

Off-label Use of ADO II® in the Closure of Various Congenital Heart Defects

Author(s)

Özge Pamukcu¹, Süleyman Sunkak², Aydın Tuncay³, Gözde Nur Erkan⁴, Ali Baykan¹, Nazmi Narin⁵

Affiliation(s)

¹Erciyes University School of Medicine, Division of Pediatric Cardiology

²Kayseri City Research and Education Hospital, Division of Pediatric Cardiology

³Erciyes University School of Medicine, Division of Cardiovascular Surgery

⁴Kırıkkale University School of Medicine, Division of Anesthesia

⁵Katip Celebi University School of Medicine, Division of Pediatric Cardiology

Article Information

Article Type: Original Articles

Received: 20.07.2022

Article Group: Pediatric Cardiology

Accepted: 16.09.2022

Available Online: 23.12.2022

Cite this article as: Pamukcu Ö, Sunkak S, Tuncay A, Erkan GN, Baykan A, Narin N. Off-label Use of ADO II® in the Closure of Various Congenital Heart Defects. *J Pediatr Acad* 2022; 3: 114-118.

Abstract

Devices may be used for special purposes different than their production purpose. For instance, Amplatzer Ductal Occluder is actually designed for duct closure and its usage for closing defects other than ductus is named as off-label. The aim of this study is to emphasize off-label use of device: not only for VSD but also for other various defects. This study is designed retrospectively, performed by the evaluation catheterization records of patients in whom ADO II and ADO II-AS devices were used in Erciyes University Medical Faculty Children Hospital, Pediatric Cardiology Department between 2011 and 2018. Patients' demographic criteria: age, weight at the time of procedure was gathered. The diagnosis, size of device, follow-up period and complications were also noted. From April 2011 to March 2018, a total of 122 patients underwent transcatheter closure by ADO II and 66 patients by ADO II AS. The number of PDA closure with ADO II was 48; with ADO II AS were 62. Rest of the procedures were all off-label. Types of off-label procedures performed were: VSD closure, residual mitral cleft closure, Aorta-Right atrium tunnel closure, pulmonary arteriovenous fistula occlusion, aorta-pulmonary window closure, and occlusion of the artery feeding accessory lobe in scimitar syndrome, Gerbode defect occlusion. Up to our knowledge; this study includes the largest pediatric case series with various different congenital heart defects which were closed with ADO II. Also our ADO-II occluded VSD case series is one of the largest series in the literature with almost 6 years' follow-up. We believe in that ADO-II device may be an alternative in percutaneous closure of various rare heart defects. It is used successfully for non-ductal defects with low complication and high compliance rates.

Keywords: ADO II, congenital heart defect, Gerbode defect, pulmonary arteriovenous malformation, mitral valve cleft



Correspondence: Suleyman Sunkak, Kayseri City Research and Education Hospital
Division of Pediatric Cardiology, Kayseri, Turkey
E-mail: suleymansunkak@gmail.com

Introduction

Off-label use is a term used for the treatment modalities or drugs for an unapproved indication or in an unapproved age group, route of administration or dosage. This is a legal issue unless breaks ethical guidelines or safety regulations. The ability to use a treatment modality beyond the officially approved indications is commonly used to good effect by healthcare professionals. Usage Amplatzer Ductal Occluder for the occlusion of defects other than PDA is off label. Safety and efficiency of ADO II and ADO II AS in PDA closure have been discussed before in literature.¹⁻⁴ However, the number of reports concerning off-label use of ADO II and ADO II AS is very limited especially in pediatric age group. According to our knowledge, this study is the largest one that discuss the off-label use of ADO II and ADO II AS in children. The aim of this study is to emphasize the usage of off-Label devices in congenital heart defects by giving different case examples.

Material and Method

It is a retrospective study. During the time interval beginning from 2011 to 2018 we have used ADO II and ADO II-AS devices (St. Jude Medical, St. Paul, MN) for off-label uses in our department. We have collected the demographic data (age, weight etc), the diagnosis, device type, size, time of follow-up period and the complications of the patients.

Erciyes University Ethic Committee approved our study (Decision No: 2019-730). A written informed consent was taken from all parents before each procedure.

Before the catheterization; detailed work-up was done. We had to use computed tomography only in the patient with Scimitar syndrome in order to determine the artery supplying accessory lobe before the procedure.

The devices used in the study were ADO II and ADO II AS (St Jude Medical, Inc.; Plymouth, MN, USA).

Physical examinations, electrocardiogram, and transthoracic echocardiography were performed before and after the procedure and repeated in 3 months' interval till 1 year and then yearly thereafter.

Results

During the time interval between April 2011 to March 2018: total defect closure by ADO II device was 122 and ADO II AS device was 66. The 48 of total 122 cases with ADO II Device was PDA and 62 of 66 cases with ADO II AS was PDA. The main procedures that ADO II device used for off label were the closure of VSD, Gerbode defect, residual mitral cleft, aorta-pulmonary window, Aorta-Right atrium tunnel, pulmonary arteriovenous fistula, closure, artery feeding accessory lobe in Scimitar syndrome, occlusion.

VSD Closure

Till April 2011 ventricular septal defects have been closed percutaneously with ADO-II device in our hospital. Procedures were performed according to the indications and techniques we used, which were mentioned in our previous studies.^{5,6}

The number of VSD closure with ADO II was 68, with ADO II-AS was 3 till now. The age and weight of patients was 83 months (48-120), 23 kg (13-27) respectively.

Highlights

- ADO II device has been used safely in PDA occlusion for many years.
- This device can also be used for occlusion of rare different congenital heart defects.
- However, since these defects are very rare and the procedure is likely to be risky, it is best to perform the procedure in experienced centers and by experienced pediatric interventional cardiology teams.

Twelve of these patients were less than 1 year of age (10 were closed with ADO II, 2 with ADO II AS).

Aorta-RA tunnel Closure

A newborn baby was admitted to emergency with tachypnea, respiratory insufficiency. Aorta-right atrium tunnel was diagnosed by TTE. The orifice of aorta right atrium tunnel was occluded with 5 × 6 ADO II AS from retrograde side.⁷

Mitral Cleft Closure

18-month-old infant operated for incomplete AVSD when he was 6-month-old. After surgery he had residual mitral cleft and second degree regurgitation through cleft, first degree insufficiency through mitral valve. Left chambers of the heart were enlarged. Family did not want their boy to have a second operation. Therefore; we have decided to close mitral cleft percutaneously. From femoral arterial route, delivery system was placed to pulmonary vein passing through mitral cleft. 3 mm × 4 mm ADO-II was used to occlude mitral cleft by transthoracic echocardiography guidance (**Video 1**). Up to our knowledge it is the first case whose mitral cleft was closed percutaneously.



Video 1: The mitral cleft was occluded using a 3×4 ADO-II device with transthoracic Echocardiography guidance.

Pulmonary Arteriovenous Malformation Closure

6-month-old infant was recognized that she was cyanotic during her vaccination. Transcutaneous oxygen saturation was 60%. All secondary causes of cyanosis were discarded. Transthoracic echocardiography and chest X ray revealed normal. Pulmonary Arteriovenous malformation was found by CT. The angiographic imaging revealed four major arteriovenous connections in the-left-lower-lobe. The largest two were closed with two separate devices: 6 mm × 6 mm ADO II and 5 mm × 6 mm ADO II (**Video 2**). Oxygen saturation of patient was increased to 98% and discharged from hospital.



Video 2: Two large pulmonary arteriovenous malformation were closed with two separate devices, one 6×6 ADO-II and one 5×6 ADO-II

Aorta-pulmonary window Occlusion

Five years old boy was admitted to the clinic with heart murmur, tachycardia and tachypnea. It was learnt from parents that he had undergone surgical repair of aortopulmonary window at 2 years of age. He was found to have a residual defect by transthoracic echocardiography, left chambers were enlarged and second degree mitral insufficiency was present. Treatment options were discussed with family and transcatheter closure was planned. Aorta-pulmonary window was closed through arterial side with 6 mm × 4 mm ADO II device successfully.

Occlusion of the artery feeding accessory lobe in scimitar syndrome

13 years old girl admitted to our clinic for dyspnea. Dextrocardia and hypoplasia of right lung was seen in chest X ray. Transthoracic echocardiography revealed that right pulmonary veins abnormally connected to the IVC. Therefore; in suspicion of Scimitar syndrome CT was performed and confirmed the diagnosis. Treatment options were discussed with family. Family did not want to have cardiac surgery; therefore, we decide perform percutaneous closure. Artery supplying accessory lobe was occluded with 6 mm × 4 mm ADO II device (**Figure 1**). After closure her symptoms were relieved. 2 months' later control CT demonstrated that sequestered lung lobe was decreased significantly.



Figure 1: The artery-supplying accessory lobe was occluded with a 6×4 ADO-II device in Scimitar Syndrome.

Gerbode defect occlusion

Ten years old boy, operated for VSD 3 years ago. He admitted to the hospital for respiratory difficulty and grade 3 holosystolic murmur. Left side of the heart was enlarged therefore we have decided to occlude the defect. We have discussed the parents about treatment method (surgery and transcatheter method). Family

did not want to have surgery. Qp/Qs ratio of the patient was calculated as 1.9. Narrowest diameter of Gerbode defect (LV to RA shunt) was measured as 2 mm. The distance of the defect to aortic valve was 6 mm. The defect was occluded with 4 mm × 4 mm ADO II (AGA Medical) device.

Discussion

Amplatzer Duct Occluder-II is originally designed for PDA closure however; recently its off-label uses increase in number. The main reasons that improves its popularity are: it is flexible, is easy to proceed through angulations, requires 4F or 5F Amplatzer® TorqVue® LP Delivery Sheath (St. Jude Medical, Plymouth, MN, USA). Therefore, using ADO II makes the procedure easier, delivery is more comfortable, and smaller sheath size decrease vascular complications.⁷ Also it is suitable for either vascular delivery.

Its improved form, the ADO II additional sizes (ADO II-AS) (St. Jude Medical, Inc.; St. Paul, Minnesota, USA) have discs that has low risk to protrude into surrounding vessels (peripheral pulmonary arteries or aorta).⁸

Most popular off-label use of ADO II is VSD occlusion. It is preferred mainly for treating aneurysmatic VSDs even when they are adjacent to aortic valve. Vijayalakshmi et al.⁹ reported VSD closure using ADO-II. They have occluded perimembranous, apical/mid muscular and Gerbode defects. The major challenge in percutaneous perimembranous VSD closure is heart block. They told that unlike the other occluder devices ADO II device because of its soft structure it does not apply pressure on the conducting system. Kanaan et al.¹⁰ have used ADO II device for 31 patients in 8-year time interval. Baspinar et al.¹¹ used ADO II for only 3 patients, 2 of them were muscular VSD and the other one was aneurysmatic perimembranous VSD. Mahmoud et al.¹² reported percutaneous closure of one muscular ventricular septal defect with ADO II AS.

We have both published our center early and midterm results of transcatheter VSD closure with ADO II.^{5,13} Between April 2011 and October 2016 VSD closure of 49 patients with ADO-II device was performed and 7 of them were <1-year-old.¹³ This number is now increased to 71. Amplatzer Ductal Occluder II was used for 68 of these patients and ADO II-AS was used for 3 patients. Twelve of these 71 patients were less than 1 year of age. The procedure and follow-up results of this age group were recently published.⁶

Gerbode defect is a connection between right atrium and left ventricle. It is accepted as different type of VSD. It is usually acquired secondary to cardiovascular surgery, endocarditis rarely to the trauma. Congenital forms are very rare. The gold standard treatment is surgery but the risk of complications is high. In recent years' percutaneous closure of these defects have been performed in adults but not so common in children. Vijayalakshmi et al reported percutaneous closure of 4 patients with Gerbode defect. Only one patient of Gerbode defect developed transient complete heart block.

Our case is the first pediatric example reported in Turkey that percutaneous acquired Gerbode defect occlusion was performed. Percutaneous closure of Gerbode defects is another option for off-label use of ADO II.

Aorta–right atrial tunnel is a rare congenital defect and etiology is unknown. Surgery is the gold standard treatment. Previously the first percutaneous aorta–right atrial tunnel closure with a coil was reported.¹⁴ The youngest child was 4-day old newborn whose tunnel closed with transcatheter method by Mahesh et al.¹⁵ In our institution the first transcatheter aorta–right atrial tunnel closure was done with the Amplatzer Vascular Plug 4 device.¹⁶ The case in our study was the first one in our center that we have used ADO II for closure.

Vijayalakshmi et al also reported one case with aorta–RV tunnel that they closed with ADO II device.

Pulmonary arteriovenous malformations (PAVM) are the abnormal vascular connections between the pulmonary artery and pulmonary vein that may cause right-to-left shunts and rarely seen in children. Percutaneous closure is preferred treatment modality for these children because success rate is high and complication rate is low.¹⁷ Various different devices were used for closure like coils, vascular plugs and ductal occluders I and II.^{18–20} Beck et al.²⁰ closed a total of 14 PAVMs (11 ADO I and 3 vascular plugs) in five adult patients. They defined that Amplatzer Ductal Occluder and vascular plugs are safe and effective in the closure of PAVMs in the acute setting and at intermediate follow-up. Giordano et al reported a 5-month-old infant with PAVM. They used ADO II AS and Amplatzer vascular plug for closure.²¹ We have used 6 mm × 6 mm ADO II and 5 mm × 6 mm ADO II for closure of 2 PAVM in a 6-month-old infant.

Aorto-pulmonary window (APW) is a rare congenital heart defect which results left-to-right shunt and typically present within the first weeks or months of life because of congestive heart failure. Transcatheter closure of APW has been done for a while. Various devices, coils, vascular plug, symmetrical membranous ventricular septal occluder have been used to occlude APW.²² Firstly, transcatheter closure of postsurgical residual defects was reported.²³ Later on; Nayak et al.²⁴ shared their experience of transcatheter native congenital APW closure via antegrade and retrograde routes using ADO II. They reported that ADO II was a suitable device because retention discs of each side are in equal size that is advantageous for retrograde closure of APW in young children. There are only case reports about APW closure in pediatric age group in the literature.

The other various defects that we used ADO II off-label were: occlusion of the artery feeding accessory lobe in scimitar syndrome and residual mitral cleft closure. These two procedures are unique that we cannot find any similar case in the literature.

Conclusion

Our study has summarized different off-label usages of ADO II device. It is important to give an idea to the clinicians in the occlusion of various non-ductal defects especially in the centers where the opportunities are restricted.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Conflict of Interest: There are no conflicts of interest in connection with this paper, and the material described is not under publication or consideration for publication elsewhere.

Ethics Committee Approval: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation (Turkey) and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees (Erciyes University clinical research ethics committee, 2019/730).

Financial Disclosure: The authors have no conflicts of interest to declare.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

References

1. Baruteau AE, Hascoët S, Baruteau J, et al. Transcatheter closure of patent ductus arteriosus: past, present and future. *Arch Cardiovasc Dis.* 2014;107:122-132. [\[CrossRef\]](#)
2. Bruckheimer E, Godfrey M, Dagan T, Levinzon M, Amir G, Birk E. The Amplatzer Duct Occluder II Additional Sizes device for transcatheter PDA closure: initial experience. *Catheter Cardiovasc Interv.* 2014;83:1097-1101. [\[CrossRef\]](#)
3. Eleftherakis NG, Vekiou A. Transcatheter closure of patent arterial duct with amplatzer duct occluder II additional sizes in children. *J Invasive Cardiol.* 2013;25:96-97. [\[CrossRef\]](#)
4. Sungur M, Karakurt C, Ozbarlas N, Baspinar O. Closure of patent ductus arteriosus in children, small infants, and premature babies with Amplatzer duct occluder II additional sizes: multicenter study. *Catheter Cardiovasc Interv.* 2013;82:245-252. [\[CrossRef\]](#)
5. Narin N, Baykan A, Pamukcu O, et al. ADO II in Percutaneous VSD Closure in Pediatric Patients. *J Interv Cardiol.* 2015;28:479-484. [\[CrossRef\]](#)
6. Narin N, Pamukcu O, Tuncay A, et al. Percutaneous Ventricular Septal Defect Closure in Patients Under 1 Year of Age. *Pediatr Cardiol.* 2018;39:1009-1015. [\[CrossRef\]](#)
7. Narin N, Pamukcu O. Percutaneous closure of aorta-right atrial tunnel in a newborn. *Cardiol Young.* 2018;28:142-143. [\[CrossRef\]](#)
8. St. Jude Medical Corporation. Amplatzer Duct Occluder II AS 2013. [\[CrossRef\]](#)
9. Vijayalakshmi IB, Narasimhan C, Singh B, Manjunath CN. Treatment of congenital non-ductal shunt lesions with the amplatzer duct occluder II. *Catheter Cardiovasc Interv.* 2017;89:E185-E193. [\[CrossRef\]](#)
10. Kanaan M, Ewert P, Berger F, Assa S, Schubert S. Follow-up of patients with interventional closure of ventricular septal defects with Amplatzer Duct Occluder II. *Pediatr Cardiol.* 2015;36:379-385. [\[CrossRef\]](#)
11. Baspinar O, Irdem A, Kilinc M. Off-label use of Amplatzer devices in congenital heart disorders during childhood. *Acta Cardiol.* 2013;68:31-35. [\[CrossRef\]](#)
12. Mahmoud HT, Santoro G, Capogrosso C, Russo MG. Off-label use of Amplatzer Duct Occluder II additional sizes. *J Cardiovasc Med (Hagerstown).* 2017;18:436-442. [\[CrossRef\]](#)
13. Pamukcu O, Narin N, Baykan A, Sunkak S, Tasci O, Uzum K. Mid-term results of percutaneous ventricular septal defect closure with Amplatzer Duct Occluder-II in children. *Cardiol Young.* 2017;27:1726-1731. [\[CrossRef\]](#)
14. Sreedharan M, Baruah B, Dash PK. Aorta-right atrial tunnel a novel therapeutic option. *Int J Cardiol.* 2006;107:410-412. [\[CrossRef\]](#)

15. Mahesh K, Francis E, Kumar RK. Aorta to right atrial tunnel prenatal: diagnosis and transcatheter management in a neonate. *JACC Cardiovasc Interv.* 2008;1:716–717. [\[CrossRef\]](#)
16. Baykan A, Narin N, Ozyurt A, Uzum K. Aorta-right atrial tunnel closure using the transcatheter technique: a case of a 3-year-old child. *Cardiol Young.* 2013;23:457-459. [\[CrossRef\]](#)
17. Pollak JS, Saluja S, Thabet A, Henderson KJ, Denbow N, White RI Jr. Clinical and anatomic outcomes after embolotherapy of pulmonary arteriovenous malformations. *J Vasc Interv Radiol.* 2006;17:35-45. [\[CrossRef\]](#)
18. Heidari R, Behjati M, Balouchi A. Meticulous observations essential before and after coil embolization of pulmonary arteriovenous malformation; lessons learned from two cases. *ARYA Atheroscler.* 2017;13:44-45. [\[CrossRef\]](#)
19. Andersen PE, Kjeldsen AD. Occlusion of pulmonary arteriovenous malformations by use of vascular plug. *Acta Radiol.* 2007;48:496-499. [\[CrossRef\]](#)
20. Beck A, Dagan T, Matitau A, Bruckheimer E. Transcatheter closure of pulmonary arteriovenous malformations with amplatzer devices. *Catheter Cardiovasc Interv.* 2006;67:932-937. [\[CrossRef\]](#)
21. Giordano M, Santoro G, Palladino MT, Russo MG. Arterial duct and pulmonary arteriovenous malformations: A shunt masking a shunt. *Ann Pediatr Cardiol.* 2018;11:89-91. [\[CrossRef\]](#)
22. Xu HX, Zheng DD, Pan M, Li XF. Transcatheter Treatment of Aortopulmonary Window with a Symmetrical Membranous Ventricular Septal Occluder. *Cardiology.* 2017;138:76-79. [\[CrossRef\]](#)
23. Noonan PM, Desai T, Degiovanni JV. Closure of an aortopulmonary window using the Amplatzer Duct Occluder II. *Pediatr Cardiol.* 2013;34:712-714. [\[CrossRef\]](#)
24. Nayak HK, Islam N, Bansal BK. Transcatheter closure of aortopulmonary window with Amplatzer duct occluder II. *Ann Pediatr Cardiol.* 2017;10:93-94. [\[CrossRef\]](#)