Amplatzer Piccolo™ Occluder

CLINICAL COMPENDIUM

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AMPLATZER PICCOLO™

AMPLATZER PICCOLO™ OCCLUDER – OVERVIEW OF PUBLISHED CLINICAL DATA

The Amplatzer Piccolo™ Occluder[1] is a percutaneous transcatheter occlusion device intended for the non-surgical closure of a patent ductus arteriosus (PDA) in infants ≥700 grams. The ductus arteriosus is a blood vessel present in the fetal circulation connecting the pulmonary artery and the aorta. While this connection usually closes after birth, it may remain patent in approximately 1 in 2000 newborns, and more frequently in premature neonates, resulting in a PDA. A PDA may result in a significant left-to-right shunt, producing symptoms of heart failure. A hemodynamically significant PDA has been associated with increased morbidity and mortality in infants.

Currently, the Amplatzer Piccolo Occluder is the only device approved by the FDA for PDA closure in patients <5 kg or <5 months, encompassing most infants, neonates and premature neonates. The device is a line extension to the ADO II device, intended for closure of a PDA with a diameter ≤4 mm and a length ≥3 mm. The device can be delivered via an anterograde (venous) or retrograde (arterial) approach and its design is well suited to the anatomy of the PDA in the smallest infants, including premature infants, weighing 0.7 – 2 kg. The device is available in short lengths (2, 4 and 6 mm) which may greatly reduce the risk of descending aortic or left pulmonary artery (LPA) stenosis that can be caused by device protrusion from either end of the PDA in these small patients. To minimize the risk of device protrusion the entire device is implanted within the duct (intraductal) in infants ≤2 kg. In larger children (>2 kg) the device is implanted so that it spans the entire length of the duct and the discs are positioned just outside the duct (extraductal), thereby minimizing the risk of device embolization. This clinical compendium provides an overview of scientific literature reporting on the clinical application of the Amplatzer Piccolo Occluder and Amplatzer Duct Occluder II Additional Sizes (ADO II AS) in a variety of patients, including premature infants, children, and older patients.

AMPLATZER PICCOLO OCCLUDER CLINICAL TRIAL FOR PERCUTANEOUS CLOSURE OF THE PATENT DUCTUS ARTERIOSUS IN PATIENTS ≥700 GRAMS

Sathanandam SK et al. *Catheter Cardiovasc Interv* 2020[1] May 20. doi: 10.1002/ccd.28973. Online ahead of print

- This article reports on a clinical trial to evaluate the safety and effectiveness of the Amplatzer Piccolo Occluder in support of FDA approval of the device for patients ≥700 g. The study was designed as a single arm, prospective, multicenter, non-randomized clinical investigation.
  - A total of 200 patients were enrolled from 9 centers. (Mean age: 3.92 ± 33.74 months, mean weight: 6.25 kg, 51% male, min/max PDA diameter: 2.6 ± 0.7 / 4.6 ± 1.5 mm, mean PDA length: 10.4 ± 2.9 mm).
  - 100 of the 200 total patients were ≤2 kg at the time of the procedure.
  - The youngest patient was 10 days old, with the smallest patient weighing 700 g. And 33 patients ≤1 kg at the time of the procedure.
- All patients underwent an implant attempt using the Amplatzer Piccolo Occluder.
  - Patients ≤2 kg: Successful implantation in 99% of the patients. Anterograde approach was used in all successful procedures, and femoral arterial access was used in 2% of the patients. The shortest devices (2 mm) were used in 83.8% of the patients.
  - Patients >2 kg: Successful implantation in 92% of the patients. Anterograde approach was used in 73.9% of successful procedures, with femoral arterial access used in 48% of the patients. Using a wider range of device sizes compared with patients ≤2 kg, the longest devices (6 mm) were used in only 11 patients.
- Intraprocedural device embolization occurred in 2% and 3% of patients ≤2 kg and >2 kg, respectively. All embolized devices were successfully snared and retrieved with no need for an open surgical procedure. Post-procedure device migration after successful device implantation was reported from 2 patients (1 each in patients ≤2 kg and >2 kg).
- At 6-month follow-up, effective closure was observed in 100% and 98.8% of patients ≤2 kg and >2 kg, respectively. Effective closure was assessed by an independent core laboratory from transthoracic echocardiography and defined as no or trivial residual PDA shunt.
- Major complications, independently adjudicated by a clinical events committee, occurred only in patients ≤2 kg, at a rate of 4.2%. Complications meeting the primary safety endpoint included device-related aortic obstruction (n=1), blood loss requiring transfusion (n=2) and hemolysis secondary to residual shunting through the device (n=1). Five patients developed new onset moderate tricuspid regurgitation.
- The overall survival at 6 months in this cohort was 96% and 98% for patients ≤2 kg and <2 kg, respectively.

[1.] Frequently referred to in the literature as the ADO II AS device.

- The authors concluded that the outcomes of this study support the safety and effectiveness of the Amplatzer Piccolo Occluder, particularly in patients ≤2 kg.

PERCUTANEOUS CLOSURE OF PATENT DUCTUS ARTERIOSUS IN PREMATURE INFANTS: A FRENCH NATIONAL SURVEY

Malekzadeh-Milani S et al. *Catheter Cardiovasc Interv* 2020[2]

- In a French four-center retrospective study PDA closure was performed in 102 premature infants.
  - 21 patients ≤1 kg, mean age: 39 ± 26 days, procedural weight: 0.880 ± 0.105 kg, PDA diameter (pulmonary side / aortic side): 3.2 mm / 3.2 mm.
  - 59 patients between 1 and 2 kg, mean age: 32 ± 13 days, procedural weight: 1.334 ± 0.234 kg, PDA diameter: 2.8 / 3.1 mm.
  - 22 patients >2 kg, mean age: 71 ± 32 days, procedural weight: 2.707 ± 0.413 kg, PDA diameter: 2.8 / 3.6 mm.

- PDA closure procedures were performed using the ADO II AS device in 91 patients, a microvascular plug (MVP, Medtronic) in 10 patients and coils in 1 patient. Implant success was achieved in 99% of the procedures. In 1 case, using the largest available ADO II AS device in a patient >2 kg, the device was retrieved because of a large residual shunt and unstable device placement. Across all procedures there were no embolizations and from the cases with implant success no residual shunts were reported. The ADO II AS devices were placed entirely within the PDA without any disc in the pulmonary artery or aorta.

- There were a total of 8 complications, including LPA stenosis (3 patients), mild gradient on the aortic isthmus with no hypertension or left ventricular hypertrophy (1 patient), tricuspid regurgitation (3 patients) and aortic coarctation (1 patient treated with a MVP). There were no procedural complications leading to severe permanent cardiac lesions and the complication rate was similar between the 3 groups.

- At a mean follow-up of 39.8 ± 13.1 months 7 deaths occurred, which were not directly attributed to the procedure. Mortality was similar between the 3 groups and appeared to be primarily related to the patient status prior to the procedure rather than the procedure itself.

- The authors concluded that transcatheter PDA closure is feasible in a large population of premature infants and provides good results even in smaller infants.

IMPROVED VENTILATION IN PREMATURE BABIES AFTER TRANSCATHETER VERSUS SURGICAL CLOSURE OF PATENT DUCTUS ARTERIOSUS

Regan W et al. *Int J Cardiol* 2020[3]

- The authors reported on a retrospective analysis of PDA closure in 147 babies in 3 European centers, comparing:
  - Transcatheter closure in 64 patients, median procedural weight: 1200 g
  - Surgical closure in 83 patients matched with transcatheter cases based on procedural weight and gestational age at birth, median procedural weight: 1100 g.

- All transcatheter closure procedures were performed using the Amplatzer Piccolo Occluder. Successful closure was achieved in 63 of the 64 transcatheter procedures (98.4%). A single case was not successful because the device was too small and unstable.

- There were no procedural deaths associated with transcatheter PDA closure. A total of 14 complications in 13 patients (20.3%) were reported from transcatheter closure:
  - Mild LPA stenoses due to device protrusion (n=6).
  - Left femoral vein thrombosis which spontaneously resolved with no treatment (n=1).
  - Device migration to the LPA, with successful percutaneous retrieval (n=2).
  - Tricuspid valve trauma and regurgitation (n=2). One of these patients had additional worsening of pre-existing LPA stenosis.
  - Aortic arch obstruction (n=2). In 1 patient mild obstruction resolved on follow-up. Another patient was treated surgically.

  For comparison, surgical ligation was successful in all 83 cases with no procedural deaths and 18 complications in 16 patients (19.3%).

- Transcatheter closure was associated with significantly shorter duration of postprocedural mechanical ventilation than surgical ligation (3 vs. 5 days, p = 0.035). This difference was even more pronounced for babies <4 weeks of age at the time of the procedure. Babies <4 weeks old were also discharged at an earlier corrected gestational age as compared to those undergoing closure later in life. This difference was not observed in patients undergoing surgical closure.

- The authors concluded that transcatheter closure of PDA offers sustained improvement in morbidity as compared to surgical ligation through a reduction in post-procedural mechanical ventilation time that is significant throughout their total stay in the neonatal intensive care unit. This improvement is more pronounced in younger patients with an additional benefit of shorter length of hospital stay.

PATENT DUCTUS ARTERIOSUS CLOSURE IN PRETERMS LESS THAN 2 KG: SURGERY VERSUS TRANSCATHETER

Pamukcu O et al. *Int J Cardiol* 2018[4]

- This single center study retrospectively compared safety and efficacy of surgical versus percutaneous PDA closure in preterms <2 kg.
  - Percutaneous closure: 26 patients, mean age: 27.6 ± 17.9 days, median weight: 1455 g (967 – 1770 g), 61.5% male, mean PDA diameter: 2 ± 0.62 mm (1 – 4 mm).
  - Surgical closure: 31 patients, mean age: 31.3 ± 13 days, median weight: 1254 g (920 – 1755 g), 35.5% male, mean PDA diameter: 2.9 ± 0.49 mm (1.9 – 4 mm).

- In the percutaneous closure group, the ADO (n=1) and ADO II AS (n=25) devices were used. Vascular access was most frequently achieved by venous approach (n=16), and by combined venous and arterial access in 8 cases and umbilical approach in 2 cases. Closure was successful in 22 cases (84.6%). Two device embolizations occurred: 1 device embolized 24 hours after the procedure and was retrieved percutaneously, and 1 patient was referred to surgery. Other major complications included right atrial perforation and iatrogenic aortic coarctation (n=1). Device-related pulmonary stenosis was recorded as a minor complication in 2 patients.

- In the surgical closure group, major complications included pneumomediastinum and chylothorax (1 of each). Patients in the surgery group had a significantly lower weight and gestational age compared to those treated with percutaneous closure, which may have affected the success rate in the surgery group.

- No statistically significant difference was found between success rates of percutaneous and surgical PDA closure. Because of the complications of prematurity, additional medical support was required in both groups. There were no procedure-related deaths in either group.

- At a mean follow-up period of 18.8 ± 16.3 months for the percutaneous closure group, 1 patient died (severe lung problems, sepsis and multiorgan failure) and 2 were still hospitalized.

- The authors concluded that percutaneous PDA closure is a safe and effective alternative to surgery in preterms weighing <2 kg.

SURGICAL LIGATION VERSUS PERCUTANEOUS CLOSURE OF PATENT DUCTUS ARTERIOSUS IN VERY LOW-WEIGHT PRETERM INFANTS: WHICH ARE THE REAL BENEFITS OF THE PERCUTANEOUS APPROACH?

Rodrıguez Ogando A et al. *Pediatr Cardiol* 2018[5]

- This was a single center, retrospective review of cases involving preterm infants undergoing PDA surgical ligation or percutaneous PDA closure using the ADO II AS device.
  - Percutaneous closure: 25 patients, gestational age: 26.5 ± 1.2 weeks, mean weight: 919 ± 223 g (all patients were <2 kg). Mean ductal diameter: 1.7 mm (1.0 – 2.5 mm).
  - Surgical ligation: 53 patients, gestational age: 25.8 ± 2 weeks, mean weight: 792 ± 251 g.
  - Subgroup of surgical ligation patients <2 kg: 28 patients, gestational age: 26.5 ± 2.4 weeks, weight: 879 ± 297 g (not significantly different in gestational age and weight from patients undergoing percutaneous closure).

- Outcomes were compared between percutaneous closure and patients <2 kg undergoing surgical ligation.

- In the group undergoing percutaneous closure, there were no major procedural complications.
  - Device embolization, recovery and successful closure: 2 patients.
  - Slight protrusion of the device in left pulmonary artery: 4 patients.
  - No complications related to vascular access. A small residual shunt (<3 mm) was seen in 3 patients.

- Pulmonary score (a validated score to evaluate basal pulmonary state, accounting for medication use, quantity of supplementary oxygen and type of ventilatory support) improved in patients undergoing percutaneous closure and surgical ligation, with an earlier improvement in the percutaneous group, beginning immediately after closure.

- Surgical ligation was associated with higher postnatal morbidity rates than those undergoing percutaneous closure, with significantly higher grade 3 - 4 intraventricular hemorrhage rate and inotropic therapy duration. The rate of recurrent vocal cord paralysis was 17% in the surgical ligation group vs. 0% with percutaneous closure.

- Percutaneous closure was associated with lower hospital mortality rates before 36 weeks of post-menstrual age. However, this effect was not significant when accounting for antenatal, perinatal and postnatal variables. Mortality in the surgical ligation group was related with sepsis and early respiratory failure.

- It was concluded that, compared with surgical ligation, percutaneous PDA closure had greater positive impact on pulmonary recovery and lower negative impact on hemodynamics and was associated with lower morbidity and mortality.

ARE THE AMPLATZER DUCT OCCLUDER II ADDITIONAL SIZES DEVICES DEDICATED ONLY FOR SMALLER CHILDREN?

Fiszer R et al. *EuroIntervention* 2017[6]

- This article reported on PDA closure using the ADO II AS device in 103 patients in 2 centers (66% female, mean age: 4.7 ± 4.7 years, range 0.1 – 24 years, median weight: 14.6 kg, range 2 – 80 kg). The cohort included 9 infants (<6 months), 39 children aged 6 months to 3 years and 55 patients >3 years. Among the older patients there were 10 teenagers and 3 adult patients. The mean ductal diameter was 2.0 ± 0.6 mm and the mean length was 6.3 ± 2.7 mm.

- In all but 3 procedures an arterial access was used. Devices were successfully implanted in 98.1% of the procedures. In 1 patient 2 devices were used. Implant failures (n=2) were related to device embolization, probably related to duct spasm during aortography and underestimation of its diameter.

- There was 1 death unrelated to the PDA occlusion. Transient pedal pulse loss requiring heparin infusion was seen in 3 patients.

- Complete ductal closure was observed at 1 day post-procedure. At a median follow-up duration of 6 months there was no obstruction or Doppler flow acceleration in the aorta or LPA.

- The authors commented that the ADO II AS may be used as an alternative to coil implantation in all age groups, given the fact that the device achieves highly effective PDA closure and a low complication rate.

SINGLE-CENTER EXPERIENCE IN PERCUTANEOUS CLOSURE OF ARTERIAL DUCT WITH AMPLATZER DUCT OCCLUDER II ADDITIONAL SIZES

Mahmoud HT et al. *Catheter Cardiovasc Interv* 2017[7]

- This article reported on the single center experience with percutaneous PDA closure using the ADO II AS device in 109 patients (4.8 ± 8.1 years, 20.7 ± 19.4 kg, 58.7% female). Fifteen patients (13.8%) were ≤6 kg. The mean ductal diameter was 2.2 ± 0.67 mm (range: 1.5 – 4.5 mm).

- The device was successfully implanted in 98.2% of the cases. Two failures occurred, one device prolapsed before final release and one device embolized soon after release.

- There were no procedural complications. No differences in ductal dimensions and procedural and follow-up data were found between patients ≤6 kg and >6 kg, except for a significantly shorter procedural duration in patients >6 kg (40.9 ± 12.4 min vs. 64.4 ± 28.7 min).

- Complete occlusion was achieved immediately in 71% of the patients. 100% of the patients had complete occlusion at their last echocardiographic follow-up (30 ± 17 months). There were no late-onset complications at mid-term follow-up.

- The authors conclude that the ADO II AS device is a safe, effective and versatile therapeutic tool for transcatheter closure of small-to-moderate sized ducts, even in challenging settings. The device is associated with high mid-term occlusion rates and no late-onset complications.

TRANSCATHETER CLOSURE OF HEMODYNAMIC SIGNIFICANT PATENT DUCTUS ARTERIOSUS IN 32 PREMATURE INFANTS BY AMPLATZER DUCTAL OCCLUDER ADDITIONAL SIZE-ADOIIAS

Morville P et al. *Catheter Cardiovasc Interv* 2017[8]

- In this study, the ADO II AS device was used for PDA closure in 32 neonates weighing <2500 g (mean gestational age: 28 ± 3 weeks, mean age at procedure: 25 days, mean weight at birth/procedure: 1054 ± 406 g / 1373 ± 535 g, 10 patients weighed ≤1000 g). The mean ductal diameter was 3.2 ± 0.6 mm (2.2 – 4 mm).

- In 31 patients the device was successfully implanted (96.9%). Complications included hemopericardium related to right ventricular perforation by a 4F vertebral catheter (n=1), LPA obstruction (n=1) and transit LPA aliasing (n=2). The patient with hemopericardium (20 days old premature infant weighing 680 g with pre-existing multiorgan failure) died within 6 hours after the procedure. Six patients had periprosthetic (n=3) or intraprosthetic (n=3) shunts, immediately after closure. All shunts closed after 24 hours. One patient had transient bleeding around the introducer requiring transfusion.

- During follow-up 4 patients died due to complications of prematurity (renal failure, hepatorenal and cardiac failure, fulminant necrotizing enterocolitis, sudden death).

- The authors conclude that their results show the feasibility, relative safety and efficacy of closing a hemodynamically significant PDA with the ADO II AS device in very small premature infants.

CATHETER CLOSURE THROUGH A VENOUS APPROACH OF PATENT DUCTUS ARTERIOSUS IN SMALL PEDIATRIC PATIENTS USING COMBINED ANGIOGRAPHIC AND ECHOCARDIOGRAPHIC GUIDANCE

Thanopoulos BD et al. *Am J Cardiol* 2016[9]

- This multicenter (n=4) study evaluated whether PDA closure using an exclusive venous approach is a safe and effective alternative to the standard technique involving arterial access, which may be associated with arterial complications, particularly in small pediatric patients. 122 patients were randomized to the standard technique (n=56, median age: 8 months, median weight: 4.3 kg) or exclusive venous approach (n=56, median age: 7 months, median weight: 3.8 kg). ADO, ADO II and ADO II AS devices were selected based on PDA size (1 to 2 mm larger than ductal pulmonary diameter).

- Standard technique (mean PDA diameter: 3.8 ± 0.9 mm, range: 2 – 5.5 mm):
  - ADO, ADO II and ADO II AS in 18, 24 and 14 patients, respectively.
  - Complete acute closure in 95% of patients.
  - Mild left pulmonary stenosis in 3 patients, no femoral pulse in 5 patients (with incomplete restoration of arterial perfusion in 1 patient), significant arterial groin hematoma in 4 patients.

- Exclusive venous approach (mean PDA diameter: 3.3 ± 0.8 mm, range: 2.5 – 6 mm):
  - ADO, ADO II and ADO II AS in 17, 23 and 16 patients, respectively.
  - Complete acute closure in 96% of patients.
  - Minor venous groin hematoma in 6 patients.

- No significant differences in procedural and radiation times between the approaches. Complete closure and good device position in all patients at 1 month post-implantation.

- The standard technique, involving arterial access, was associated with a 16% arterial complication rate. In view of this, the authors state that the exclusive venous approach should be the method of choice for PDA closure in small pediatric patients and premature infants.

TRANSCATHETER CLOSURE OF PATENT DUCTUS ARTERIOSUS IN UNDER 6 KG AND PREMATURE INFANTS

Baspinar O et al. *J Interven Cardiol* 2015[10]

- This article reported on attempted transcatheter PDA closure using various devices in 69 patients, including:
  - Patients <6 kg (n=53, 77.4% female), with mean age: 5.4 ± 2.7 months, mean weight: 4.6 ± 0.8 kg and mean PDA diameter: 2.9 ± 1.5 mm.

- Premature infants (n=16, 62.5% female), with mean age: 30.3 ± 19.9 days, mean weight: 1.7 ± 0.3 kg, mean PDA diameter: 2.7 ± 0.7 mm.

There may be some overlap between cohorts included in this study and the multicenter study reported by Sungur et al.[11]

- Overall, transcatheter PDA closure was successful in 91.3% of the patients. In all patients with successful PDA closure, complete closure was observed within 24 hours of the procedure.
  - Patients <6 kg: Successful closure in 50/53 patients (94.3%) (ADO I, ADO II, ADO II AS, and other devices used in 17, 17, 10, and 6 patients, respectively). All cases using an ADO II AS device were successful.
  - Premature infants: Successful closure in 13/16 patients (81.2%) (ADO II, ADO II AS, and coils used in 1, 14 , and 1 patients, respectively). In all 3 unsuccessful cases the ADO II AS device was used. In one of these patients with multiple comorbidities, the procedure was complicated by pericardial tamponade and suspected perforation due to catheter manipulations, leading to the patient's death.

- Complications, specifically reported for the ADO II AS device included iatrogenic aortic coarctation in a patient <6 kg and mild aortic coarctation in a premature infant.

- The authors concluded that transcatheter PDA closure is relatively safe and effective in premature infants and infants weighing <6 kg.

THE AMPLATZER DUCT OCCLUDER II ADDITIONAL SIZES DEVICE FOR TRANSCATHETER PDA CLOSURE: INITIAL EXPERIENCE

Bruckheimer E et al. *Catheter Cardiovasc Interv* 2014[12]

- This article described the initial single center experience with the ADO II AS device in 60 patients (55% female, median age: 3.3 years, range 0.6 – 15.8 years, median weight: 14.5 kg, range 4 – 79 kg). The mean width of the pulmonary end was 1.6 ± 0.4 mm.

- Successful device deployment was achieved in 56/60 patients (93.3%), with 52 successful cases using a retrograde aortic approach. Implant failures were related to device instability (n=3) and device embolization (n=1), and were subsequently resolved by implantation of alternative device.

- Early echocardiographic evaluation (usually 1 day post-procedure) of the successful cases showed a hemodynamically insignificant residual shunt in 1 patient and a closed PDA in the remaining 98.2% of the patients.

- At a median follow-up period of 2.3 months no complications were seen and minimal flow acceleration in the LPA was observed in 2 patients.

- It was concluded that the ADO II AS device is safe and effective for transcatheter PDA closure of small to moderate ducts (narrowing at pulmonary end <3 mm). The device is preferably delivered by retrograde aortic approach.

EARLY CLINICAL EXPERIENCE WITH A MODIFIED AMPLATZER DUCTAL OCCLUDER FOR TRANSCATHETER ARTERIAL DUCT OCCLUSION IN INFANTS AND SMALL CHILDREN

Kenny D et al. *Catheter Cardiovasc Interv* 2013[13]

- Early clinical experience was reported from implantation of the ADO II AS device in 17 patients (58.5% female, median age: 6 months, range 1.0 – 48.1 months, median weight: 5.7 kg, range 1.7 – 17.4 kg). The mean ductal diameter was 2.2 ± 0.7 mm, mean ductal length was 6.8 ± 1.7 mm.

- Complete ductal occlusion was achieved at the end of the procedure in 13 patients (76.5%). Three patients required device resizing. There was 1 early device embolization (1 day post-procedure) resolved by surgical device retrieval and ductal ligation (n=1). Significant protrusion into the descending aorta was seen in another patient and resolved intra-operatively by using a smaller device. One premature infant had diminished lower limb pulses.

- At a median follow-up duration of 4.2 months (range 1 – 10 months), complete ductal occlusion without aortic arch or LPA stenosis was achieved in all 16 patients with successful transcatheter PDA occlusion.

- It was concluded that the ADO II AS device achieves ductal closure in small infants and children with significant persistent flow through the arterial duct. Careful device diameter sizing may be required in larger ductal diameters to avoid embolization.

COMPARISON OF THE RESULTS OF TRANSCATHETER CLOSURE OF PATENT DUCTUS ARTERIOSUS WITH NEWER AMPLATZER DEVICES

Liddy S et al. *Catheter Cardiovasc Interv* 2013[14]

- Success and complications rates for various devices and PDA types were compared by retrospective review of all transcatheter PDA closures at a single center.

- The review included 177 patients treated with ADO (n=89), ADO II (n=50), ADO II AS (n=9), Flipper coil (n=25) and other devices (n=4). Institutional policy was to use coils for PDAs of minimum diameter <2 mm and ADO devices for larger PDAs.

- Patients treated with ADO II AS had a mean age of 2.0 years (0.4 – 4.1 years), a mean weight of 10.4 kg (3.9 – 18.4 kg), and a mean minimal ductal diameter of 2.5 mm (1.1 – 3.8 mm). ADO II AS devices were most frequently implanted by arterial approach (8 of 9 cases).

- All ADO II AS devices were successfully implanted. Fluoroscopy times differed significantly between the devices, with shortest time for the ADO II AS device (4.2 min). This was correlated with a shorter fluoroscopy time for arterial versus venous delivery.

- For the ADO II AS device, a residual shunt was seen in 1 patient immediately after the procedure and in no patients at 6 months follow-up.

- The authors state that the ADO II AS device offers similar advantages to ADO II with reduced risk of device protrusion, potentially making the device more suitable for younger infants.

CLOSURE OF PATENT DUCTUS ARTERIOSUS IN CHILDREN, SMALL INFANTS, AND PREMATURE BABIES WITH AMPLATZER DUCT OCCLUDER II ADDITIONAL SIZES: MULTICENTER STUDY

Sungur M et al. *Catheter Cardiovasc Interv* 2013[11]

- This retrospective multicenter (n=4) study evaluated the safety and efficacy of the ADO II AS device in 60 patients. Median age was 6.5 months (0.5 – 168 months) and median weight was 6.8 kg (1.19 – 57 kg), with 26 children weighing ≤6 kg, of which 9 weighed ≤3 kg. The median narrowest duct diameter was 2 mm (range: 1.2 – 4 mm). Among the 26 children ≤6 kg included in this cohort there may be some overlap with the single-center cohort reported by Baspinar et al.[10]

- Successful closure was achieved in 58 patients (96.6%). In 2 patients (both <6 kg) the device was not released due to significant residual shunt (treated using an ADO II device in 1 patient and by surgery in the other patient). A pulmonary disc freely floating out in the LPA without residual shunt or LPA gradient was observed in 1 patient and disappeared at 6 months follow-up. There were no procedure-related deaths. Complications included reduced pedal pulse (n=2) and blood loss requiring transfusion (n=1).

- Among the 58 patients with successful implantation, immediate closure was achieved in 87.5% and 97% of patients weighing ≤6 kg and >6 kg, respectively. Echocardiographic evaluation at the day after the procedure showed complete closure in all patients.

- At follow-up (median: 6 and 12 months for patients ≤6 kg and >6 kg, respectively) no evidence of obstruction or Doppler flow acceleration in the aortic arch or LPA was observed.

- It was concluded that percutaneous closure of medium and small sized PDAs using the ADO II AS is safe and effective in small infants and ex-premature babies (gestational age ≥37 weeks).

CLOSURE OF THE PATENT DUCTUS ARTERIOSUS WITH THE NEW DUCT OCCLUDER II ADDITIONAL SIZES DEVICE

Agnoletti G et al. *Catheter Cardiovasc Interv* 2012[15]

- The objective of this study was to evaluate technical feasibility, safety and efficacy of the ADO II AS device in 7 patients (5 females, median age: 1.5 years, median weight: 11.4 kg). PDA diameter ranged between 0.99 and 2.26 mm and PDA length was between 2.1 and 5.86 mm.

- Six of the 7 cases were performed by venous approach. All implantations were successfully completed without complications. Immediate trivial (<1 mm) residual shunt was present in 1 patient and echocardiographic evaluation at 24 hours post-procedure did not show any residual shunt. At a median follow-up duration of 2 months, complete PDA occlusion without obstruction of the aorta or pulmonary arteries was seen.

- The authors concluded that the low profile and symmetry of the ADO II AS device allows for venous or arterial approach and small delivery catheter size. Compared with other devices, the ADO II AS device might be preferred for closure of small to moderately sized PDAs.

PERCUTANEOUS CLOSURE OF PATENT DUCTUS ARTERIOSUS IN INFANTS ≤1.5 KG: A META-ANALYSIS

Bischoff AR et al. *J Pediatr* 2020[16]

- This was a meta-analysis on PDA closure in infants ≤1.5 kg, including data from 373 patients collected in 28 studies. Six of these studies, specifically reporting on relatively large cohorts implanted with the Piccolo device, were also included in this clinical compendium. Other studies included in the meta-analysis reported on a small number of patients ≤1.5 kg and/or patients implanted with other devices (other Amplatzer devices in most studies, but also using the Medtronic Microvascular Plug and coils). Overall, 243 patients (65.1%) were implanted with a Piccolo occluder.

- Technical success was defined as the patient leaving the procedure room with a device or coil in the PDA. The overall technical success rate in all 373 patients was 97.3%. In 6 cases, the PDA was eventually closed by surgical ligation due to potential device protrusion into adjacent structures (n=3), cardiac tamponade (n=1), aortic coarctation and surgical device removal (n=1) and surgical retrieval of an embolized device (n=1). Other failures were related to cardiac perforation / hemopericardium resulting in death (n=3) and an aborted procedure due to IVC dissection during sheath advancement (n=1). The age at the time of the procedure was a significant independent predictor for technical success.

- Major and minor adverse events occurred at a rate of 8% and 18%, respectively. Overall mortality was 6% with 5 procedure-related deaths (1.3%). Patients with weight between 1.5 and 6 kg, included in a separate meta-analysis, showed a significantly lower technical success rate (92.9%) as well as a higher overall incidence of adverse events (21.8%) and a higher rate of minor adverse events (13.4%), compared to patients ≤1.5 kg.

- The technical success rate was similar in centers reporting on ≥10 procedures versus those reporting fewer procedures. Major and minor adverse events were significantly more frequent in centers with <10 procedures.

DATA SUMMARY: STUDIES REPORTING ON THE CLINICAL USE OF PICCOLO OR ADO II AS AS DEVICE

ARTICLE	PATIENTS (N) IMPLANTED WITH PICCOLO OR ADO II AS	TECHNICAL SUCCESS RATE	COMPLETE / EFFECTIVE CLOSURE RATE	MINOR COMPLICATION RATE	MAJOR COMPLICATION RATE
Sathanandam SK et al.[1] ≤2 kg	100	99.0%	100%	NR	4.2%
Sathanandam SK et al.[1] >2 kg	100	92.0%	98.8%	NR	0%
Malekzadeh-Milani et al.[2]	91	98.9%	100%[a]	7.7%[b]	
Regan et al.[3]	64	98.4%	NR	20.3%[c]	
Pamukcu O et al.[4]	25[d]	84.6%	NR	7.7%	15.4%
Rodrıguez Ogando A et al.[5]	25	100%[e]	88%[a]	0%[f]	0%
Fiszer R et al.[6]	103	98.1%	100%	2.9%	1.0%
Mahmoud HT et al.[7]	109	98.2%	100%	0%	0%
Morville P et al.[8]	32	96.9%	100%	12.5%	3.1%
Thanopoulos BD et al.[9]	30	NR	NR	NR	NR
Baspinar O et al.[10]	24	87.5%[g]	100%	NR[h]	NR[h]
Bruckheimer E et al.[12]	60	93.3%	98.2%[a]	0%	0%
Kenny D et al.[13]	17	94.1%[i]	100%	5.9%	5.9%
Liddy S et al.[14]	9	100%	100%	NR	0%
Sungur M et al.[11]	60	96.6%	100%	6.7%	0%
Agnoletti G et al.[15]	7	100%	100%	0%	0%

All outcomes as reported in the articles for ADO II AS device specifically.
Technical success rate: as reported in the article, usually the rate of successfully deployed devices. Related to all patients in whom implantation was attempted. Complete closure rate: Observed at time of last follow-up and related to all patients with successful device implantation. Minor / major complication rates: Related to all patients in whom implantation was attempted.

ADO II AS = AMPLATZER™ Duct Occluder II Additional Sizes; NR = not reported (or not reported for ADO II AS specifically).

Notes:

a. Immediate outcome.
b. Not reported as minor or major complications and reported for multiple device types. Of the 8 reported complications, 7 may have occurred during a procedure using the ADO II AS device.
c. Not reported as minor or major complications.
d. Rates for Pamukcu et al. reported for 26 patients, including 25 ADO II AS devices and 1 ADO device.
e. In 2 cases, an embolized device was recovered and successfully replaced by an oversized device.
f. Slight protrusion in LPA in 4 cases.
g. In patients <6 kg and premature patients, implantation of the ADO II AS device was successful in 10/10 and 11/14 patients, respectively, resulting in an overall success rate of 21/24 (87.5%).
h. Study using multiple devices. Complications specifically reported for ADO II AS device: pericardial tamponade with fatal outcome (n=1), aortic coarctation (n=2).
i. In 17 cases, there was 1 device embolization followed by surgical retrieval and ligation.

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