov 2016	For percutaneous transcatheter closure of a patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke. ⁴
GORE HELEX Septal Occluder	W.L. Gore & Associates	Aug 2006 (discontinued)	Percutaneous, transcatheter closure of ostium secundum ASDs
GORE CARDIOFORM Septal Occluder	W.L. Gore & Associates	Mar 2018 (supplement)	PFO closure to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke

PMA: premarket approval. FDA product code: MLV.

ATRIAL SEPTAL DEFECT CLOSURE DEVICES

The FDA has approved three devices for ASD closure through the premarket approval process or a premarket approval supplement: the Amplatzer Septal Occluder, the GORE HELEX Septal Occluder (discontinued), and the GORE CARDIOFORM Septal Occluder (see Table 2). FDA product code: MLV.

Table 2. Atrial Septal Defect Closure Devices Approved by the U.S. Food and Drug Administration

Device	Manufacturer	PMA Approval Date	Indications
Amplatzer™ Septal Occluder	St. Jude Medical (Abbot Medical)	Dec 2001	<ul style="list-style-type: none"> • Occlusion of ASDs in the secundum position • Use in patients who have had a fenestrated Fontan procedure who require closure of the fenestration • Patients indicated for ASD closure have echocardiographic evidence of ostium secundum ASD and clini-

Device	Manufacturer	PMA Approval Date	Indications
GORE HELEX Septal Occluder	W.L. Gore & Associates	Aug 2006 (discontinued)	cal evidence of right ventricular volume overload. • Percutaneous, transcatheter closure of ostium secundum ASDs
GORE CARDIOFORM ASD Occluder (formerly GORE CARDIOFORM Septal Occluder)	W.L. Gore & Associates	May 2019 (supplement; name change) Oct 2016 (supplement)	• Percutaneous, transcatheter closure of ostium secundum ASDs

ASD: atrial septal defect; PMA: premarket approval.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Messe SR, Kasner SE. Is closure recommended for patent foramen ovale and cryptogenic stroke? Patent foramen ovale in cryptogenic stroke: not to close. *Circulation*. Nov 04 2008;118(19):1999-2004. PMID 18981314
2. Slottow TL, Steinberg DH, Waksman R. Overview of the 2007 Food and Drug Administration Circulatory System Devices Panel meeting on patent foramen ovale closure devices. *Circulation*. Aug 07 2007;116(6):677-82. PMID 17679629
3. U.S. Food and Drug Administration. Summary of safety and effectiveness data. Gore Cardioform Septal Occluder. March 30, 2018. https://www.accessdata.fda.gov/cdrh_docs/pdf5/P050006s060b.pdf. Accessed March 19, 2020.
4. Food and Drug Administration (FDA). Summary of Safety and Effectiveness Data (SSED): Patent Foramen Ovale (PFO) Occluder (PMA P120021). 2016; https://www.accessdata.fda.gov/cdrh_docs/pdf12/P120021B.pdf. Accessed March 19, 2020.
5. Meier B, Kalesan B, Mattle HP, et al. Percutaneous closure of patent foramen ovale in cryptogenic embolism. *N Engl J Med*. Mar 21 2013;368(12):1083-91. PMID 23514285
6. Carroll JD, Saver JL, Thaler DE, et al. Closure of patent foramen ovale versus medical therapy after cryptogenic stroke. *N Engl J Med*. Mar 21 2013;368(12):1092-100. PMID 23514286
7. Saver JL, Carroll JD, Thaler DE, et al. Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke. *N Engl J Med*. Sep 14 2017;377(11):1022-1032. PMID 28902590
8. Rogers T, Slack M, Waksman R. Overview of the 2016 US Food and Drug Administration Circulatory System Devices Panel Meeting on the Amplatzer Patent Foramen Ovale Occluder. *Am J Cardiol*. Jan 01 2017;119(1):153-155. PMID 27810099

9. Lee PH, Song JK, Kim JS, et al. Cryptogenic Stroke and High-Risk Patent Foramen Ovale: The DEFENSE-PFO Trial. *J Am Coll Cardiol*. May 22 2018;71(20):2335-2342. PMID 29544871
10. Sondergaard L, Kasner SE, Rhodes JF, et al. Patent Foramen Ovale Closure or Antiplatelet Therapy for Cryptogenic Stroke. *N Engl J Med*. Sep 14 2017;377(11):1033-1042. PMID 28902580
11. Mas JL, Derumeaux G, Guillon B, et al. Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke. *N Engl J Med*. Sep 14 2017;377(11):1011-1021. PMID 28902593
12. Kent DM, Dahabreh IJ, Ruthazer R, et al. Device Closure of Patent Foramen Ovale After Stroke: Pooled Analysis of Completed Randomized Trials. *J Am Coll Cardiol*. Mar 01 2016;67(8):907-17. PMID 26916479
13. Li J, Liu J, Liu M, et al. Closure versus medical therapy for preventing recurrent stroke in patients with patent foramen ovale and a history of cryptogenic stroke or transient ischemic attack. *Cochrane Database Syst Rev*. Sep 08 2015;(9):CD009938. PMID 26346232
14. Shah R, Nayyar M, Jovin IS, et al. Device Closure Versus Medical Therapy Alone for Patent Foramen Ovale in Patients With Cryptogenic Stroke: A Systematic Review and Meta-analysis. *Ann Intern Med*. Mar 06 2018;168(5):335-342. PMID 29310136
15. De Rosa S, Sievert H, Sabatino J, et al. Percutaneous Closure Versus Medical Treatment in Stroke Patients With Patent Foramen Ovale: A Systematic Review and Meta-analysis. *Ann Intern Med*. Mar 06 2018;168(5):343-350. PMID 29310133
16. Alushi B, Lauten A, Cassese S, et al. Patent foramen ovale closure versus medical therapy for prevention of recurrent cryptogenic embolism: updated meta-analysis of randomized clinical trials. *Clin Res Cardiol*. Sep 2018;107(9):788-798. PMID 29644412
17. Rigatelli G, Pedon L, Zecchel R, et al. Long-Term Outcomes and Complications of Intracardiac Echocardiography-Assisted Patent Foramen Ovale Closure in 1,000 Consecutive Patients. *J Interv Cardiol*. Oct 2016;29(5):530-538. PMID 27500752
18. Wintzer-Wehekind J, Alperi A, Houde C, et al. Long-Term Follow-Up After Closure of Patent Foramen Ovale in Patients With Cryptogenic Embolism. *J Am Coll Cardiol*. Jan 29 2019;73(3):278-287. PMID 30678757
19. Dowson A, Mullen MJ, Peatfield R, et al. 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*. Mar 18 2008;117(11):1397-404. PMID 18316488
20. Mattle HP, Evers S, Hildick-Smith D, et al. Percutaneous closure of patent foramen ovale in migraine with aura, a randomized controlled trial. *Eur Heart J*. Jul 07 2016;37(26):2029-36. PMID 26908949
21. Tobis JM, Charles A, Silberstein SD, et al. Percutaneous Closure of Patent Foramen Ovale in Patients With Migraine: The PREMIUM Trial. *J Am Coll Cardiol*. Dec 05 2017;70(22):2766-2774. PMID 29191325
22. Lip PZ, Lip GY. Patent foramen ovale and migraine attacks: a systematic review. *Am J Med*. May 2014;127(5):411-20. PMID 24355354
23. Biasco L, Infantino V, Orzan F, et al. Impact of transcatheter closure of patent foramen ovale in the evolution of migraine and role of residual shunt. *J Cardiol*. Nov 2014;64(5):390-4. PMID 24713153
24. Snijder RJ, Luermans JG, de Heij AH, et al. Patent Foramen Ovale With Atrial Septal Aneurysm Is Strongly Associated With Migraine With Aura: A Large Observational Study. *J Am Heart Assoc*. Dec 01 2016;5(12). PMID 27930349
25. Tobis J, Shenoda M. Percutaneous treatment of patent foramen ovale and atrial septal defects. *J Am Coll Cardiol*. Oct 30 2012;60(18):1722-32. PMID 23040567
26. Mojadidi MK, Gevorgyan R, Nouredin N, et al. The effect of patent foramen ovale closure in patients with platypnea-orthodeoxia syndrome. *Catheter Cardiovasc Interv*. Oct 2015;86(4):701-7. PMID 26063336
27. Du ZD, Hijazi ZM, Kleinman CS, et al. Comparison between transcatheter and surgical closure of secundum atrial septal defect in children and adults: results of a multicenter nonrandomized trial. *J Am Coll Cardiol*. Jun 05 2002;39(11):1836-44. PMID 12039500

28. Butera G, Biondi-Zoccai G, Sangiorgi G, et al. Percutaneous versus surgical closure of secundum atrial septal defects: a systematic review and meta-analysis of currently available clinical evidence. *EuroIntervention*. Jul 2011;7(3):377-85. PMID 21729841
29. Abaci A, Unlu S, Alsancak Y, et al. Short and long term complications of device closure of atrial septal defect and patent foramen ovale: meta-analysis of 28,142 patients from 203 studies. *Catheter Cardiovasc Interv*. Dec 01 2013;82(7):1123-38. PMID 23412921
30. Suchon E, Pieculewicz M, Tracz W, et al. Transcatheter closure as an alternative and equivalent method to the surgical treatment of atrial septal defect in adults: comparison of early and late results. *Med Sci Monit*. Dec 2009;15(12):CR612-7. PMID 19946231
31. Berger F, Vogel M, Alexi-Meskishvili V, et al. Comparison of results and complications of surgical and Amplatzer device closure of atrial septal defects. *J Thorac Cardiovasc Surg*. Oct 1999;118(4):674-8; discussion 678-80. PMID 10504632
32. Kotowycz MA, Therrien J, Ionescu-Iltu R, et al. Long-term outcomes after surgical versus transcatheter closure of atrial septal defects in adults. *JACC Cardiovasc Interv*. May 2013;6(5):497-503. PMID 23602461
33. Chen TH, Hsiao YC, Cheng CC, et al. In-Hospital and 4-Year Clinical Outcomes Following Transcatheter Versus Surgical Closure for Secundum Atrial Septal Defect in Adults: A National Cohort Propensity Score Analysis. *Medicine (Baltimore)*. Sep 2015;94(38):e1524. PMID 26402807
34. Xu XD, Liu SX, Zhao XX, et al. Comparison of medium-term results of transcatheter correction versus surgical treatment for secundum type atrial septal defect combined with pulmonary valve stenosis. *Int Heart J*. 2014; 55(4):326-30. PMID 24898601
35. Fischer G, Stieh J, Uebing A, et al. Experience with transcatheter closure of secundum atrial septal defects using the Amplatzer septal occluder: a single centre study in 236 consecutive patients. *Heart*. Feb 2003; 89(2):199-204. PMID 12527678
36. Javois AJ, Rome JJ, Jones TK, et al. Results of the U.S. Food and Drug Administration continued access clinical trial of the GORE HELEX septal occluder for secundum atrial septal defect. *JACC Cardiovasc Interv*. Aug 2014; 7(8):905-12. PMID 25147036
37. Baruteau AE, Petit J, Lambert V, et al. Transcatheter closure of large atrial septal defects: feasibility and safety in a large adult and pediatric population. *Circ Cardiovasc Interv*. Dec 2014;7(6):837-43. PMID 25423959
38. Du ZD, Koenig P, Cao QL, et al. Comparison of transcatheter closure of secundum atrial septal defect using the Amplatzer septal occluder associated with deficient versus sufficient rims. *Am J Cardiol*. Oct 15 2002; 90(8):865-9. PMID 12372575
39. Oho S, Ishizawa A, Akagi T, et al. Transcatheter closure of atrial septal defects with the Amplatzer septal occluder--a Japanese clinical trial. *Circ J*. Sep 2002;66(9):791-4. PMID 12224813
40. Brochu MC, Baril JF, Dore A, et al. Improvement in exercise capacity in asymptomatic and mildly symptomatic adults after atrial septal defect percutaneous closure. *Circulation*. Oct 01 2002;106(14):1821-6. PMID 12356636
41. Furlan AJ, Reisman M, Massaro J, et al. Closure or medical therapy for cryptogenic stroke with patent foramen ovale. *N Engl J Med*. Mar 15 2012;366(11):991-9. PMID 22417252
42. Grohmann J, Hohn R, Fleck T, et al. Transcatheter closure of atrial septal defects in children and adolescents: single-center experience with the GORE(R) septal occluder. *Catheter Cardiovasc Interv*. Nov 15 2014;84(6): E51-7. PMID 24664494
43. Nyboe C, Hjortdal VE, Nielsen-Kudsk JE. First experiences with the GORE((R)) Septal Occluder in children and adults with atrial septal defects. *Catheter Cardiovasc Interv*. Nov 15 2013;82(6):929-34. PMID 23404677
44. Yilmazer MM, Guven B, Vupa-Cilengiroglu O, et al. Improvement in cardiac structure and functions early after transcatheter closure of secundum atrial septal defect in children and adolescents. *Turk J Pediatr*. Jul-Aug 2013;55(4):401-10. PMID 24292034

45. Jalal Z, Hascoet S, Gronier C, et al. Long-Term Outcomes After Percutaneous Closure of Ostium Secundum Atrial Septal Defect in the Young: A Nationwide Cohort Study. *JACC Cardiovasc Interv.* Apr 23 2018;11(8):795-804. PMID 29673513
46. Lansberg MG, O'Donnell MJ, Khatri P, et al. Antithrombotic and thrombolytic therapy for ischemic stroke: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* Feb 2012;141(2 Suppl): e601S-e636S. PMID 22315273
47. Messe SR, Gronseth G, Kent DM, et al. Practice advisory: Recurrent stroke with patent foramen ovale (update of practice parameter): Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology.* Aug 23 2016;87(8):815-21. PMID 27466464
48. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* Jul 2014;45(7):2160-236. PMID 24788967
49. Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* Apr 02 2019;73(12):e81-e192. PMID 30121239