



RECOMENDACIÓN T3

BÚSQUEDA Y SÍNTESIS DE EVIDENCIA DE EFECTOS DESEABLES E INDESEABLES

Guía de Práctica Clínica Ataque cerebrovascular - 2018

A. PREGUNTA CLÍNICA

En personas mayores de 15 años con ataque cerebrovascular (ACV) isquémico aguda ¿Se debe realizar cierre del foramen oval permeable MÁS tratamiento antitrombótico en comparación a realizar sólo tratamiento antitrombótico?

Análisis y definición de los componentes de la pregunta en formato PICO

Población: Personas mayores de 15 años con ataque cerebrovascular (ACV) isquémico aguda.

Intervención: Realizar cierre del foramen oval permeable MÁS tratamiento antitrombótico.

Comparación: Realizar sólo tratamiento antitrombótico.

Desenlace (outcome): Accidente cerebrovascular, fibrilación o flutter auricular, sangrado mayor.

B. BÚSQUEDA DE EVIDENCIA

Se realizó una búsqueda general de revisiones sistemáticas asociadas al tema de "Stroke". Las bases de datos utilizadas fueron: Cochrane database of systematic reviews (CDSR); Database of Abstracts of Reviews of Effectiveness (DARE); HTA Database; PubMed; LILACS; CINAHL; PsycINFO; EMBASE; EPPI-Centre Evidence Library; 3ie Systematic Reviews and Policy Briefs Campbell Library; Clinical Evidence; SUPPORT Summaries; WHO institutional Repository for information Sharing; NICE public health guidelines and systematic reviews; ACP Journal Club; Evidencias en Pediatría; y The JBI Database of Systematic Reviews and implementation Reports. No se aplicaron restricciones en base al idioma o estado de publicación. Dos revisores de manera independiente realizaron la selección de los títulos y los resúmenes, la evaluación del texto completo y la extracción de datos. Un investigador experimentado resolvió cualquier discrepancia entre los distintos revisores. En caso de considerarse necesario, se integraron estudios primarios.¹

Seleccionadas las revisiones sistemáticas o estudios primarios asociadas a la temática, se clasificaron en función de las potenciales preguntas a las que daban respuesta. Al momento de definir la pregunta la evidencia ya se encontraba previamente clasificada según intervenciones comparadas. Los resultados se encuentran alojados en la plataforma Living Overview of the Evidence (L-OVE), sistema que permite la actualización periódica de la evidencia.

¹ Para revisar la metodología, las estrategias y los resultados de la búsqueda, favor revisar el informe "*Búsqueda sistemática de evidencia de los efectos deseables e indeseables*" en la sección de método de la Guía de Práctica Clínica respectiva.

C. SÍNTESIS DE EVIDENCIA

Resumen de la evidencia identificada

Se identificaron 47 revisiones sistemáticas que incluyen 88 estudios primarios, de los cuales 8 corresponden a ensayos aleatorizados. Para más detalle ver “*Matriz de evidencia*²”, en el siguiente enlace: [Cierre de foramen oval en accidente cerebrovascular](#).

Tabla 1: Resumen de la evidencia seleccionada

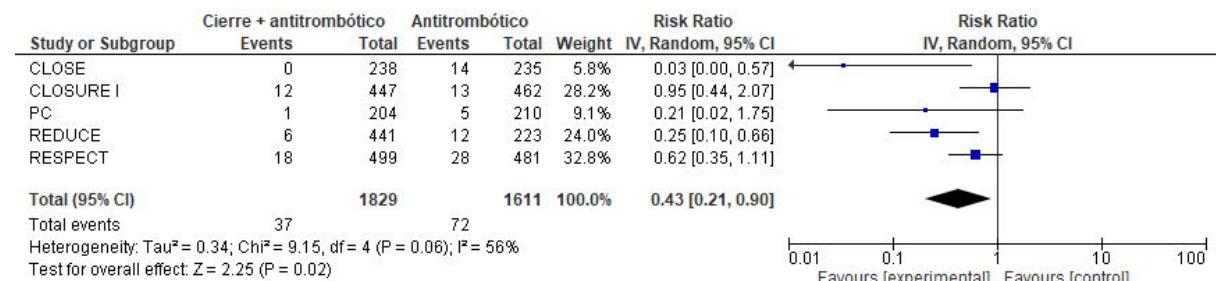
Revisión Sistemática	47 [1-47]
Estudios primarios	8 ensayos aleatorizados [48-54], 80 observacionales [57-134]

Estimador del efecto

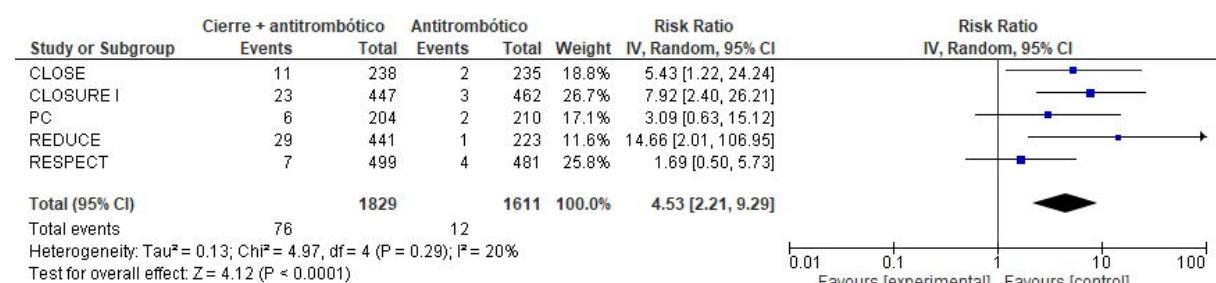
Se realizó un análisis de la matriz de evidencia, decidiendo excluir un ensayo [49] ya que no compara cierre versus no cierre, sino diferentes dispositivos. Se incluyeron 5 ensayos aleatorizados [48, 50-54]. Los estudios observacionales no aumentaban la certeza de la evidencia ni entregaban información adicional. Se identificó una revisión sistemática [22] que incluye todos los ensayos relevantes, por lo que se decidió reutilizar sus metanálisis para construir la tabla de resumen de resultados.

Metanálisis

Accidente cerebrovascular



Fibrilación o flutter auricular



² **Matriz de Evidencia**, tabla dinámica que grafica el conjunto de evidencia existente para una pregunta (en este caso, la pregunta del presente informe). Las filas representan las revisiones sistemáticas y las columnas los estudios primarios que estas revisiones han identificado. Los recuadros en verde corresponden a los estudios incluidos en cada revisión. La matriz se actualiza periódicamente, incorporando nuevas revisiones sistemáticas pertinentes y los respectivos estudios primarios.

Sangrado mayor

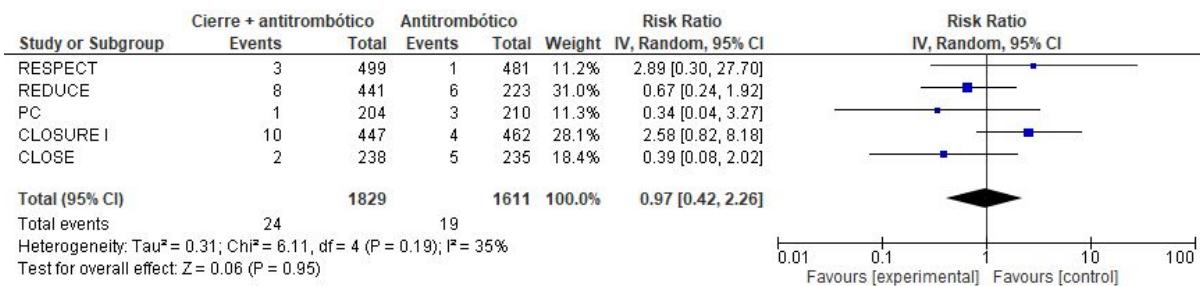


Tabla de Resumen de Resultados (Summary of Findings)

CIERRE DEL FORAMEN OVAL PERMEABLE PARA ATAQUE CEREBROVASCULAR ISQUÉMICO AGUDO						
Población	Personas mayores de 15 años con ataque cerebrovascular (ACV) isquémico agudo.					
Intervención	Realizar cierre del foramen oval permeable más tratamiento antitrombótico.					
Comparación	Realizar sólo tratamiento antitrombótico.					
Desenlaces	Efecto relativo (IC 95%)	Efecto absoluto estimado*			Certeza de la evidencia (GRADE)	Mensajes clave en términos sencillos
	-- Estudios/ pacientes	antitrombóticos	Cierre + antitrombóticos	Diferencia (IC 95%)		
Accidente cerebrovascular	RR 0,43 (0,21 a 0,90) -- 5 ensayos / 3340 pacientes [50-54]	45 por 1000	19 por 1000	Diferencia: 26 menos (4 a 35 menos)	⊕⊕○○ ^{1,2} Baja	Realizar cierre del foramen oval permeable más tratamiento antitrombótico comparado con sólo tratamiento antitrombótico podría disminuir el riesgo de accidente cerebrovascular, pero la certeza de la evidencia es baja.
Fibrilación o flutter auricular	RR 4,53 (2,21 a 9,29) -- 5 ensayos / 3340 pacientes [50-54]	7 por 1000	34 por 1000	Diferencia: 27 más (9 a 62 más)	⊕⊕⊕ ¹ Alta	Realizar cierre del foramen oval permeable más tratamiento antitrombótico comparado con sólo tratamiento antitrombótico aumenta el riesgo de fibrilación o flutter auricular.
Sangrado mayor	RR 0,97 (0,42 a 2,26) -- 5 ensayos / 3440 pacientes [50-54]	12 por 1000	12 por 1000	Diferencia: 0 (7 menos a 15 más)	⊕⊕○○ ^{1,3} Baja	Realizar cierre del foramen oval permeable más tratamiento antitrombótico comparado con sólo tratamiento antitrombótico podría disminuir los sangrados mayores, pero la certeza de la evidencia es baja.

IC 95%: Intervalo de confianza del 95%.

RR: Riesgo relativo.

GRADE: Grados de evidencia Grading of Recommendations Assessment, Development and Evaluation.

* El **riesgo CON antitrombóticos** está basado en el riesgo del grupo control en los estudios. El **riesgo CON cierre + antitrombóticos**(y su intervalo de confianza) está calculado a partir del efecto relativo (y su intervalo de confianza).

¹ Se disminuyó un nivel de certeza de evidencia por riesgo de sesgo, ya que ningún ensayo fue ciego. No se disminuyó por este factor para el desenlace fibrilación auricular, ya que el sesgo probablemente reforzaría esta conclusión.

² Se disminuyó un nivel de certeza de evidencia por inconsistencia (I2 50%)

³ Se disminuyó un nivel de certeza de evidencia por imprecisión ya que cada extremo del intervalo de confianza conlleva una decisión diferente

Fecha de elaboración de la tabla: Octubre, 2018.

Referencias

1. Abdelaziz HK, Saad M, Abuomara HZ, Nairooz R, Pothineni NVK, Madmani ME, Roberts DH, Mahmud E. Long-term outcomes of patent foramen ovale closure or medical therapy after cryptogenic stroke: A meta-analysis of randomized trials. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions.* 2018;
2. Abo-Salem E, Chaitman B, Helmy T, Boakye EA, Alkhawam H, Lim M. Patent foramen ovale closure versus medical therapy in cases with cryptogenic stroke, meta-analysis of randomized controlled trials. *Journal of neurology.* 2018;265(3):1-8.
3. Agarwal S, Bajaj NS, Kumbhani DJ, Tuzcu EM, Kapadia SR. Meta-analysis of transcatheter closure versus medical therapy for patent foramen ovale in prevention of recurrent neurological events after presumed paradoxical embolism. *JACC. Cardiovascular interventions.* 2012;5(7):777-89.
4. Ahmad Y, Howard JP, Arnold A, Shin MS, Cook C, Petraco R, Demir O, Williams L, Iglesias JF, Sutaria N, Malik I, Davies J, Mayet J, Francis D, Sen S. Patent foramen ovale closure vs. medical therapy for cryptogenic stroke: a meta-analysis of randomized controlled trials. *European heart journal.* 2018;39(18):1638-1649.
5. Almekhlafi MA, Wilton SB, Rabi DM, Ghali WA, Lorenzetti DL, Hill MD. Recurrent cerebral ischemia in medically treated patent foramen ovale: a meta-analysis. *Neurology.* 2009;73(2):89-97.
6. Alushi B, Lauten A, Cassese S, Colleran R, Schüpke S, Rai H, Schunkert H, Meier B, Landmesser U, Kastrati A. Patent foramen ovale closure versus medical therapy for prevention of recurrent cryptogenic embolism: updated meta-analysis of randomized clinical trials. *Clinical research in cardiology : official journal of the German Cardiac Society.* 2018;107(9):788-798.
7. Anantha-Narayanan M., Anugula D., Das G.. Patent foramen ovale closure reduces recurrent stroke risk in cryptogenic stroke: A systematic review and metaanalysis of randomized controlled trials. *World Journal of Cardiology.* 2018;10(6):41-48.
8. Ando T, Holmes AA, Pahuja M, Javed A, Briassoulis A, Telila T, Takagi H, Schreiber T, Afonso L, Grines CL, Bangalore S. Meta-Analysis Comparing Patent Foramen Ovale Closure Versus Medical Therapy to Prevent Recurrent Cryptogenic Stroke. *The American journal of cardiology.* 2018;121(5):649-655.
9. Chen L, Luo S, Yan L, Zhao W. 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. *Journal of the neurological sciences.* 2014;337(1-2):3-7.
10. Chen X, Chen SD, Dong Y, Dong Q. Patent foramen ovale closure for patients with cryptogenic stroke: A systematic review and comprehensive meta-analysis of 5 randomized controlled trials and 14 observational studies. *CNS neuroscience & therapeutics.* 2018;24(10):853-862.
11. Darmoch F, Al-Khadra Y, Soud M, Fanari Z, Alraies MC. Transcatheter Closure of Patent Foramen Ovale versus Medical Therapy after Cryptogenic Stroke: A Meta-Analysis of Randomized Controlled Trials. *Cerebrovascular diseases (Basel, Switzerland).* 2018;45(3-4):162-169.
12. De Rosa S, Sievert H, Sabatino J, Polimeni A, Sorrentino S, Indolfi C. Percutaneous Closure Versus Medical Treatment in Stroke Patients With Patent Foramen Ovale: A Systematic Review and Meta-analysis. *Annals of internal medicine.* 2018;168(5):343-350.

13. Dentali F, Gianni M, Mumoli N, Cei M, Bertolini A, Guasti L, Ageno W. Efficacy and safety of patent foramen ovale closure in patients with a cryptogenic stroke: Systematic review and meta-analysis. *Thrombosis and haemostasis*. 2014;111(4):773-6.
14. Garcia Pena A.A., Rodriguez J.A.. Are many patent foramen ovale closure procedures being performed in Colombia? Patent foramen ovale, atrial septal aneurysm and the risk of recurring cryptogenic stroke. Systematic review of literature. *Revista Colombiana de Cardiología*. 2016;23(5):389-402.
15. Garg L, Haleem A, Varade S, Sivakumar K, Shah M, Patel B, Agarwal M, Agrawal S, Leary M, Kluck B. Patent Foramen Ovale Closure in the Setting of Cryptogenic Stroke: A Meta-Analysis of Five Randomized Trials. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2018;27(9):2484-2493.
16. Hakeem A, Marmagkiolis K, Hacioglu Y, Uretsky BF, Gundogdu B, Leesar M, Bailey SR, Cilingiroglu M. 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. *Cardiovascular revascularization medicine : including molecular interventions*. 2013;14(6):349-55.
17. Kent DM, Dahabreh IJ, Ruthazer R, Furlan AJ, Reisman M, Carroll JD, Saver JL, Smalling RW, Jüni P, Mattle HP, Meier B, Thaler DE. Device Closure of Patent Foramen Ovale After Stroke: Pooled Analysis of Completed Randomized Trials. *Journal of the American College of Cardiology*. 2016;67(8):907-17.
18. Khan AR, Bin Abdulhak AA, Sheikh MA, Khan S, Erwin PJ, Tleyjeh I, Khuder S, Eltahawy EA. Device closure of patent foramen ovale versus medical therapy in cryptogenic stroke: a systematic review and meta-analysis. *JACC. Cardiovascular interventions*. 2013;6(12):1316-23.
19. Kheiri B, Abdalla A, Osman M, Ahmed S, Hassan M, Bachuwa G. Patent foramen ovale closure versus medical therapy after cryptogenic stroke: An updated meta-analysis of all randomized clinical trials. *Cardiology journal*. 2018;
20. Kitsios GD, Dahabreh IJ, Abu Dabrh AM, Thaler DE, Kent DM. Patent foramen ovale closure and medical treatments for secondary stroke prevention: a systematic review of observational and randomized evidence. *Stroke; a journal of cerebral circulation*. 2012;43(2):422-31.
21. Kwong JS, Lam YY, Yu CM. Percutaneous closure of patent foramen ovale for cryptogenic stroke: a meta-analysis of randomized controlled trials. *International journal of cardiology*. 2013;168(4):4132-8.
22. Lattanzi S, Brigo F, Cagnetti C, Di Napoli M, Silvestrini M. Patent Foramen Ovale and Cryptogenic Stroke or Transient Ischemic Attack: To Close or Not to Close? A Systematic Review and Meta-Analysis. *Cerebrovascular diseases (Basel, Switzerland)*. 2018;45(5-6):193-203.
23. Li J, Liu J, Liu M, Zhang S, Hao Z, Zhang J, Zhang C. 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 of Systematic Reviews*. 2015;9(9):CD009938.
24. Nagaraja V, Raval J, Eslick GD, Burgess D, Denniss AR. Is Transcatheter Closure Better than Medical Therapy for Cryptogenic Stroke with Patent Foramen Ovale? A Meta-analysis of Randomised Trials. *Heart, lung & circulation*. 2013;22(11):903-9.

25. Ntaios G, Papavasileiou V, Makaritsis K, Michel P. PFO closure vs. medical therapy in cryptogenic stroke or transient ischemic attack: a systematic review and meta-analysis. *International journal of cardiology*. 2013;169(2):101-5.
26. Ntaios G, Papavasileiou V, Sagris D, Makaritsis K, Vemmos K, Steiner T, Michel P. Closure of Patent Foramen Ovale Versus Medical Therapy in Patients With Cryptogenic Stroke or Transient Ischemic Attack: Updated Systematic Review and Meta-Analysis. *Stroke*. 2018;49(2):412-418.
27. Palaiodimos L, Kokkinidis DG, Faillace RT, Foley TR, Dangas GD, Price MJ, Mastoris I. Percutaneous closure of patent foramen ovale vs. medical treatment for patients with history of cryptogenic stroke: A systematic review and meta-analysis of randomized controlled trials. *Cardiovascular revascularization medicine : including molecular interventions*. 2018;
28. Pandit A, Aryal MR, Pandit AA, Jalota L, Kantharajpur S, Hakim FA, Lee HR. 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 & circulation*. 2014;23(4):303-308.
29. Patti G, Pelliccia F, Gaudio C, Greco C. Meta-Analysis of Net Long-Term Benefit of Different Therapeutic Strategies in Patients With Cryptogenic Stroke and Patent Foramen Ovale. *The American journal of cardiology*. 2015;115:837-43.
30. Pickett CA, Villines TC, Ferguson MA, Hulten EA. Percutaneous closure versus medical therapy alone for cryptogenic stroke patients with a patent foramen ovale: meta-analysis of randomized controlled trials. *Texas Heart Institute journal / from the Texas Heart Institute of St. Luke's Episcopal Hospital, Texas Children's Hospital*. 2014;41(4):357-67.
31. Pineda AM, Nascimento FO, Yang SC, Kirtane AJ, Sommer RJ, Beohar N. 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. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2013;82(6):968-75.
32. Reinthaler M, Ozga AK, Sinning D, Curio J, Al-Hindwan HS, Bäckemo Johansson J, Jung F, Lendlein A, Rauch G, Landmesser U. Revival of transcatheter PFO closure: A meta-analysis of randomized controlled trials - impact of shunt size and age. *American heart journal*. 2018;201:95-102.
33. Rengifo-Moreno P, Palacios IF, Junpaparp P, Witzke CF, Morris DL, Romero-Corral A. Patent foramen ovale transcatheter closure vs. medical therapy on recurrent vascular events: a systematic review and meta-analysis of randomized controlled trials. *European heart journal*. 2013;34(43):3342-52.
34. Riaz IB, Dhoble A, Mizyed A, Hsu CH, Husnain M, Lee JZ, Lotun K, Lee KS. Transcatheter patent foramen ovale closure versus medical therapy for cryptogenic stroke: a meta-analysis of randomized clinical trials. *BMC cardiovascular disorders*. 2013;13(no pagination):116.
35. Saber H, Palla M, Kazemlou S, Azarpazhooh MR, Seraji-Bozorgzad N, Behrouz R. Network meta-analysis of patent foramen ovale management strategies in cryptogenic stroke. *Neurology*. 2018;91(1):e1-e7.
36. Salas-Gutierrez, I, Reyes-Melo, I, Chiquete, E., Ruiz-Flores, ML, Cantu-Brito, C. Efficacy of percutaneous closure of patent foramen ovale in preventing recurrent events, compared with standard medical therapy in patients with cryptogenic ischemic stroke: Systematic review and meta-analysis. *Revista Mexicana de Neurociencia*. 2013;14: 299–305(6):299-305.

37. Schulze V, Lin Y, Karathanos A, Brockmeyer M, Zeus T, Polzin A, Perings S, Kelm M, Wolff G. Patent foramen ovale closure or medical therapy for cryptogenic ischemic stroke: an updated meta-analysis of randomized controlled trials. *Clinical research in cardiology : official journal of the German Cardiac Society*. 2018;107(9):745-755.
38. Shah R, Nayyar M, Jovin IS, Rashid A, Bondy BR, Fan TM, Flaherty MP, Rao SV. Device Closure Versus Medical Therapy Alone for Patent Foramen Ovale in Patients With Cryptogenic Stroke: A Systematic Review and Meta-analysis. *Annals of internal medicine*. 2018;168(5):335-342.
39. Spencer FA, Lopes LC, Kennedy SA, Guyatt G. Systematic review of percutaneous closure versus medical therapy in patients with cryptogenic stroke and patent foramen ovale. *BMJ open*. 2014;4(3):e004282.
40. Stortecky S, da Costa BR, Mattle HP, Carroll J, Hornung M, Sievert H, Trelle S, Windecker S, Meier B, Jüni P. Percutaneous closure of patent foramen ovale in patients with cryptogenic embolism: a network meta-analysis. *European heart journal*. 2015;36(2):120-128.
41. Tsivgoulis G, Katsanos AH, Mavridis D, Frogoudaki A, Vrettou AR, Ikonomidis I, Parissis J, Deftereos S, Karapanayiotides T, Palaiodimou L, Filippatou A, Perren F, Hadjigeorgiou G, Alexandrov AW, Mitsias PD, Alexandrov AV. Percutaneous patent foramen ovale closure for secondary stroke prevention: Network meta-analysis. *Neurology*. 2018;91(1):e8-e18.
42. Turc G, Calvet D, Guérin P, Sroussi M, Chatellier G, Mas JL, CLOSE Investigators. Closure, Anticoagulation, or Antiplatelet Therapy for Cryptogenic Stroke With Patent Foramen Ovale: Systematic Review of Randomized Trials, Sequential Meta-Analysis, and New Insights From the CLOSE Study. *Journal of the American Heart Association*. 2018;7(12).
43. Udell JA, Opotowsky AR, Khairy P, Silversides CK, Gladstone DJ, O'Gara PT, Landzberg MJ. Patent foramen ovale closure vs medical therapy for stroke prevention: meta-analysis of randomized trials and review of heterogeneity in meta-analyses. *The Canadian journal of cardiology*. 2014;30(10):1216-24.
44. Vaduganathan M, Qamar A, Gupta A, Bajaj N, Golwala HB, Pandey A, Bhatt DL. Patent Foramen Ovale Closure for Secondary Prevention of Cryptogenic Stroke: Updated Meta-Analysis of Randomized Clinical Trials. *The American journal of medicine*. 2018;131(5):575-577.
45. Wang TKM, Wang MTM, Ruygrok P. Patent Foramen Ovale Closure Versus Medical Therapy for Cryptogenic Stroke: Meta-Analysis of Randomised Trials. *Heart, lung & circulation*. 2018;
46. Wolfrum M, Froehlich GM, Knapp G, Casaubon LK, Dinicolantonio JJ, Lansky AJ, Meier P. Stroke prevention by percutaneous closure of patent foramen ovale: a systematic review and meta-analysis. *Heart (British Cardiac Society)*. 2014;100(5):389-95.
47. Zhang B, Zhou J, Li H, Zhou M, Chen A, Zhao Q. Transcatheter closure of patent foramen ovale does not reduce the risk of recurrent ischemic stroke versus medical therapy alone: a meta-analysis of randomized controlled trials. *International journal of cardiology*. 2013;169(6):e106-8.
48. Zhang XL, Kang LN, Wang L, Xu B. Percutaneous closure versus medical therapy for stroke with patent foramen Ovale: a systematic review and meta-analysis. *BMC cardiovascular disorders*. 2018;18(1):45.
49. Amplatzer versus CardioSEAL-STARflex versus Helex occluder). Hornung M, Bertog SC, Franke J, Id D, Taaffe M, Wunderlich N, Vaskelyte L, Hofmann I, Sievert H. Long-term results of a randomized trial comparing three different devices for percutaneous closure of a patent foramen ovale. *European heart journal*. 2013;34(43):3362-9.

50. CLOSE. Mas JL, Derumeaux G, Guillon B, Massardier E, Hosseini H, Mechtouff L, Arquizan C, Béjot Y, Vuillier F, Detante O, Guidoux C, Canaple S, Vaduva C, Dequatre-Ponchelle N, Sibon I, Garnier P, Ferrier A, Timsit S, Robinet-Borgomano E, Sablot D, Lacour JC, Zuber M, Favrole P, Pinel JF, Apoil M, Reiner P, Lefebvre C, Guérin P, Piot C, Rossi R, Dubois-Randé JL, Eicher JC, Meneveau N, Lusson JR, Bertrand B, Schleich JM, Godart F, Thambo JB, Leborgne L, Michel P, Pierard L, Turc G, Barthelet M, Charles-Nelson A, Weimar C, Moulin T, Juliard JM, Chatellier G, CLOSE Investigators. Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke. *The New England journal of medicine*. 2017;377(11):1011-1021.
51. CLOSURE I Trial. Furlan AJ, Reisman M, Massaro J, Mauri L, Adams H, Albers GW, Felberg R, Herrmann H, Kar S, Landzberg M, Raizner A, Wechsler L, CLOSURE I Investigators. Study design of the CLOSURE I Trial: a prospective, multicenter, randomized, controlled trial to evaluate the safety and efficacy of the STARFlex septal closure system versus best medical therapy in patients with stroke or transient ischemic attack due to presumed paradoxical embolism through a patent foramen ovale. *Stroke; a journal of cerebral circulation*. 2010;41(12):2872-83.
52. PC-Trial. Meier B, Kalesan B, Mattle HP, Khattab AA, Hildick-Smith D, Dudek D, Andersen G, Ibrahim R, Schuler G, Walton AS, Wahl A, Windecker S, Jüni P, PC Trial Investigators. Percutaneous closure of patent foramen ovale in cryptogenic embolism. *The New England journal of medicine*. 2013;368(12):1083-91.
53. REDUCE. Søndergaard L, Kasner SE, Rhodes JF, Andersen G, Iversen HK, Nielsen-Kudsk JE, Settergren M, Sjöstrand C, Roine RO, Hildick-Smith D, Spence JD, Thomassen L, Gore REDUCE Clinical Study Investigators. Patent Foramen Ovale Closure or Antiplatelet Therapy for Cryptogenic Stroke. *The New England journal of medicine*. 2017;377(11):1033-1042.
54. RESPECT. Saver JL, Carroll JD, Thaler DE, Smalling RW, MacDonald LA, Marks DS, Tirschwell DL, RESPECT Investigators. Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke. *The New England journal of medicine*. 2017;377(11):1022-1032.
55. Alameddine F, Block PC. Transcatheter patent foramen ovale closure for secondary prevention of paradoxical embolic events: acute results from the FORECAST registry. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2004;62(4):512-6.
56. Alushi B, Biasco L, Orzan F, Omedé P, Sciuto F, Moretti C, Belli R, Defilippi G, Barisone G, Cerrato P, Gaita F. Patent foramen ovale treatment strategy: an Italian large prospective study. *Journal of cardiovascular medicine (Hagerstown, Md.)*. 2014;15(10):761-8.
57. Anzola GP, Morandi E, Casilli F, Onorato E. Does transcatheter closure of patent foramen ovale really "shut the door?" A prospective study with transcranial Doppler. *Stroke; a journal of cerebral circulation*. 2004;35(9):2140-4.
58. Anzola GP, Zavarize P, Morandi E, Rozzini L, Parrinello G. Transcranial Doppler and risk of recurrence in patients with stroke and patent foramen ovale. *European journal of neurology : the official journal of the European Federation of Neurological Societies*. 2003;10(2):129-35.
59. Aslam F, Iliadis AE, Blankenship JC. Percutaneous closure of patent foramen ovale: success and outcomes of a low-volume procedure at a rural medical center. *The Journal of invasive cardiology*. 2007;19(1):20-4.
60. Balbi M, Casalino L, Gnecco G, Bezante GP, Pongiglione G, Marasini M, Del Sette M, Barsotti A. Percutaneous closure of patent foramen ovale in patients with presumed paradoxical

- embolism: periprocedural results and midterm risk of recurrent neurologic events. *American heart journal*. 2008;156(2):356-60.
61. Beitzke A, Schuchlenz H, Gamillscheg A, Stein JI, Wendelin G. Catheter closure of the persistent foramen ovale: mid-term results in 162 patients. *Journal of interventional cardiology*. 2001;14(2):223-9.
 62. Billinger K, Ostermayer SH, Carminati M, Degiovanni JV, Ewert P, Hess J, Maymone-Martins FA, Qureshi SA, Salmon AP, Schneider M, Wilson N, Sievert H. HELEX Septal Occluder for transcatheter closure of patent foramen ovale: multicentre experience. *EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology*. 2006;1(4):465-71.
 63. Bogousslavsky J, Garazi S, Jeanrenaud X, Aebscher N, Van Melle G. Stroke recurrence in patients with patent foramen ovale: the Lausanne Study. *Lausanne Stroke with Paradoxal Embolism Study Group*. *Neurology*. 1996;46(5):1301-5.
 64. Braun M, Giech V, Boscheri A, Schoen S, Gahn G, Reichmann H, Haass M, Schraeder R, Strasser RH. Transcatheter closure of patent foramen ovale (PFO) in patients with paradoxical embolism. Periprocedural safety and mid-term follow-up results of three different device occluder systems. *European heart journal*. 2004;25(5):424-30.
 65. Braun MU, Fassbender D, Schoen SP, Haass M, Schraeder R, Scholtz W, Strasser RH. Transcatheter closure of patent foramen ovale in patients with cerebral ischemia. *Journal of the American College of Cardiology*. 2002;39(12):2019-25.
 66. Butera G, Bini MR, Chessa M, Bedogni F, Onofri M, Carminati M. Transcatheter closure of patent foramen ovale in patients with cryptogenic stroke. *Italian heart journal : official journal of the Italian Federation of Cardiology*. 2001;2(2):115-8.
 67. Casaubon L, McLaughlin P, Webb G, Yeo E, Merker D, Jaigobin C. Recurrent stroke/TIA in cryptogenic stroke patients with patent foramen ovale. *The Canadian journal of neurological sciences*. Le journal canadien des sciences neurologiques. 2007;34(1):74-80.
 68. Cerrato P, Priano L, Imperiale D, Bosco G, Destefanis E, Villar AM, Ribezzo M, Trevi GP, Bergamasco B, Orzan F. Recurrent cerebrovascular ischaemic events in patients with interatrial septal abnormalities: a follow-up study. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*. 2006;26(6):411-8.
 69. Chatterjee T, Petzsch M, Ince H, Rehders TC, Körber T, Weber F, Schneider H, Auf der Maur C, Nienaber CA. Interventional closure with Amplatzer PFO occluder of patent foramen ovale in patients with paradoxical cerebral embolism. *Journal of interventional cardiology*. 2005;18(3):173-9.
 70. Cujec B, Mainra R, Johnson DH. Prevention of recurrent cerebral ischemic events in patients with patent foramen ovale and cryptogenic strokes or transient ischemic attacks. *The Canadian journal of cardiology*. 1999;15(1):57-64.
 71. De Castro S, Cartoni D, Fiorelli M, Rasura M, Anzini A, Zanette EM, Beccia M, Colonnese C, Fedele F, Fieschi C, Pandian NG. Morphological and functional characteristics of patent foramen ovale and their embolic implications. *Stroke; a journal of cerebral circulation*. 2000;31(10):2407-13.
 72. Demkow M, Ruzyłło W, Kepka C, Pruszczak P, Opuchlik A, Szyluk B, Konka M, Wilczyński J, Szulc M, Kwieciński H. Transcatheter closure of patent foramen ovale in patients with cryptogenic stroke. *Kardiologia polska*. 2004;61(8):101-9; discussion 109.

73. Du ZD, Cao QL, Joseph A, Koenig P, Heischmidt M, Waight DJ, Rhodes J, Brorson J, Hijazi ZM. Transcatheter closure of patent foramen ovale in patients with paradoxical embolism: intermediate-term risk of recurrent neurological events. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2002;55(2):189-94.
74. Dubiel M, Bruch L, Liebner M, Schmehl I, Winkelmann A, Rux S, Sonntag S, Wulff H, Grad MO, Kleber FX. Exclusion of patients with arteriosclerosis reduces long-term recurrence rate of presumed arterial embolism after PFO closure. *Journal of interventional cardiology*. 2007;20(4):275-81.
75. Dubiel M, Bruch L, Schmehl I, Liebner M, Winkelmann A, Stretz A, Grad MO, Kleber FX. Migraine headache relief after percutaneous transcatheter closure of interatrial communications. *Journal of interventional cardiology*. 2008;21(1):32-7.
76. Eged M, Andron M, Albouaini K, Alahmar A, Grainger R, Morrison WL. Percutaneous closure of patent foramen ovale and atrial septal defect: procedure outcome and medium-term follow-up. *Journal of interventional cardiology*. 2007;20(5):395-401.
77. Ende DJ, Chopra PS, Rao PS. Transcatheter closure of atrial septal defect or patent foramen ovale with the buttoned device for prevention of recurrence of paradoxical embolism. *The American journal of cardiology*. 1996;78(2):233-6.
78. Faggiano P, Frattini S, Piovesana P, Lorusso R, Chiari E, Scolari F, Padovani A, Cas LD. Low cerebrovascular event rate in subjects with patent foramen ovale and different clinical presentations: results from a prospective non randomized study on a population including patients with and without patent foramen ovale closure. *International journal of cardiology*. 2012;156(1):47-52.
79. Fischer D, Fuchs M, Schaefer A, Schieffer B, Jategaonkar S, Hornig B, Drexler H, Meyer GP. Transcatheter closure of patent foramen ovale in patients with paradoxical embolism. Procedural and follow-up results after implantation of the Starflex occluder device with conjunctive intensified anticoagulation regimen. *Journal of interventional cardiology*. 2008;21(2):183-9.
80. Giardini A, Donti A, Formigari R, Bronzetti G, Prandstraller D, Bonvicini M, Palareti G, Guidetti D, Gaddi O, Picchio FM. Comparison of results of percutaneous closure of patent foramen ovale for paradoxical embolism in patients with versus without thrombophilia. *The American journal of cardiology*. 2004;94(8):1012-6.
81. Giardini A, Donti A, Formigari R, Salomone L, Palareti G, Guidetti D, Picchio FM. Long-term efficacy of transcatheter patent foramen ovale closure on migraine headache with aura and recurrent stroke. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2006;67(4):625-9.
82. Greutmann M, Greutmann-Yantiri M, Kretschmar O, Senn O, Roffi M, Jenni R, Luescher TF, Eberli FR. Percutaneous PFO closure with Amplatzer PFO occluder: predictors of residual shunts at 6 months follow-up. *Congenital heart disease*. 2009;4(4):252-7.
83. Gu Y, Wang G, Pan G, Fawcett JP, A J, Sun J. Transport and bioavailability studies of astragaloside IV, an active ingredient in Radix Astragali. *Basic & clinical pharmacology & toxicology*. 2004;95(6):295-8.
84. Hammerstingl C, Bauriedel B, Stüsser C, Momcilovic D, Tuleta I, Nickenig G, Skowasch D. Risk and fate of residual interatrial shunting after transcatheter closure of patent foramen ovale: a long term follow up study. *European journal of medical research*. 2011;16(1):13-9.

85. Hanna JP, Sun JP, Furlan AJ, Stewart WJ, Sila CA, Tan M. Patent foramen ovale and brain infarct. Echocardiographic predictors, recurrence, and prevention. *Stroke; a journal of cerebral circulation*. 1994;25(4):782-6.
86. Harms V, Reisman M, Fuller CJ, Spencer MP, Olsen JV, Krabill KA, Gray WA, Jesurum JT. Outcomes after transcatheter closure of patent foramen ovale in patients with paradoxical embolism. *The American journal of cardiology*. 2007;99(9):1312-5.
87. Harrer JU, Wessels T, Franke A, Lucas S, Berlit P, Klötzsch C. Stroke recurrence and its prevention in patients with patent foramen ovale. *The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques*. 2006;33(1):39-47.
88. Hausmann D, Mügge A, Daniel WG. Identification of patent foramen ovale permitting paradoxical embolism. *Journal of the American College of Cardiology*. 1995;26(4):1030-8.
89. Hong TE, Thaler D, Brorson J, Heitschmidt M, Hijazi ZM, Amplatzer PFO Investigators. Transcatheter closure of patent foramen ovale associated with paradoxical embolism using the amplatzer PFO occluder: initial and intermediate-term results of the U.S. multicenter clinical trial. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2003;60(4):524-8.
90. Horner S, Niederkorn K, Gattringer T, Furtner M, Topakian R, Lang W, Maier R, Gamillscheg A, Fazekas F. Management of right-to-left shunt in cryptogenic cerebrovascular disease: results from the observational Austrian paradoxical cerebral embolism trial (TACET) registry. *Journal of neurology*. 2013;260(1):260-7.
91. Hung J, Landzberg MJ, Jenkins KJ, King ME, Lock JE, Palacios IF, Lang P. Closure of patent foramen ovale for paradoxical emboli: intermediate-term risk of recurrent neurological events following transcatheter device placement. *Journal of the American College of Cardiology*. 2000;35(5):1311-6.
92. Kiblawi FM, Sommer RJ, Levchuck SG. Transcatheter closure of patent foramen ovale in older adults. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2006;68(1):136-42; discussion 143-4.
93. Kim M, Kim S, Moon J, Oh PC, Park YM, Shin DH, Lee YB, Lee JY, Hwang HY, Kang WC. Effect of patent foramen ovale closure for prevention on recurrent stroke or transient ischemic attack in selected patients with cryptogenic stroke. *Journal of interventional cardiology*. 2018;31(3):368-374.
94. Knebel F, Gliech V, Walde T, Panda A, Sanad W, Eddicks S, Baumann G, Borges AC. Percutaneous closure of interatrial communications in adults - prospective embolism prevention study with two- and three-dimensional echocardiography. *Cardiovascular ultrasound*. 2004;2:5.
95. Kutty S, Brown K, Asnes JD, Rhodes JF, Latson LA. Causes of recurrent focal neurologic events after transcatheter closure of patent foramen ovale with the CardioSEAL septal occluder. *The American journal of cardiology*. 2008;101(10):1487-92.
96. Lee JY, Song JK, Song JM, Kang DH, Yun SC, Kang DW, Kwon SU, Kim JS. Association between anatomic features of atrial septal abnormalities obtained by omni-plane transesophageal echocardiography and stroke recurrence in cryptogenic stroke patients with patent foramen ovale. *The American journal of cardiology*. 2010;106(1):129-34.
97. Luermans JG, Post MC, Schräder R, Sluysmans T, Vydt T, Vermeersch P, Chessa M, Onorato E, Goy JJ, Budts WI. Outcome after percutaneous closure of a patent foramen ovale using the Intrasept device: a multi-centre study. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2008;71(6):822-8.

98. Martín F, Sánchez PL, Doherty E, Colon-Hernandez PJ, Delgado G, Inglessis I, Scott N, Hung J, King ME, Buonanno F, Demirjian Z, de Moor M, Palacios IF. Percutaneous transcatheter closure of patent foramen ovale in patients with paradoxical embolism. *Circulation*. 2002;106(9):1121-6.
99. Mas JL, Arquizan C, Lamy C, Zuber M, Cabanes L, Derumeaux G, Coste J. Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both. *The New England journal of medicine*. 2001;345(24):1740-6.
100. Mas JL, Zuber M. Recurrent cerebrovascular events in patients with patent foramen ovale, atrial septal aneurysm, or both and cryptogenic stroke or transient ischemic attack. French Study Group on Patent Foramen Ovale and Atrial Septal Aneurysm. *American heart journal*. 1995;130(5):1083-8.
101. Mazuelos F, Suárez de Lezo J, Pan M, Mesa D, Delgado M, Ruiz M, Ojeda S, Esteban F. [Percutaneous closure of patent foramen ovale in young patients with cryptogenic stroke: long-term follow-up]. *Revista española de cardiología*. 2008;61(6):640-3.
102. Mazzucco S, Bovi P, Carletti M, Tomelleri G, Golia G, Stegagno C, Variola A, Anselmi M, Nicolis D, Olivato S, Anzola GP, Ribichini F, VEROSTROKE Study Group. A model of multi-disciplinary approach to the diagnosis and treatment of young patients with cryptogenic stroke and patent foramen ovale. *Cardiology in the young*. 2012;22(3):327-34.
103. Mirzada N, Ladenwall P, Hansson PO, Eriksson P, Dellborg M. Recurrent stroke in patients with patent foramen ovale: An observational prospective study of percutaneous closure of PFO versus non-closure. *International journal of cardiology*. 2015;195:293-9.
104. Moon J, Kang WC, Kim S, Oh PC, Park YM, Chung WJ, Choi DY, Lee JY, Lee YB, Hwang HY, Ahn T. Comparison of Outcomes after Device Closure and Medication Alone in Patients with Patent Foramen Ovale and Cryptogenic Stroke in Korean Population. *Yonsei medical journal*. 2016;57(3):621-5.
105. Onorato E, Melzi G, Casilli F, Pedon L, Rigatelli G, Carrozza A, Maiolino P, Zanchetta M, Morandi E, Angeli S, Anzola GP. Patent foramen ovale with paradoxical embolism: mid-term results of transcatheter closure in 256 patients. *Journal of interventional cardiology*. 2003;16(1):43-50.
106. Paciaroni M, Agnelli G, Bertolini A, Pezzini A, Padovani A, Caso V, Venti M, Alberti A, Palmiero RA, Cerrato P, Silvestrelli G, Lanari A, Previdi P, Corea F, Balducci A, Ferri R, Falcinelli F, Filippucci E, Chiocchi P, Grandi FC, Ferigo L, Musolino R, Bersano A, Ghione I, Sacco S, Carolei A, Baldi A, Ageno W, FORI (Foramen Ovale Registro Italiano) Investigators. 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. *Cerebrovascular diseases (Basel, Switzerland)*. 2011;31(2):109-16.
107. Papa M, Gaspardone A, Fragasso G, Fracasso G, Ajello S, Gioffrè G, Iamele M, Iani C, Margonato A. Usefulness of transcatheter patent foramen ovale closure in migraineurs with moderate to large right-to-left shunt and instrumental evidence of cerebrovascular damage. *The American journal of cardiology*. 2009;104(3):434-9.
108. Pezzini A, Grassi M, Lodigiani C, Patella R, Gandolfo C, Zini A, DeLodovici ML, Paciaroni M, Del Sette M, Toriello A, Musolino R, Calabrò RS, Bovi P, Adami A, Silvestrelli G, Sessa M, Cavallini A, Marcheselli S, Marco Bonifati D, Checcarelli N, Tancredi L, Chiti A, Del Zotto E, Tomelleri G, Spalloni A, Giorli E, Costa P, Giacalone G, Ferrazzi P, Poli L, Morotti A, Piras V, Rasura M, Simone AM, Gamba M, Cerrato P, Zedde ML, Micieli G, Melis M, Massucco D, Guido D, De Giuli V, Bonaiti S, D'Amore C, La Starza S, Iacoviello L, Padovani A, Italian Project

- on Stroke in Young Adults (IPSY) Investigators. Propensity Score-Based Analysis of Percutaneous Closure Versus Medical Therapy in Patients With Cryptogenic Stroke and Patent Foramen Ovale: The IPSY Registry (Italian Project on Stroke in Young Adults). *Circulation. Cardiovascular interventions*. 2016;9(9).
109. Post MC, Van Deyk K, Budts W. Percutaneous closure of a patent foramen ovale: single-centre experience using different types of devices and mid-term outcome. *Acta cardiologica*. 2005;60(5):515-9.
110. Presbitero P, Lanzone AM, Albiero R, Lisignoli V, Zavalloni Parenti D, Gasparini GL, Lodigiani C, Barbaro C, Fappani A, Barberis G, Rossi ML, Pagnotta P. Anatomical patterns of patent foramen ovale (PFO): do they matter for percutaneous closure?. *Minerva cardioangiologica*. 2009;57(3):275-84.
111. Rigatelli G, Dell'Avvocata F, Giordan M, Ronco F, Braggion G, Schenal N, Aggio S, Cardaioli P. Transcatheter patent foramen ovale closure in spite of interatrial septum hypertrophy or lipomatosis: a case series. *Journal of cardiovascular medicine (Hagerstown, Md.)*. 2010;11(2):91-5.
112. Schuchlenz HW, Weihs W, Berghold A, Lechner A, Schmidt R. Secondary prevention after cryptogenic cerebrovascular events in patients with patent foramen ovale. *International journal of cardiology*. 2005;101(1):77-82.
113. Serena J, Martí-Fàbregas J, Santamarina E, Rodríguez JJ, Pérez-Ayuso MJ, Masjuan J, Segura T, Gállego J, Dávalos A, CODICIA, Right-to-Left Shunt in Cryptogenic Stroke Study, Stroke Project of the Cerebrovascular Diseases Study Group, Spanish Society of Neurology. Recurrent stroke and massive right-to-left shunt: results from the prospective Spanish multicenter (CODICIA) study. *Stroke; a journal of cerebral circulation*. 2008;39(12):3131-6.
114. Shafi NA, McKay RG, Kiernan FJ, Silverman IE, Ahlquist M, Silverman DI. Determinants and clinical significance of persistent residual shunting in patients with percutaneous patent foramen ovale closure devices. *International journal of cardiology*. 2009;137(3):314-6.
115. Sievert H, Horvath K, Zadan E, Krumsdorf U, Fach A, Merle H, Scherer D, Schräder R, Spies H, Nowak B, Lissmann-Jensen H. Patent foramen ovale closure in patients with transient ischemia attack/stroke. *Journal of interventional cardiology*. 2001;14(2):261-6.
116. Sievert H, Ruygrok P, Salkeld M, Baumgartner H, Meier B, Windecker S, Juliard JM, Aubry P, Tiefenbacher C, Krumsdorf U, Vermeersch P, Ewert P, Piéchaud JF. Transcatheter closure of patent foramen ovale with radiofrequency: acute and intermediate term results in 144 patients. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2009;73(3):368-73.
117. Slavin L, Tobis JM, Rangarajan K, Dao C, Krivokapich J, Liebeskind DS. Five-year experience with percutaneous closure of patent foramen ovale. *The American journal of cardiology*. 2007;99(9):1316-20.
118. Spies C, Khandelwal A, Timmemann I, Kavinsky CJ, Schräder R, Hijazi ZM. Recurrent events following patent foramen ovale closure in patients above 55 years of age with presumed paradoxical embolism. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2008;72(7):966-70.
119. Spies C, Timmermanns I, Reissmann U, van Essen J, Schräder R. Patent foramen ovale closure with the Intrasept occluder: Complete 6-56 months follow-up of 247 patients after presumed paradoxical embolism. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2008;71(3):390-5.

120. Taaffe M, Fischer E, Baranowski A, Majunke N, Heinisch C, Leetz M, Hein R, Bayard Y, Büscheck F, Reschke M, Hoffmann I, Wunderlich N, Wilson N, Sievert H. Comparison of three patent foramen ovale closure devices in a randomized trial (Amplatzer versus CardioSEAL-STARflex versus Helex occluder). *The American journal of cardiology*. 2008;101(9):1353-8.
121. Thaman R, Faganello G, Gimeno JR, Szantho GV, Nelson M, Curtis S, Martin RP, Turner MS. Efficacy of percutaneous closure of patent foramen ovale: comparison among three commonly used occluders. *Heart (British Cardiac Society)*. 2011;97(5):394-9.
122. Thanopoulos BV, Dardas PD, Karanasios E, Mezilis N. Transcatheter closure versus medical therapy of patent foramen ovale and cryptogenic stroke. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2006;68(5):741-6.
123. Varma C, Benson LN, Warr MR, Yeo E, Yip J, Jaigobin CS, Webb G, McLaughlin PR. Clinical outcomes of patent foramen ovale closure for paradoxical emboli without echocardiographic guidance. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2004;62(4):519-25.
124. Vigna C, Inchingolo V, Giannatempo G, Pacilli MA, Di Viesti P, Fusilli S, Amico CM, Santoro T, Lanna P, Fanelli R, Simone P, Loperfido F. Clinical and brain magnetic resonance imaging follow-up after percutaneous closure of patent foramen ovale in patients with cryptogenic stroke. *The American journal of cardiology*. 2008;101(7):1051-5.
125. Wahl A, Jüni P, Mono ML, Kalesan B, Praz F, Geister L, Räber L, Nedeltchev K, Mattle HP, Windecker S, Meier B. Long-term propensity score-matched comparison of percutaneous closure of patent foramen ovale with medical treatment after paradoxical embolism. *Circulation*. 2012;125(6):803-12.
126. Wahl A, Kunz M, Moschovitis A, Nageh T, Schwerzmann M, Seiler C, Mattle HP, Windecker S, Meier B. Long-term results after fluoroscopy-guided closure of patent foramen ovale for secondary prevention of paradoxical embolism. *Heart (British Cardiac Society)*. 2008;94(3):336-41.
127. Wahl A, Praz F, Tai T, Findling O, Walpot N, Nedeltchev K, Schwerzmann M, Windecker S, Mattle HP, Meier B. Improvement of migraine headaches after percutaneous closure of patent foramen ovale for secondary prevention of paradoxical embolism. *Heart (British Cardiac Society)*. 2010;96(12):967-73.
128. Wahl A, Tai T, Praz F, Schwerzmann M, Seiler C, Nedeltchev K, Windecker S, Mattle HP, Meier B. Late results after percutaneous closure of patent foramen ovale for secondary prevention of paradoxical embolism using the amplatzer PFO occluder without intraprocedural echocardiography: effect of device size. *JACC. Cardiovascular interventions*. 2009;2(2):116-23.
129. Weimar C, Holle DN, Benemann J, Schmid E, Schminke U, Haberl RL, Diener HC, Goertler M, German Stroke Study Collaboration. Current management and risk of recurrent stroke in cerebrovascular patients with right-to-left cardiac shunt. *Cerebrovascular diseases (Basel, Switzerland)*. 2009;28(4):349-56.
130. Windecker S, Wahl A, Nedeltchev K, Arnold M, Schwerzmann M, Seiler C, Mattle HP, Meier B. Comparison of medical treatment with percutaneous closure of patent foramen ovale in patients with cryptogenic stroke. *Journal of the American College of Cardiology*. 2004;44(4):750-8.

131. Zanchetta M, Pedon L, Olivieri A, Benacchio L. Randomized study comparing mechanical with electronic 2-dimensional intracardiac ultrasound monitoring (MEDIUM) during percutaneous closure of patent foramen ovale in adult patients with cryptogenic stroke. *Echocardiography* (Mount Kisco, N.Y.). 2008;25(5):496-503.
132. Zhang CJ, Huang YG, Huang XS, Huang T, Huang WH, Shen JJ, Xun ZR. Transcatheter closure of patent foramen ovale with the Spider patent foramen ovale occluder: a prospective, single-center trial. *Chinese medical journal*. 2010;123(7):834-7.
133. van de Wyngaert F, Kefer J, Hermans C, Ovaert C, Pasquet A, Beguin C, Sindic C, Sluysmans T. Absence of recurrent stroke after percutaneous closure of patent foramen ovale despite residual right-to-left cardiac shunt assessed by transcranial Doppler. *Archives of cardiovascular diseases*. 2008;101(7-8):435-41.
134. von Bardeleben RS, Richter C, Otto J, Himmrich L, Schnabel R, Kampmann C, Rupprecht HJ, Marx J, Hommel G, Münzel T, Horstick G. Long term follow up after percutaneous closure of PFO in 357 patients with paradoxical embolism: Difference in occlusion systems and influence of atrial septum aneurysm. *International journal of cardiology*. 2009;134(1):33-41.