International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Evaluation of Safety and Performance of Bioresorbable Occluder Implant in Treating Atrial Septal Defect

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Abstract: ***A large, long - term atrial septal defect (ASD) or imperfection can harm the heart and lungs. Medical procedure like heart surgery is fundamental procedure to fix an atrial septal defect by medical device and to prevent complications. The goal of the current study is to evaluate the efficacy and safety of a bioresorbable occluder that was developed in - house for patients with ASD disease. This study depicts information based on animal study in porcine heart model for the developed bioresorbable ASD occluder, as well as the safety of the device in the designated area after the implantation. For assurance of present research, animal study has been performed to occlude an atrial septal wall utilizing a standard technique and successfully implanted a bioresorbable ASD occluder device in the defect size of 0.9 cm affirmed by angiography and Transthoracic Echocardiogram (TTE), After 180 days of animal study, it is claimed that the, present research work could be recommended for a preclinical study to treat atrial septal defect in humans.***

Keywords: Arial Septal Defect (ASD), Bioresorbable Occluder (BRO), porcine heart model

1. Introduction

An atrial septal defect (ASD) is a hole in the heart between the upper chambers generally known as atria. The hole builds up the pressure of the blood that course through the lungs. It can be congenital (inherited heart defect). ASD is a typical underlying intrinsic coronary disease with an expected rate of 100 for each 100, 000 live births. An opening in the atrial septum will be shaped by the unusual early stage advancement of the first atrial septum. However, if addressed a number of adverse effects including physical activity, atrial tachyarrhythmia, right ventricular dysfunction and pneumonic hypertension will manifest as people age. Furthermore, due to the persistent existence of alloy occluders the effects of removal or on the other hand shedding will worsen during adolescent cardiac growth. Newly biodegradable materials particularly polylactide based are leading in expanding consideration due to its biocompatible properties. An occluder utilized in the present study is composed of Poly L - lactic acid (PLLA) which is biodegradable in nature so, it will degrade over its definite time. Due to some circumstances if the septal defect arises again in the future, it can be occluded again by utilizing bioresorbable occluder. In this way, bioresorbable occluder utilized in this study is clinically more relevant as compared to alloy occluders.

To comprehend the reason for ASD, it is useful to know how the heart regularly functions. The normal heart is made of four chambers two upper chambers (atria) and two lower chambers (ventricles). The right half of the heart moves blood to the lungs. In the lungs, blood gets oxygen and afterward returns it to the heart's left side. The left half of the heart then pumps the blood through the body's principal artery (aorta) and out to the remainder of the body. A huge atrial septal defect can make additional blood overload to the lungs and overwork to the right side of the heart. On the other hand if not treated, it gradually expands and becomes powerless leading to pulmonary hypertension.

Therefore in this study, attention has been focused on biodegradable occluder for ASD which is utilized as a percutaneous option in contrast to cardiac surgery for closure of atrial septal defects. The waist size decides the left and right atrial discs dimension, which can estimate the aorta and make an expected gamble for disintegration. Utilizing a sheath, bioresorbable occluder crosses the defect and located in the superior pulmonary vein and size of the sheath is determined by the size of the device. Then after, device is deployed and tested by pushing back and forth on the link to affirm steadiness proceeding to release of the device.

2. Materials and Methods

Firstly an animal was treated with anticoagulants like aspirin and clopidogrel before 3 days prior to the procedural day, preceding implantation of the test thing and continued from day 1 to day 31 with reduced dose of aspirin e. g; 150 mg. The animal was fasted and kept only on water before 12 hours prior to procedure. Animal was weighed, anesthetized, instrumented, and monitored using 15 mg/kg (IM) of ketamine, 2.5 mg/kg (IM) of xylazine, 0.5 mg/kg (IV bolus) of propofol followed by inhalation of 1 - 3% of anesthesia through facemask. The neck, chest and thigh area was clipped free of hair for femoral vein, artery approach and ECG applications respectively. Thus the animal was prepared and draped for aseptic procedures with medications.

After that, animal was prepared for the surgical procedure with following medication. Medication for anesthesia was administered in accordance with standard operating procedure to respective animal. Anesthesia was maintained using 1 - 3% of isoflurane through endotracheal intubation. Medication administered on each animal during the clinical study was recorded individually. The right and left groin of an animal was shaved. Percutanuos approach utilizing

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seldinger method was used to embed sheath of 8F into right femoral vein and 6F into left femoral artery sheaths. Activated clotting time (ACT) measurement was done during pre and post heparinisation (the therapeutic administration of heparin).

The first and the main bolus dose was given at 80 - 120 IU/kg IV/IA and ensuing dosages was titrated in light of ACT values. Femoral artery was embedded with 6F sheath where catheter is set in the aortic root above an aortic valve. Femoral vein was embedded with 5F JR catheter over a stiff of 0.035x150 cm guide wire to be secured in left subclavian, the JR catheter was removed keeping the guide wire in left subclavian vein. The 8F Sheath was removed and yet again embedded with the 8F of mullins sheath with the dilator, Guide wire was removed and mullins sheath was withdrawn from subclavian vein to anchor the fossa ovalis in the right atrium and insertion of the ross needle into mullins sheath. Septal cut needle (Ross) was pushed in the mullin sheath under TTE and angiography utilizing left anterior oblique (LAO), right anterior oblique (RAO) and arterial pressure (AP) orientation. The septum is penetrated involving the guidance of pigtail catheter by pushing the mullin sheath in the septum from right to left atrium. After that, needle was removed and guide wire was placed transeptally into the left ventricle. Balloon was passed through the transeptal puncture and inflated in order to perform angiography for the affirmation of ASD.

The ASD BRO was embedded utilizing the delivery system navigated through the sheath. Chest Radiography and TTE was done of pre and post implantation. Animal was recuperated after this methodology and was able to survive for 180 days.

The span of the review was of 180 days. The animal was under anticoagulant treatment till terminal day (Day 180) and monitored with cage side perceptions for any deviation in the health status and record of their water and food consumption was ensured. During 180th day the animal was observed basically for ill health. Cage side perceptions was observed and recorded once in a day of every individual animal. Early electives was euthanized in light of empathetic end points followed by gross and histopathological assessment for the reason of mortality or morbidity. On day 180 subsequent angiography and TTE was performed on the animal for recedual shunting and affirming the positioning of the occluder device as shown in the fig.01, 02 and 03.

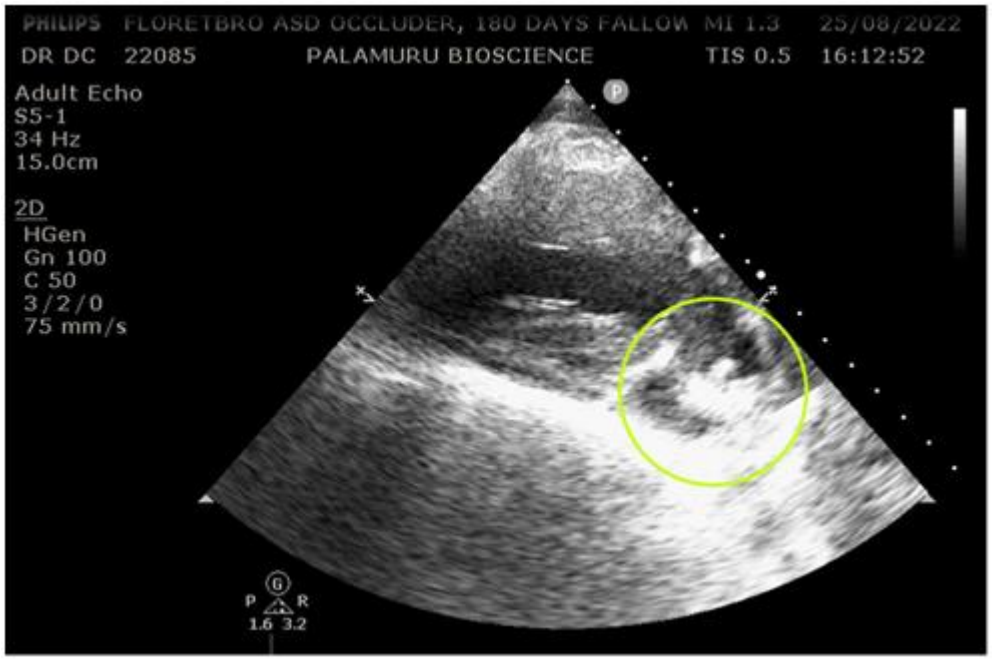

Figure 1: ASD occluder device in Right Parasternal long axis view on Day 180

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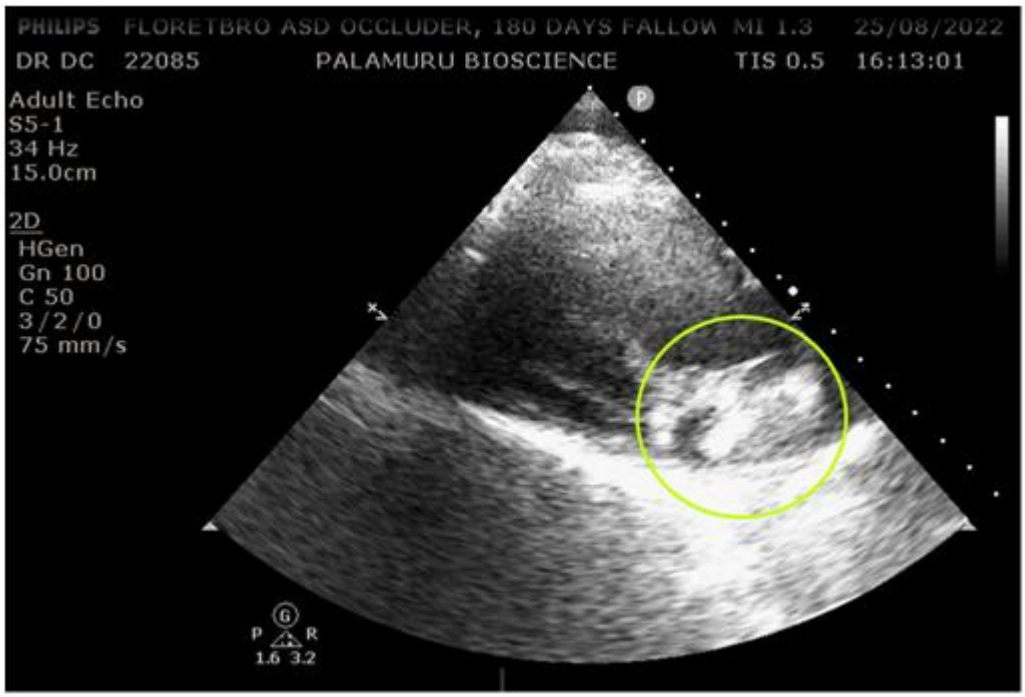

Figure 2: ASD occluder device in Left Parasternal long axis view on Day 180

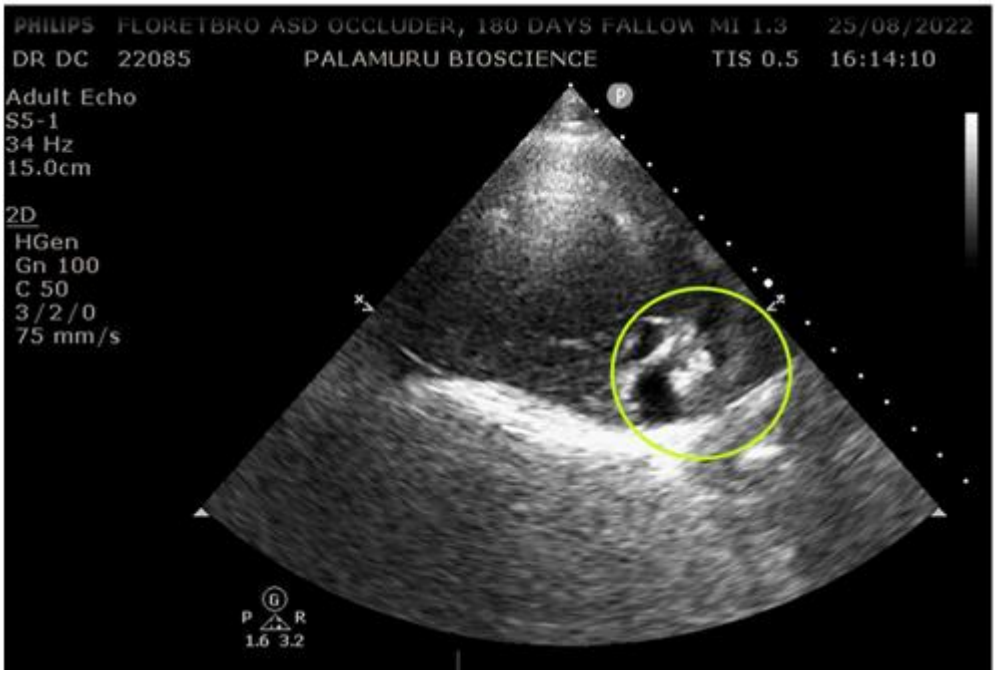

Figure 3: ASD occluder device in Short axis view on Day 180

3. Result and Discussion

The purpose behind this study is to assess the safety and execution of the bioresorbable atrial septal defect occluder in porcine model. This study gave data on the performance of the ASD BRO as well as the safety of the device in the designated area of implantation. One animal was taken for this study for the creation of ASD by utilizing a standard technique and embedding an ASD BRO device in the defect size of 0.9cm affirmed by angiography and TTE. Swine was chosen as the test system since this species has the circulatory system necessities like those of a adult human and gives a comparable size, cardiac output, pulse, blood pressure etc. This is a generally involved animal model to test cardio - vascular devices as size and circulatory results are key boundaries. More modest phylogenetically lower species are not suitable for in - vivo studies with this sort of device.

The device size setup was 18mm Left disc, 14mm right disc and waist was 6mm in diameter. Animal was recovered and checked for cage side observations till 180 days. The standard and 180 days termination hematology and biochemistry parameters were within the normal physiological ranges. During the 180th day of monitoring animal, it was found healthy and responsive and showed no reduction in body weight. At the preplanned termination of the research on 180th day, animal was accommodatingly forfeited after fluoroscopy and TTE for the necropsy and

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histopathological assessment of the atrial septum with implanted device. The fluoroscopy and TTE showed no disgorging, shunting or movement of the device. There were no lesions in the standard organs observed during necropsy. The device was seen appropriately integrated in the atrial septal tissue during necropsy observation. The histopathological assessment showed moderate infilteration of the inflammatory cells yet the device was appropriately epithelialised and there were no conspicious fibres of the device left uncovered by the epithelium after 180 days of animal study as shown in the fig.04, fig.05 & 06.

Hence, this study provided information on the performance of the bioresorbable atrial septal defect occluder device as well as the early residual shunting, thrombosis, pericardial effusion, mitral regurgitation. The minimum acceptance criteria of the study was successful implantation of the test items and animal's survival throughout the implantation procedure.

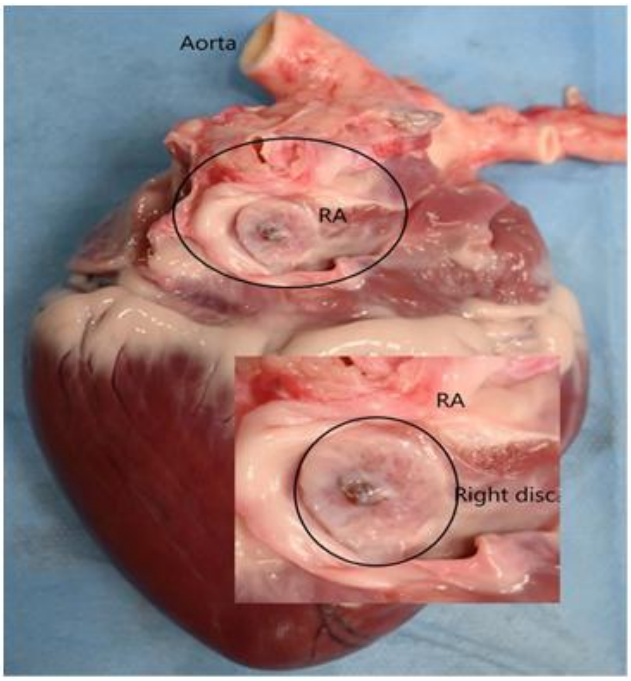

Figure 4: Posterior view of heart showing right atrium with right disc of bioresorbable ASD occluder device of animal on 180th day

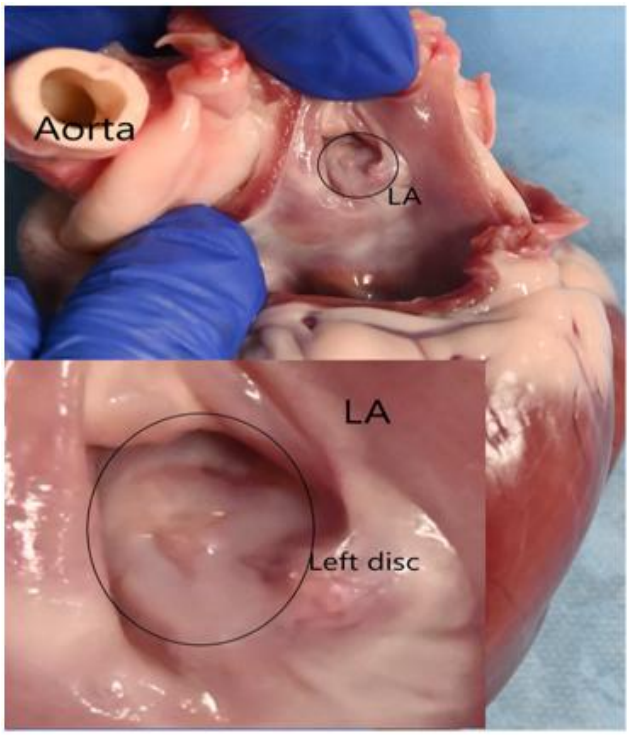

Figure 5: Left lateral view of heart showing left atrium with left disc of bioresorbable ASD occluder device of animal on 180th day.

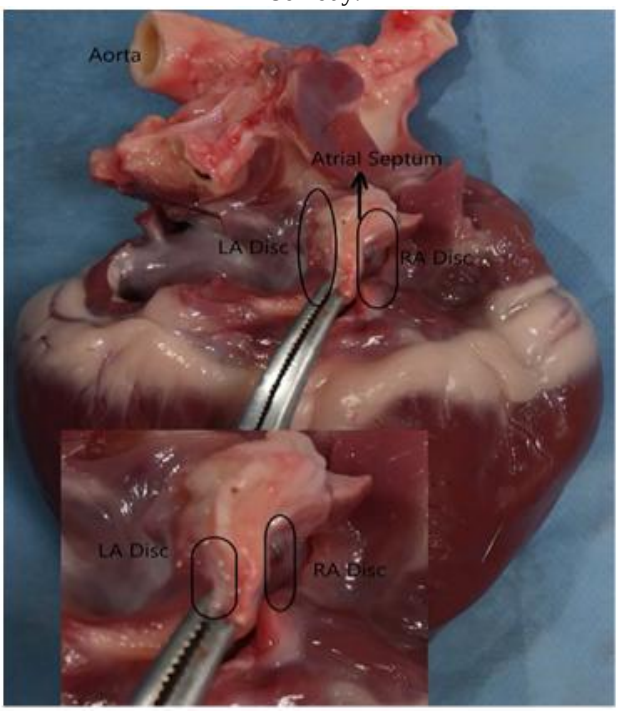

Figure 6: Posterior view of heart showing right and left disc of bioresorbable ASD occluder device in atrial septum of animal on 180th day

Conclusion

Hence, it is concluded that the present research study satisfied the base acknowledgment measures of the study as there was effective implantation of the test things and animal's survival all through the implantation strategy. So the implantation method and results got through this study can be taken as a rule for executing future clinical implantation for useful security or a safety of bioresorbable

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occluder device that can close the defect of atrial septal defect in coronary arteries of a human. This study gave data on the exhibition of bioresorbable ASD occluder device as well as the early residual shunting, thrombosis, pericardial effusion and mitral regurgitation etc.

References

[1] Atrial septal defect closure. Vasquez AF, Lasala JM. Cardiol Clin.2013 Aug; 31 (3): 385 - 400. doi: 10.1016/j. ccl.2013.05.003.
[2] Atrial septal defect closure with an Amplatzer septal occluder fenestrated with a coronary stent in a child with pulmonary arterial hypertension. Skinner GJ, Tulloh RM, Tometzki AJ, Schulze - Neick I, Morgan GJ. Cardiol Young.2013 Oct; 23 (5): 692 - 6. doi: 10.1017/S1047951112001771.
[3] Current practice in atrial septal defect occlusion in children and adults. Alkashkari W, Albugami S, Hijazi ZM. Expert Rev Cardiovasc Ther.2020 Jun; 18 (6): 315 - 329. doi: 10.1080/14779072.2020.1767595.
[4] Assessment of Transcatheter or Surgical Closure of Atrial Septal Defect using Interpretable Deep Keypoint Stadiometry. Wang J, Xie W, Cheng M, Wu Q, Wang F, Li P, Fan B, Zhang X, Wang B, Liu X. Research (Wash D C).2022 Oct 21; 2022: 9790653. doi: 10.34133/2022/9790653.
[5] Catheter intervention for adult patients with congenital heart disease. Akagi T. J Cardiol.2012 Sep; 60 (3): 151 - 9. doi: 10.1016/j. jjcc.2012.06.014.
[6] Transcatheter closure of secundum atrial septal defects: results in patients with large and extreme defects. Romanelli G, Harper RW, Mottram PM. Heart Lung Circ.2014 Feb; 23 (2): 127 - 31. doi: 10.1016/j. hlc.2013.07.020.
[7] Transcatheter closure as an alternative and equivalent method to the surgical treatment of atrial septal defect in adults: comparison of early and late results. Suchon E, Pieculewicz M, Tracz W, Przewlocki T, Sadowski J, Podolec P. Med Sci Monit.2009 Dec; 15 (12): CR612 - 7.
[8] Atrial Septal Defect Repair in Adolescent and Adult Patients, a Cross Sectional Study at Jordan University Hospital, a Tertiary Hospital in a Developing Country. Bani Hani A, Salhiyyah K, Salameh M, Abu Abeeleh M, Al Smady M, Al Rawashdeh M, Abu Fares H, Al - Ammouri I. Int J Gen Med.2022 Mar 30; 15: 3517 - 3524. doi: 10.2147/IJGM. S356502.
[9] Impact of Right Ventricular Dilatation in Patients with Atrial Septal Defect. Nakayama R, Takaya Y, Akagi T, Nakagawa K, Watanabe N, Nobusada S, Matsushita T, Toh N, Kanazawa S, Ito H. J Interv Cardiol.2020 Apr 27; 2020: 9509105. doi: 10.1155/2020/9509105.
[10] Targeted therapy is required for management of pulmonary arterial hypertension after defect closure in adult patients with atrial septal defect and associated pulmonary arterial hypertension. Fujino T, Yao A, Hatano M, Inaba T, Muraoka H, Minatsuki S, Imamura T, Maki H, Kinugawa K, Ono M, Nagai R, Komuro I. Int Heart J.2015; 56 (1): 86 - 93. doi: 10.1536/ihj.14 - 183.
[11] Hemodynamics of patients developing pulmonary arterial hypertension after shunt closure. D'Alto M, Romeo E, Argiento P, Correra A, Santoro G, Gaio G, Sarubbi B, Calabrò R, Russo MG. Int J Cardiol.2013 Oct 9; 168 (4): 3797 - 801. doi: 10.1016/j. ijcard.2013.06.036.
[12] Subsequent shunt closure after targeted medical therapy can be an effective strategy for secundum atrial septal defect with severe pulmonary arterial hypertension: two case reports: strategy for ASD with severe PAH. Taniguchi Y, Emoto N, Miyagawa K, Nakayama K, Kinutani H, Tanaka H, Shinke T, Okada K, Okita Y, Hirata KI. Heart Vessels.2014 Mar; 29 (2): 282 - 5. doi: 10.1007/s00380 - 013 - 0351 - 0.
[13] Comparative changes of pulmonary artery pressure values and tricuspid valve regurgitation following transcatheter atrial septal defect closure in adults and the elderly. Yalonetsky S, Lorber A. Congenit Heart Dis.2009 Jan - Feb; 4 (1): 17 - 20. doi: 10.1111/j.1747 - 0803.2008.00245.
[14] Similar cardiac remodelling after transcatheter atrial septal defect closure in children and young adults. Santoro G, Pascotto M, Caputo S, Cerrato F, Cappelli Bigazzi M, Palladino MT, Iacono C, Carrozza M, Russo MG, Calabrò R. Heart.2006 Jul; 92 (7): 958 - 62. doi: 10.1136/hrt.2005.070169.
[15] Intermediate - term effects of transcatheter secundum atrial septal defect closure on cardiac remodeling in children and adults. Kaya MG, Baykan A, Dogan A, Inanc T, Gunebakmaz O, Dogdu O, Uzum K, Eryol NK, Narin N. Pediatr Cardiol.2010 May; 31 (4): 474 - 82. doi: 10.1007/s00246 - 009 - 9623 - y.
[16] Atrial fibrillation and stroke in adult patients with atrial septal defect and the long - term effect of closure. Nyboe C, Olsen MS, Nielsen - Kudsk JE, Hjortdal VE. Heart.2015 May; 101 (9): 706 - 11. doi: 10.1136/heartjnl - 2014 - 306552.
[17] Incidence and clinical course of thrombus formation on atrial septal defect and patient foramen ovale closure devices in 1, 000 consecutive patients. Krumsdorf U, Ostermayer S, Billinger K, Trepels T, Zadan E, Horvath K, Sievert H. J Am Coll Cardiol.2004 Jan 21; 43 (2): 302 - 9. doi: 10.1016/j. jacc.2003.10.030.
[18] Device closure rates of simple atrial septal defects optimized by the STARFlex device. Nugent AW, Britt A, Gauvreau K, Piercey GE, Lock JE, Jenkins KJ. J Am Coll Cardiol.2006 Aug 1; 48 (3): 538 - 44. doi: 10.1016/j. jacc.2006.03.049.
[19] Effect of percutaneous atrial septal defect and patent foramen ovale device closure on degree of aortic regurgitation. Loar RW, Johnson JN, Cabalka AK, Cetta F, Hagler DJ, Eidem BW, Taggart NW. Catheter Cardiovasc Interv.2013 Jun 1; 81 (7): 1234 - 7. doi: 10.1002/ccd.24779.
[20] Impact of Percutaneous Closure of Interatrial Shunts on Migraine Attacks: Single - Operator Series and Review of the Literature. Manolis AS. Rev Recent Clin Trials.2017; 12 (2): 129 - 138. doi: 10.2174/1574887112666170328124939.

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