Protocol

Closure Devices for Patent Foramen Ovale and Atrial Septal Defects

(20209)

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

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 PFO 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	Interventions of interest are: • Atrial septal defect closure with a transcatheter device	Comparators of interest are: • Surgical ASD 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. 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. 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 migraine. 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 three randomized controlled trials (RCTs) comparing device-based PFO closure with medical therapy, multiple nonrandomized comparative studies, and multiple systematic reviews and meta-analyses of these studies. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity and mortality. None of the three trials reported statistically significant improvements on their main outcomes using intention-to-treat analysis. In all three trials, low numbers of outcome events in both groups limited the power to detect differences between groups. One trial showed a significant benefit for the closure group on per protocol analysis and another showed significant benefit on secondary outcomes. Meta-analyses of these trials have also come to different conclusions, with some reporting statistically significant reductions in recurrent events on pooled analysis and others reporting a trend for benefit that was not statistically significant. A high-quality meta-analysis reported a significantly lower risk of recurrent ischemic stroke with device therapy, but a higher risk of atrial fibrillation. While these results suggest that a benefit might be present, the evidence is not definitive and the risk-benefit ratio of transcatheter PFO closure as an alternative to medical therapy is not well-defined. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have PFO and migraines who receive PFO closure with a transcatheter device, the evidence includes two 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 end point evaluation did not demonstrate improvements in migraine days after PFO closure, but likely it was underpowered. Nonrandomized studies have shown highly variable rates of migraine improvement 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 over-load 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 transcatheter 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

Closure of patent foramen ovale using a transcatheter approach is considered **investigational**.

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.

Policy Guidelines

Three devices have been approved by the FDA for ASD closure: the Amplatzer™ Septal Occluder, the GORE HELEX Septal Occluder (discontinued), and the GORE CARDIOFORM Septal Occluder.

The labeled indications for these devices are similar and include:

- Patients with echocardiographic evidence of ostium secundum atrial septal defect; AND
- Clinical evidence of right ventricular volume overload (i.e., 1.5:1 degree of left-to-right shunt or right ventricular enlargement).

Generally recognized indications for closure include a pulmonary-to-systemic flow ratio of greater than 1.5, right atrial and right ventricular enlargement, and paradoxical embolism.

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 a 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 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. There has been interest in open surgery and transcatheter approaches to close the PFO in patients with a history of cryptogenic stroke to prevent recurrent stroke.

Atrial Septal Defects

Unlike PFO, which represents the postnatal persistence of normal fetal cardiovascular physiology, 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 tricus-pid 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

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 device so that smaller catheters can be used, developing techniques to properly center the device 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

Several devices have been developed to treat PFO and ASDs via a transcatheter approach, including the CardioSEAL® STARFlex™ Septal Occlusion System, the Amplatzer® PFO Occluder, the Figulla® ASD Occluder (Occlutech GmbH, Jena, Germany), and the CeraFlex™ ASD Occluder (Lifetech Scientific, Shenzhen, China).

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

Regulatory Status

Patent Foramen Ovale Closure Devices

In 2002, two transcatheter devices were cleared for marketing by the FDA through a humanitarian device exemption (HDE) 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, St. Paul, MN). HDE approval is applicable to devices designed to treat a patient population of fewer than 4000 patients per year. This approval process requires the manufacturer to submit data on the safety and the probable clinical benefit. Clinical trials validating the device effectiveness are not required. The labeled indications of both limited the use of these devices to closure of PFO in patients with recurrent crypto-genic stroke due to presumed paradoxical embolism through a PFO and who have failed conventional drug therapy.

Following this limited FDA approval, use of PFO closure devices increased by more than 50-fold, well in excess of the 4000 per year threshold intended under the HDE.[2] As a result, in 2006, FDA withdrew the HDE approval for these devices.

In November 2016, the Amplatzer® PFO Occluder was approved by the FDA through the premarket approval (PMA) process for the following indication[3]:

> "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 crypto-

genic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke."

The PMA was based on analysis of the RESPECT trial, initial results of which were published in 2013.

FDA product code: MLV.

Atrial Septal Defect Closure Devices

Three devices have been approved by the FDA through the PMA process or a PMA supplement for transcatheter atrial septal defect closure (see Table 1).

Table 1. ASD Closure Devices Approved by the Food and Drug Administration

Device	Manufacturer	PMA Approval Date	Indications
Amplatzer™ Septal Occluder	St. Jude Medical (Plymouth, MN)	Dec 2001	• 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 clinical evidence of right ventricular volume overload.)
GORE HELEX Septal Occluder[a]	W.L. Gore & Associates (Flagstaff, AZ)	Aug 2006	• Percutaneous, transcatheter closure of ostium secundum ASDs
GORE CARDIOFORM Septal Occluder	W.L. Gore & Associates (Flagstaff, AZ)	Oct 2016 (supp.)	• Percutaneous, transcatheter closure of ostium secundum ASDs

ASD: atrial septal defect; PMA: premarket approval.
[a] Discontinued.

FDA product code: MLV.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment 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 4 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 7 2007; 116(6):677-682. PMID 17679629

3. Food and Drug Administration (FDA). PMA P120021: FDA Summary of Safety and Effectiveness Data. 2016; https://www.accessdata.fda.gov/cdrh_docs/pdf12/P120021B.pdf. Accessed April 30, 2017.
4. 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):991-999. PMID 22417252
5. 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):1092-1100. PMID 23514286
6. 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
7. Food and Drug Administration (FDA). FDA Executive Summary: P120021 AMPLATZER Patent Foramen Ovale (PFO) Occluder. 2016; https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM502193.pdf. Accessed April 30, 2017.
8. 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):1083-1091. PMID 23514285
9. 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):907-917. PMID 26916479
10. 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
11. Rengifo-Moreno P, Palacios IF, Junpaparp P, et al. Patent foramen ovale transcatheter closure vs. medical therapy on recurrent vascular events: a systematic review and meta-analysis of randomized controlled trials. Eur Heart J. Jul 19 2013. PMID 23847132
12. Kitsios GD, Thaler DE, Kent DM. Potentially large yet uncertain benefits: a meta-analysis of patent foramen ovale closure trials. Stroke. Sep 2013; 44(9):2640-2643. PMID 23868270
13. Chen L, Luo S, Yan L, et al. A systematic review of closure versus medical therapy for preventing recurrent stroke in patients with patent foramen ovale and cryptogenic stroke or transient ischemic attack. J Neurol Sci. Feb 15 2014; 337(1-2):3-7. PMID 24300230
14. Hakeem A, Marmagkiolis K, Hacioglu Y, et al. Safety and efficacy of device closure for patent foramen ovale for secondary prevention of neurological events: Comprehensive systematic review and meta-analysis of randomized controlled trials. Cardiovasc Revasc Med. Nov-Dec 2013; 14(6):349-355. PMID 24080379
15. Khan AR, Bin Abdulhak AA, Sheikh MA, et al. Device closure of patent foramen ovale versus medical therapy in cryptogenic stroke: a systematic review and meta-analysis. JACC Cardiovasc Interv. Dec 2013; 6(12):1316-1323. PMID 24139929
16. Kwong JS, Lam YY, Yu CM. Percutaneous closure of patent foramen ovale for cryptogenic stroke: a meta-analysis of randomized controlled trials. Int J Cardiol. Oct 9 2013; 168(4):4132-4138. PMID 23890879
17. Nagaraja V, Raval J, Eslick GD, et al. Is transcatheter closure better than medical therapy for cryptogenic stroke with patent foramen ovale? A meta-analysis of randomised trials. Heart Lung Circ. Nov 2013; 22(11):903-909. PMID 24035325
18. Ntaios G, Papavasileiou V, Makaritsis K, et al. PFO closure vs. medical therapy in cryptogenic stroke or transient ischemic attack: a systematic review and meta-analysis. Int J Cardiol. Oct 30 2013; 169(2):101-105. PMID 24041984
19. Pandit A, Aryal MR, Pandit AA, et al. Amplatzer PFO occluder device may prevent recurrent stroke in patients with patent foramen ovale and cryptogenic stroke: a meta-analysis of randomised trials. Heart Lung Circ. Apr 2014; 23(4):303-308. PMID 24495944
20. Pineda AM, Nascimento FO, Yang SC, et al. A meta-analysis of transcatheter closure of patent foramen ovale versus medical therapy for prevention of recurrent thromboembolic events in patients with cryptogenic cerebrovascular events. Catheter Cardiovasc Interv. Nov 15 2013; 82(6):968-975. PMID 23832613

21. Udell JA, Opotowsky AR, Khairy P, et al. Patent foramen ovale closure vs. medical therapy for stroke prevention: meta-analysis of randomized trials and review of heterogeneity in meta-analyses. Can J Cardiol. Oct 2014; 30(10):1216-1224. PMID 25154803
22. Wolfrum M, Froehlich GM, Knapp G, et al. Stroke prevention by percutaneous closure of patent foramen ovale: a systematic review and meta-analysis. Heart. Mar 2014; 100(5):389-395. PMID 23793373
23. Pickett CA, Villines TC, Ferguson MA, et al. Percutaneous closure versus medical therapy alone for cryptogenic stroke patients with a patent foramen ovale: meta-analysis of randomized controlled trials. Tex Heart Inst J. Aug 2014; 41(4):357-367. PMID 25120387
24. Stortecky S, da Costa BR, Mattle HP, et al. Percutaneous closure of patent foramen ovale in patients with cryptogenic embolism: a network meta-analysis. Eur Heart J. Jan 7 2015; 36(2):120-128. PMID 25112661
25. Patti G, Pelliccia F, Gaudio C, et al. Meta-analysis of net long-term benefit of different therapeutic strategies in patients with cryptogenic stroke and patent foramen ovale. Am J Cardiol. Mar 15 2015; 115(6):837-843. PMID 25620037
26. Capodanno D, Milazzo G, Vitale L, et al. Updating the evidence on patent foramen ovale closure versus medical therapy in patients with cryptogenic stroke: a systematic review and comprehensive meta-analysis of 2,303 patients from three randomised trials and 2,231 patients from 11 observational studies. EuroIntervention. Mar 20 2014; 9(11):1342-1349. PMID 24240356
27. Khairy P, O'Donnell CP, Landzberg MJ. Transcatheter closure versus medical therapy of patent foramen ovale and presumed paradoxical thromboemboli: a systematic review. Ann Intern Med. Nov 4 2003; 139(9):753-760. PMID 14597460
28. Kitsios GD, Dahabreh IJ, Abu Dabrh AM, et al. Patent foramen ovale closure and medical treatments for secondary stroke prevention: a systematic review of observational and randomized evidence. Stroke. Feb 2012; 43(2):422-431. PMID 22180252
29. Wohrle J. Closure of patent foramen ovale after cryptogenic stroke. Lancet. Jul 29 2006; 368(9533):350-352. PMID 16876648
30. 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 1 2013; 82(7):1123-1138. PMID 23412921
31. Pezzini A, Grassi M, Lodigiani C, et al. Propensity score-based analysis of percutaneous closure versus medical therapy in patients with cryptogenic stroke and patent foramen ovale: The IPSYS Registry (Italian Project on Stroke in Young Adults). Circ Cardiovasc Interv. Sep 2016; 9(9). PMID 27582111
32. Alushi B, Biasco L, Orzan F, et al. Patent foramen ovale treatment strategy: an Italian large prospective study. J Cardiovasc Med (Hagerstown). Oct 2014; 15(10):761-768. PMID 24978876
33. Wahl A, Juni P, Mono ML, et al. Long-term propensity score-matched comparison of percutaneous closure of patent foramen ovale with medical treatment after paradoxical embolism. Circulation. Feb 14 2012; 125(6):803-812. PMID 22238228
34. Windecker S, Wahl A, Nedeltchev K, et al. Comparison of medical treatment with percutaneous closure of patent foramen ovale in patients with cryptogenic stroke. J Am Coll Cardiol. Aug 18 2004; 44(4):750-758. PMID 15312853
35. Harrer JU, Wessels T, Franke A, et al. Stroke recurrence and its prevention in patients with patent foramen ovale. Can J Neurol Sci. Feb 2006; 33(1):39-47. PMID 16583720
36. Paciaroni M, Agnelli G, Bertolini A, et al. Risk of recurrent cerebrovascular events in patients with cryptogenic stroke or transient ischemic attack and patent foramen ovale: the FORI (Foramen Ovale Registro Italiano) study. Cerebrovasc Dis. 2011; 31(2):109-116. PMID 21088390
37. Cifarelli A, Musto C, Parma A, et al. Long-term outcome of transcatheter patent foramen ovale closure in patients with paradoxical embolism. Int J Cardiol. Jun 11 2010; 141(3):304-310. PMID 19178959
38. Onorato E, Melzi G, Casilli F, et al. Patent foramen ovale with paradoxical embolism: mid-term results of transcatheter closure in 256 patients. J Interv Cardiol. Feb 2003; 16(1):43-50. PMID 12664817

39. Martin F, Sanchez PL, Doherty E, et al. Percutaneous transcatheter closure of patent foramen ovale in patients with paradoxical embolism. Circulation. Aug 27 2002; 106(9):1121-1126. PMID 12196339
40. Windecker S, Wahl A, Chatterjee T, et al. Percutaneous closure of patent foramen ovale in patients with paradoxical embolism: long-term risk of recurrent thromboembolic events. Circulation. Feb 29 2000; 101(8):893-898. PMID 10694529
41. Butera G, Saracino A, Danna P, et al. Transcatheter PFO closure with GORE((R)) septal occluder: early and mid-term clinical results. Catheter Cardiovasc Interv. Nov 15 2013; 82(6):944-949. PMID 23897659
42. Eeckhout E, Martin S, Delabays A, et al. Very long-term follow-up after percutaneous closure of patent foramen ovale. EuroIntervention. Apr 2015; 10(12):1474-1479. PMID 24429213
43. Inglessis I, Elmariah S, Rengifo-Moreno PA, et al. Long-term experience and outcomes with transcatheter closure of patent foramen ovale. JACC Cardiovasc Interv. Nov 2013; 6(11):1176-1183. PMID 24262618
44. Nagpal SV, Lerakis S, Flueckiger PB, et al. Long-term outcomes after percutaneous patent foramen ovale closure. Am J Med Sci. Sep 2013; 346(3):181-186. PMID 23328836
45. Rhodes JF, Jr., Goble J. Combined prospective United States clinical study data for the GORE((R)) HELEX((R)) septal occluder device. Catheter Cardiovasc Interv. May 1, 2014; 83(6):944-952. PMID 23674380
46. Thomson JD, Hildick-Smith D, Clift P, et al. Patent foramen ovale closure with the gore septal occluder: initial UK experience. Catheter Cardiovasc Interv. Feb 15 2014; 83(3):467-473. PMID 23766247
47. Wallenborn J, Bertog SC, Franke J, et al. Recurrent events after percutaneous closure of patent foramen ovale. Catheter Cardiovasc Interv. Oct 1 2013; 82(4):541-546. PMID 22707325
48. Neuser J, Akin M, Bavendiek U, et al. Mid-term results of interventional closure of patent foramen ovale with the Occlutech Figulla(R) Flex II Occluder. BMC Cardiovasc Disord. Nov 10 2016; 16(1):217. PMID 27832757
49. 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
50. 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):1397-1404. PMID 18316488
51. 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):2029-2036. PMID 26908949
52. Late-Breaking Abstracts: 57th Annual Scientific Meeting of the American Headache Society. Headache. 2015; 55:249-265.
53. Lip PZ, Lip GY. Patent foramen ovale and migraine attacks: a systematic review. Am J Med. May 2014; 127(5):411-420. PMID 24355354
54. 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):390-394. PMID 24713153
55. 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
56. Tobis J, Shenoda M. Percutaneous treatment of patent foramen ovale and atrial septal defects. J Am Coll Cardiol. Oct 30 2012; 60(18):1722-1732. PMID 23040567
57. Mojadidi MK, Gevorgyan R, Noureddin N, et al. The effect of patent foramen ovale closure in patients with platypnea-orthodeoxia syndrome. Catheter Cardiovasc Interv. Oct 2015; 86(4):701-707. PMID 26063336
58. Instruction for Use: Amplatzer® Septal Occluder System. In: AGA Medical Corporation; Golden Valley M, ed.
59. 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 5 2002; 39(11):1836-1844. PMID 12039500

60. 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):377-385. PMID 21729841
61. 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):CR612-617. PMID 19946231
62. 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):674-678; discussion 678-680. PMID 10504632
63. Kotowycz MA, Therrien J, Ionescu-Ittu 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
64. 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
65. 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. Jul 10 2014; 55(4):326-330. PMID 24898601
66. 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
67. 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):905-912. PMID 25147036
68. 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):837-843. PMID 25423959
69. 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):865-869. PMID 12372575
70. 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):791-794. PMID 12224813
71. 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 1 2002; 106(14):1821-1826. PMID 12356636
72. 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):E51-57. PMID 24664494
73. 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):929-934. PMID 23404677
74. 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):401-410. PMID 24292034
75. 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-636S. PMID 22315273
76. 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):815-821. PMID 27466464

77. 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):2160-2236. PMID 24788967
78. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to develop guidelines on the management of adults with congenital heart disease). Circulation. Dec 2 2008; 118(23):e714-833. PMID 18997169