# Long-Term Outcome After Transcatheter Atrial Septal Defect Closure in Adults: A Systematic Review and Meta-Analysis

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**Condensed Abstract:** ***Aims:*** **We performed a systematic review and meta-analysis of published studies to characterize the current literature and help determine the long-term outcomes after transcatheter ASD closure in adults.** ***Methods and Results:*** **Two investigators searched the manuscript databases for all eligible studies in accordance with the considered keywords. The pooled prevalence of each event according to the meta-analysis and considering the weight calculated for each study included 10.1% (for arrhythmia), 1.8% (for emboli), 2.3% (for stroke), 12.5% (for residual shunt), 1.8% (for erosion), and 2.5% (for death).** ***Conclusion:*** **The present meta-analysis show high long-term successfulness of transcatheter ASD closure in adults. (Curr Probl Cardiol 2021;46:100595.)**

## INTRODUCTION

Atrial septal defect (ASD) is one of the most frequent congenital heart diseases in adulthood.[1] There is now a shift of paradigm for therapeutic approaches of ASD over the recent years. Devices and modalities applied for transcatheter strategy have been recently evolved leading high successfulness with minimal complications and thus this modality has been accepted as the choice for repairing ASD in adults as compared to invasive surgical procedures.[2,3] However it

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should be noted that various factors can influence the efficacy of transcatheter ASD closure such as patients' age, preprocedural criteria for patients' selection, and postprocedural care management. Moreover, in view of all these arrangements, occurring potential un-negligible complications may be encountered during and following procedure especially in long-term such as cardiac arrhythmia, embolic events, reducing functional class, erosions, residual shunt, and even death.[4] Thus, considering the most appropriate criteria for selection of candidates for procedure, paying particular attention to the morphologic characteristics of the lesion, especially its size and, consequently, the selection of the appropriate size for device, establishing the best procedural strategy with the goal of device implantation with maximized cautions, as well as minutely postprocedural assessment of possible complications is very important to achieve the most proper outcome. However, there are individual issues which are often in debate including procedure-guiding modalities, sizing the defect, and closing complex defects. Additionally, the statistics reported from various studies widely vary in respect to the occurrence of postprocedural adverse events. As a result, long-term safety is an unresolved concern for many patients and health care providers. To solve these controversies, we performed a systematic review and meta-analysis of published studies to characterize the current literature and help determine the long-term outcomes after transcatheter ASD closure in adults.

# MATERIALS AND METHODS

## *Search strategy*

This study was performed according to established methods and in compliance with PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis) Protocols.[5] Two investigators searched the manuscript databases including Medline, Web of knowledge, Google scholar, Scopus, and Cochrane for all eligible studies in accordance with the considered keywords including: "arterial septal defect," "closure," "adult," and "transcatheter." The studies were restricted to English language. The inclusion criterion for retrieved the studies was to assess the mid-term and long-term outcome (with equal to or more than 3 years of follow-up) of transcatheter arterial septal defect closure in adults (with the age higher than 18 years). The exclusion criteria were thus as follows: (1) a lack of clear and

reproducible results, (2) non-English studies, (3) lack of access to the manuscripts full texts, and (4) case reports, case series, and review paper.

## Data abstraction and validity assessment

Data abstraction was independently performed by 2 un-blinded reviewers on structure collection forms without divergences in data collection. The study quality was evaluated based on the following criteria: (1) the systematic review and meta-analysis based on the questions primarily described and formulated; (2) inclusion and exclusion criteria predefined in the studies as eligibility criteria; (3) searching the literature performed on a systematic and comprehensive approach; (4) to minimize the bias, the full texts of the article were dually reviewed; (5) the quality of included studies were rated independently by the reviewers for appraising internal validity; (6) studies' characteristics and findings were comprehensively listed; (7) the publication and risk of bias were listed; and (8) heterogeneity was also assessed.[6] Along with comparing efficacy of two modalities, the year of publishing, number of patients, the outcome measured, and the complications due to treatment were also assessed. Of total 118 studies that initially assessed based on the keywords, 14 met the endpoints that were finally analyzed[7-20] that were published between 2010 and 2019 (Fig 1).

## Statistical analysis:

Dichotomous variables are reported as proportions and percentages, and continuous variables as mean values. Binary outcomes from individual studies were to be combined with both the Mantel-Hansel fixed effect model. The odds ratio (OR) and 95% confidence interval (CI) were used as summary statistics for the comparison of dichotomous variables between the subgroups with and without postprocedural complications. Cochran's Q test was used to determine the statistical heterogeneity of this study. This test was complemented with the $I^2$ statistic, which quantifies the proportion of total variation across studies that is due to heterogeneity rather than chance. A value of I2 of 0%-25% indicates insignificant heterogeneity, 26%-50% low heterogeneity, 51%-75% moderate heterogeneity and 76%-100% high heterogeneity. Publication bias was assessed by the rank correlation test and also confirmed by the funnel plot analysis. Reported values were 2-tailed, and hypothesis testing results were considered statistically significant at

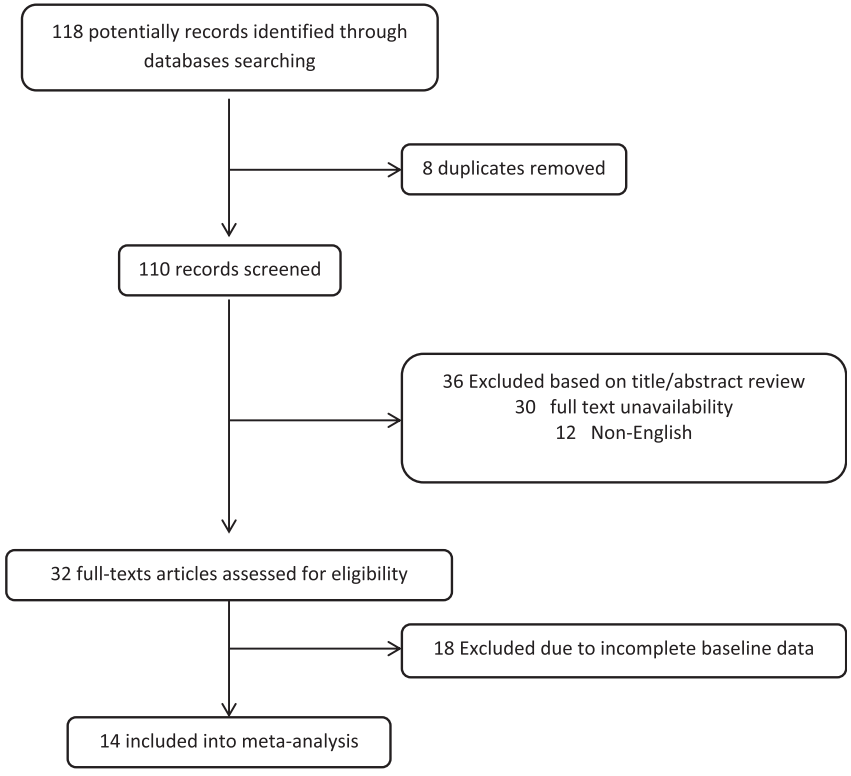


**Fig. 1.** The consort related to how selecting the published papers.

$P = 0.05$. Statistical analysis was performed using the Stata software (version 13.1, Stata Corp, College Station, TX).

# RESULTS

## *Patients' characteristics*

In total, 14 studies assessed the outcomes after transcatheter ASD closure in adults within a follow-up time ranged 3-9 years. The studies all planned as the prospective cohort studies. The total number of patients was 2354 widely ranged from 30 to 1026 in different literatures. The average age of the cases was 48.6 years and 64% of the subjects were female. The postprocedural events assessed in the studies included death, cardiac arrhythmias, embolic events, erosion, brain stroke, migraine,

congestive heart failure, the change in NYHA functional status, and residual shunt (Table 1).

### *The rate of complications*

Table 2 presents the rate of postprocedural complications pointed in each study. In this regard, the occurrence of cardiac arrhythmia ranged from 0.0% to 15.5%, embolic problems from 0.0% to 3.8%, stroke from 0.0% to 6.0%, residual shunt from 1.2% to 22.1%, erosion from 0.0% to 1.8% and even death from 0.0% to 6.7%. Overall, the pooled prevalence of each event according to the meta-analysis and considering the weight calculated for each study (Table 3) included 10.1% (for arrhythmia), 1.8% (for emboli), 2.3% (for stroke), 12.5% (for residual shunt), 1.8% (for erosion), and 2.5% (for death; Fig 2). The statistical heterogeneity differed for assessing the complications that was high for assessment of cardiac arrhythmia and residual shunt (Table 3). There was also significant publication bias as evidenced by either funnel plot asymmetry or Egger test for assessment of arrhythmia and residual shunt (Fig 3).

## DISCUSSION

Repairing ASD via surgical procedure is accepted as a choice procedure with minimal morbidity and rare mortality; however it may not favorable in older ages.[21] Recently, minimally invasive techniques such as transcatheter closure have lead to proper outcome in different age subgroups with high safety.[22] Despite unfavorable outcome of both invasive and minimal invasive even in a few of cases operated, postprocedural follow-up of the patients even for long-time is highly recommended with regard to echocardiographic assessment, echocardiographic evaluation of systolic dysfunction and tracking residual shunting, physical functional state especially functional class, and also assessing the evidences of neurological defects especially cerebrovascular embolic events once every 5 year. This following-up is essential for older adults and in this regard, the guidelines do not recommend following the patients younger than 25 years.[23]

Nowadays, transcatheter device closure is globally accepted as the choice for repairing ASD in adults. It provides similar efficacy and hemodynamic benefits, but reduced complication rates and duration of hospital stay compared with surgery particularly in older adults.[24] Moreover, some candidates are preferred to manage only with transcatheter approaches such as in cases with secundum ASD size more than 38 mm,

**TABLE 1.** The details of baseline characteristics in studies analyzed

| Author, year | Number of cases | Mean age (year) | Female gender | ASD size (mm) | Follow-up year | Reported outcomes |
|---|---|---|---|---|---|---|
| Knepp, 2010 | 42 | 50 ± 15 | — | 19 | 6 | Shunt, arrhythmia migraine |
| Luermans, 2010 | 133 | 46 ± 12 | 73% | 18 | 4 | Death, arrhythmia, emboli, stroke |
| Hanninen, 2011 | 54 | 69 ± 13 | 72% | 24 | 3 | NYHA class arrhythmia |
| Kutty, 2012 | 84 | 42 ± 17 | 78% | — | 8 | Death, NYHA class arrhythmia, emboli |
| Nakagawa, 2012 | 30 | 75 ± 4 | 66% | 23 | 3 | Death, stroke arrhythmia |
| Kefer, 2012 | 112 | 46 ± 17 | 71% | 20 | 5 | Arrhythmia, erosion |
| Rigatelli, 2012 | 81 | 48 ± 14 | 65% | 26 | 9 | Arrhythmia, erosion |
| Hoashi, 2014 | 1026 | 26 ± 2 | 64% | 18 | 7 | Death |
| Scacciatella, 2015 | 110 | 51 ± 17 | 75% | 18 | 5 | Arrhythmia, erosion, valve dis. |
| Snijder, 2015 | 104 | 46 ± 17 | 75% | 18 | 6 | Arrhythmia, shunt, stroke |
| Takaya, 2015 | 244 | 66± 9 | 62% | 22 | 3 | Death, stroke, heart failure |
| Chen, 2017 | 35 | 31 ± 8 | 60% | 39 | 3 | Death, arrhythmia, emboli |
| Kobayashi, 2018 | 30 | 57 ± 19 | 70% | 19 | 3 | Death, erosion, arrhythmia, emboli |
| Jung, 2019 | 216 | 39 ± 14 | 73% | 27 | 4 | Death, shunt, arrhythmia, emboli |
|  | 53 | 38 ± 14 | 68% | 36 | 5 |  |

**TABLE 2.** The postprocedural complications of transcatheter atrial septal defect closure in adults

| Author, year | Number of cases | Death | Arrhythmia | Emboli | Stroke | Residual shunt | Erosion |
|---|---|---|---|---|---|---|---|
| Knepp, 2010 | 94 | 0.0 | 7.4 | 0.0 | 0.0 | 3.2 | 0.0 |
| Luermans, 2010 | 133 | 0.0 | 9.8 | 3.8 | 2.3 | 17.3 | 0.0 |
| Hanninen, 2011 | 54 | 1.8 | 11.1 | 0.0 | 1.8 | 0.0 | 0.0 |
| Kutty, 2012 | 148 | 3.0 | 15.5 | 3.0 | 6.0 | 2.4 | 0.6 |
| Nakagawa, 2012 | 30 | 6.7 | 3.3 | 0.0 | 3.3 | 6.7 | 0.0 |
| Kefer, 2012 | 112 | 0.8 | 3.2 | 0.0 | 0.8 | 3.2 | 0.8 |
| Rigatelli, 2012 | 81 | 1.2 | 4.8 | 1.2 | 1.2 | 1.2 | 1.2 |
| Hoashi, 2014 | 345 | 0.2 | 13.6 | 0.2 | 0.2 | 0.0 | 0.2 |
| Scacciatella, 2015 | 110 | 1.8 | 0.0 | 0.0 | 0.0 | 3.6 | 1.8 |
| Snijder, 2015 | 104 | 4.9 | 3.8 | 0.0 | 3.8 | 22.1 | 0.9 |
| Takaya, 2015 | 244 | 3.3 | 0.0 | 0.0 | 1.2 | 0.0 | 0.0 |
| Chen, 2017 | 35 | 2.5 | 2.5 | 0.0 | 0.0 | 0.0 | 0.0 |
| Kobayashi, 2018 | 30 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Jung, 2019 | 216 | 0.0 | 0.5 | 2.5 | 0.0 | 3.7 | 0.0 |

**TABLE 3.** The pooled prevalence of complications of transcatheter atrial septal defect closure in adults

| Event | Pooled prevalence | Lower limit | Upper limit | Heterogeneity $I^2$ (*P* value) | Publication bias (*P* value) |
|---|---|---|---|---|---|
| Death | 2.5% | 1.7% | 3.6% | 25.635 (0.178) | 0.080 |
| Arrhythmia | 10.1% | 8.4% | 12.0% | 73.719 (0.001) | 0.001 |
| Emboli | 1.8% | 1.2% | 2.8% | 4.397 (0.403) | 0.584 |
| Stroke | 2.3% | 1.6% | 3.4% | 33.136 (0.110) | 0.476 |
| Shunt | 12.5% | 10.3% | 15.0% | 86.622 (0.001) | 0.008 |
| Erosion | 1.8% | 1.1% | 2.9% | 39.615 (0.063) | 0.600 |

those with inadequate septal rims for device anchorage, and those in which the device would interfere with atrioventricular valve function or venous drainage are not eligible and referred for surgical closure.[25] According to some studies, the success closure rate of transcatheter

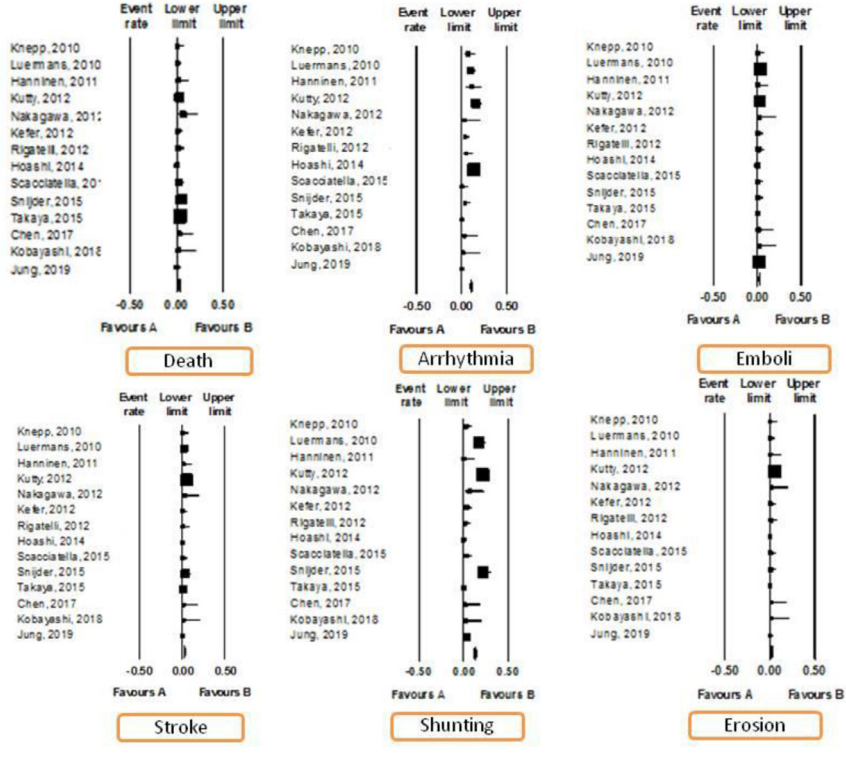


**Fig. 2.** The pooled prevalence of complications of transcatheter atrial septal defect closure in adults.

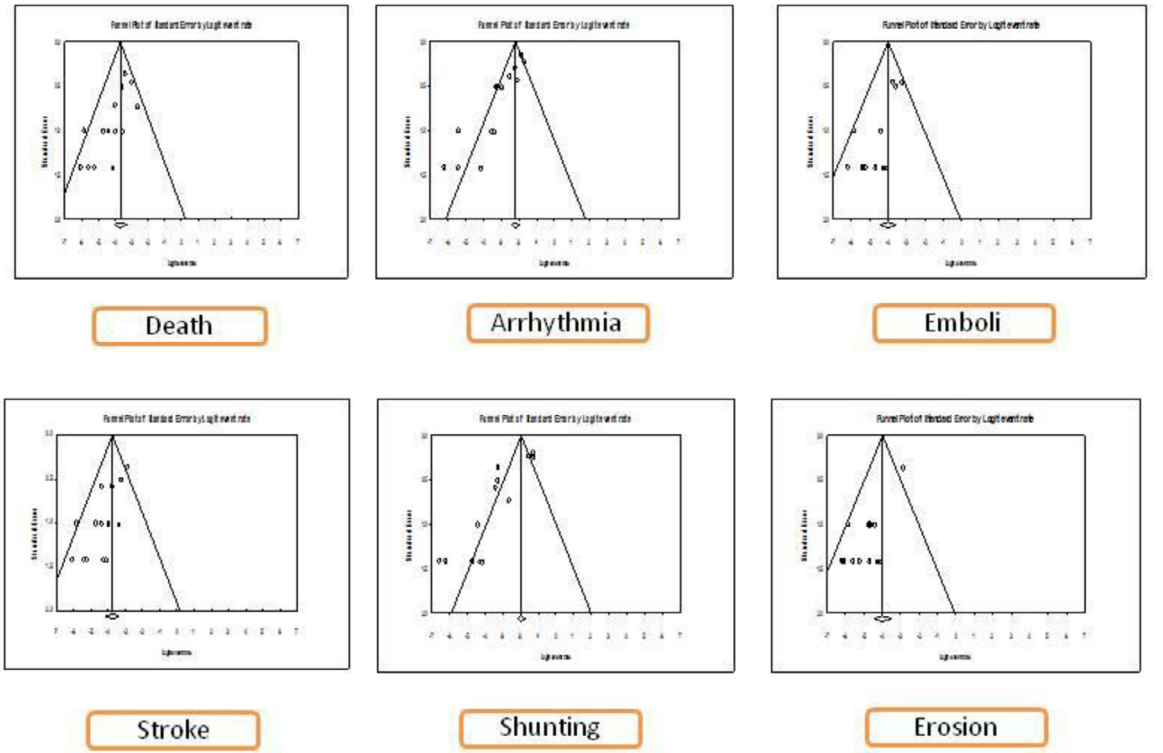


**Fig. 3.** The publication bias on assessing the complications of transcatheter atrial septal defect closure in adults.

approach has been estimated to be higher than 95% with a complication rate of less than 1%,[26-28] but the likelihood of some complications such as embolic events, erosion, or allergy to the materials used in the devices have remained significant.[29,30] In total, although early outcome of transcatheter ASD closure is evidenced to be appropriate, long-term outcome especially with regard to occurrence of residual shunt or cardiac arrhythmias is paradoxical. According the present meta-analysis, the most common long-term postprocedural events included residual shunting in 12.5% and arrhythmia in 10.1%. However in our analysis, paying attention to some points should be considered. First, weights calculating for the studies widely varied due to the wide spectrum for sample numbers (ranged from 30 to more than 1000 cases). Second, the results related to the pooled prevalence of these two prevalent events remains unreliable due to the high heterogeneity across the studies. Thus, to achieve reliable rates for prevalence of residual shunting and arrhythmia long-time after transcatheter ASD closure more studies should be performed. As another important point, the publication bias for assessment of these two events is also significant in the studies. Publication bias in medical journals refers to the publication of more articles that contain positive conclusions or significant statistical results. In fact, this bias suggests that articles containing negative or non-significant statistical results are less likely to be published. The first cause of this bias, in fact, is researchers themselves who do not want to report their negative or non-significant statistical results. Also, some organizations that provide funding for medical research may refuse to publish such findings or, at least, delay publication. Thus, the results published on the prevalence rate of residual shunting and arrhythmia after transcatheter ASD closure might be unreliable needing predesign and pre-implementation.

## Limitation

Our analyses were substantially limited in the number and quality of studies available .Non-English and lack of access to the full texts studies were exclusion criteria.

## In conclusion

The present systematic review and meta-analysis show high long-term successfulness of transcatheter ASD closure in adults, however, high rate of some events such as residual shunting and cardiac arrhythmia emphasizes further examination of the techniques used, the criteria for selecting patients, and the use of better devices for practice.

## Impact of daily practice

Transcatheter Device closure can safely be performed with a minimal device.


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## Author Contribution

Samin Behdad: Writing - Original Draft, Formal analysis. Ehsan Shirvani: Writing - Original Draft, Investigation. Mehdi Ghaderian: Conceptualization, Validation

## REFERENCES


1. Geva T1, Martins JD2, Wald RM3. Atrial septal defects. *Lancet* 2014;383:1921–32. https://doi.org/10.1016/S0140-6736(13)62145-5. Epub 2014 Apr 8.
2. Behjati-Ardakani M1, Golshan M2, Akhavan-Karbasi S3, Hosseini SM3, Behjati-Ardakani MA3, Sarebanhassanabadi M1. The clinical course of patients with atrial septal defects. *Iran J Pediatr* 2016;26:e4649.. eCollection 2016 Aug.
3. Rao PS, Harris AD. Recent advances in managing septal defects: atrial septal defects. *F1000Res* 2017;6:2042.
4. Brown KN, Kanmanthareddy A. Catheter Management of Atrial Septal Defect. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. 2019 Sep 18.
5. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;349(jan02 1):g7647.. Jan 2.
6. Zeng X, Zhang Y, Kwong JS, et al. The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. *J Evid Based Med* 2015;8:2–10.
7. Knepp MD, Rocchini AP, Lloyd TR, Aiyagari RM. Long-term follow up of secundum atrial septal defect closure with the amplatzer septal occluder. *Congenital heart disease* 2010;5:32–7.
8. Luermans JG1, Post MC, ten Berg JM, Plokker HW, Suttorp MJ. Long-term outcome of percutaneous closure of secundum-type atrial septal defects in adults. *EuroIntervention* 2010;6:604–10. https://doi.org/10.4244/EIJV6I5A101.
9. Hanninen M1, Kmet A, Taylor DA, Ross DB, Rebeyka I, Vonder Muhll IF. Atrial septal defect closure in the elderly is associated with excellent quality of life, functional improvement, and ventricular remodelling. *Can J Cardiol* 2011;27:698–704. https://doi.org/10.1016/j.cjca.2011.04.003. Epub 2011 Oct 5.
10. Kutty S, Hazeem AA, Brown K, et al. Long-term (5- to 20-year) outcomes after transcatheter or surgical treatment of hemodynamically significant isolated secundum atrial septal defect. *Am J Cardiol* 2012;109:1348–52.

11. Nakagawa K1, Akagi T, Taniguchi M, et al. Transcatheter closure of atrial septal defect in a geriatric population. *Catheter Cardiovasc Interv* 2012;80:84–90. https://doi.org/10.1002/ccd.23457. Epub 2012 Jan 10.
12. Kefer J, Sluysmans T, Hermans C, et al. Percutaneous transcatheter closure of interatrial septal defect in adults: procedural outcome and long-term results. *Catheterization Cardiovasc Intervent* 2012;79:322–30.
13. Rigatelli G, Dell'avvocata F, Cardaioli P, et al. Safety and long-term outcome of modified intracardiac echocardiography-assisted "no-balloon" sizing technique for transcatheter closure of ostium secundum atrial septal defect. *J Intervent Cardiol* 2012;25:628–34.
14. Hoashi T, Yazaki S, Kagisaki K, et al. Management of ostium secundum atrial septal defect in the era of percutaneous transcatheter device closure: 7-year experience at a single institution. *J Cardiol* 2015;65:418–22.
15. Scacciatella P, Marra S, Pullara A, et al. Percutaneous closure of atrial septal defect in adults: very long-term clinical outcome and effects on aortic and mitral valve function. *J Invasive Cardiol* 2015;27:65–9.
16. Snijder RJ, Suttorp MJ, Berg JM and Post MC. Percutaneous closure of secundum type atrial septal defects: more than 5-year follow-up. World J Cardiol
17. Takaya Y1, Akagi T2, Kijima Y1, Nakagawa K1, Sano S3, Ito H1. Long-term outcome after transcatheter closure of atrial septal defect in older patients: impact of age at procedure. *JACC Cardiovasc Interv* 2015;8:600–6. https://doi.org/10.1016/j.jcin.2015.02.002.
18. Chen Q1, Cao H2, Zhang GC2, Chen LW2, Xu F2, Zhang JX2. Midterm follow-up of transthoracic device closure of an atrial septal defect using the very large domestic occluder (44-48 mm), a single Chinese cardiac center experience. *J Cardiothorac Surg* 2017;12:74. https://doi.org/10.1186/s13019-017-0639-8.
19. Kobayashi A1, Kunii H1, Yokokawa T1, et al. Safety and effectiveness of transcatheter closure of atrial septal defects: initial results in Fukushima Prefecture. *Fukushima J Med Sci* 2018;64:151–6. https://doi.org/10.5387/fms.2018-13. Epub 2018 Nov 6.
20. Jung SY1, Kim AY1, Jung JW1, Choi JY2. Procedural, early and long-term outcomes after percutaneous closure of atrial septal defect: comparison between large and very large atrial septal defect groups. *Korean Circ J* 2019;49:975–86. https://doi.org/10.4070/kcj.2018.0391. Epub 2019 Apr 25.
21. Nyboe C, Fenger-Grøn M, Nielsen-Kudsk JE, Hjortdal V. Closure of secundum atrial septal defects in the adult and elderly patients. *Eur J Cardiothorac Surg* 2013;43:752–7.
22. Hopkins RA, Bert AA, Buchholz B, Guarino K, Meyers M. Surgical patch closure of atrial septal defects. *Ann Thorac Surg* 2004;77:2144–9.
23. Baumgartner H, Bonhoeffer P, Groot NMSD, et al. ESC Guidelines for the management of grown-up congenital heart disease (new version 2010) The Task Force on the Management of Grownup Congenital Heart Disease of the European Society of Cardiology (ESC). *Eur Heart J* 2010;31:2915–57.

24. Rosas M, Zabal C, Garcia-Montes J, Buendia A, Webb G, Attie F. Transcatheter versus surgical closure of secundum atrial septal defect in adults: impact of age at intervention. A concurrent matched comparative study. *Congenit Heart Dis.* 2007;2:148–55.
25. Podnar T, Martanovic P, Gavora P, Masura J. Morphological variations of secundum-type atrial septal defects: feasibility for percutaneous closure using Amplatzer septal occluders. *Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv* 2001;53:386–91.
26. Majunke N, Bialkowski J, Wilson N, et al. Closure of atrial septal defect with the Amplatzer septal occluder in adults. *Am J Cardiol* 2009;103:550–4.
27. Krumsdorf U, Ostermayer S, Billinger K, et al. Incidence and clinical course of thrombus formation on atrial septal defect and patient foramen ovale closure devices in 1,000 consecutive patients. *J Am Coll Cardiol* 2004;43:302–9.
28. Abaci A, Unlu S, Alsancak Y, Kaya U, Sezenoz B. 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: complications of ASD and PFO Closure. *Catheter Cardiovasc Interv* 2013;82:1123–38.
29. Mullen MJ, Hildick-Smith D, De Giovanni JV, et al. BioSTAR Evaluation STudy (BEST): a prospective, multicenter, phase I clinical trial to evaluate the feasibility, efficacy, and safety of the BioSTAR bioabsorbable septal repair implant for the closure of atrial-level shunts. *Circulation* 2006;114:1962–7.
30. Kuijpers Joey M, Mulder Barbara JM, Bouma Berto J. Secundum atrial septal defect in adults: a practical review and recent developments. *Neth Heart J* 2015;23:205–11.