Original Article

Transcatheter Closure of Adult Patent Ductus Arteriosus with Severe Pulmonary Hypertension

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The purpose of this study was to investigate the application of trial balloon occlusion for permanent closure of patent ductus arteriosus (PDA) with severe pulmonary hypertension (PH) in adults, and to assess its immediate and short-term results. From September 1999 to September 2005, a total of ten adults (two males, ages ranging from 20 to 54 years) with PDA who met the criterion for severe PH (basal pulmonary vascular resistance >8 Wood units) received trial balloon occlusion *via* an embolectomy balloon catheter. Post-occlusion hemodynamics, along with an overall clinical and hemodynamic assessment, was used to consider the indication of closure of PDA. Nine of the patients underwent successful transcatheter closure of PDA and subsequently used Amplatzer occluder devices. Chest X-ray, cardiography and echocardiography were used for follow-up evaluation of the treatment within 6 months after successful closure of PDA. No patient had a detectable residual shunt by color flow mapping or any other complications (device migration, hemolysis, endocarditis, *etc.*) at follow-up. In conclusion, trial balloon occlusion helps to determine anticipated hemodynamics after closure of PDA, so it is conducive to indicating permanent closure of adult PDA with reversible but severe PH. Furthermore, satisfactory immediate and short-term outcomes have proven this method to be safe and valid. (*Hypertens Res* 2008; 31: 1997–2002)

***Key Words*: patent ductus arteriosus, pulmonary hypertension, trial balloon occlusion, Amplatzer occluder device**

Introduction

Patent ductus arteriosus (PDA) accounts for approximately 8% of congenital heart disease. More common in female, it may be asymptomatic and thus is sometimes not diagnosed until adulthood when a murmur is incidentally auscultated or, occasionally, correlated symptoms are found (*1*, *2*). A prolonged abnormal aorto-pulmonary shunt may result in silently progressing hypertension and left ventricular dysfunction.

Since the first percutaneous closure of PDA performed by Porstmann in 1968, various occluder devices and coils have been introduced into clinical practice. Transcatheter occlusion of PDA with various devices and coils is a well-established alternative to surgical closure. Despite its encouraging success in general PDA patients, its use in PDA with severe pulmonary hypertension (PH) has been limited. There have been only a few reports on transcatheter closure of PDA with severe PH in adults (*3*, *4*).

Achieving a clinical cure using transcatheter closure of PDA with severe PH in adults is possible, with low risk. In a few cases, however, there is a risk of pulmonary hypertensive crisis, or even acute right heart failure. The result may be a long-term aorto-pulmonary shunt and consequent irreversible pulmonary vascular disease impairing patients' quality of life and shortening their life expectancy (*4*, *5*). How can we confirm the reversibility of pulmonary vascular disease to avoid the above-mentioned complications? There is no single defin-

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Table 1. Basal Clinical, X-Ray, ECG, and Echocardiogram Data of Patients

No.	Age (years)	Gender	SaO_2 (%)	Cyanosis	Murmur	CTR (%)	ECG	LVIDd (mm)	SPAP (mmHg)	Blood flow direction in duct
1	40	F	94	No	systolic+short diastolic	58	LVH	60	120	L-to-R
2	54	F	95	No	systolic	62	BVH	68	125	bidirectional (major: L-to-R)
3	25	F	92	No	systolic	54	LVH	58	102	L-to-R
4	36	F	91	No	systolic+short diastolic	60	BVH	66	128	L-to-R
5	24	M	93	No	systolic+short diastolic	59	BVH	69	95	L-to-R
6	20	M	94	No	systolic+short diastolic	60	BVH	67	98	L-to-R
7	35	F	90	occasional	systolic	65	BVH	68	95	no obvious shunt
8	26	F	95	No	none	63	BVH	69	115	bidirectional (major: L-to-R)
9	26	F	93	No	systolic	55	LVH	64	85	L-to-R
10	44	F	92	after exercise	none	64	BVH	73	126	bidirectional (major: L-to-R)

F, female; M, male; SaO_2, oxygen saturation (blood samples were taken in right femoral artery, without supplemental oxygen inhalation); CTR, cardio-thoracic ratio in chest X-ray; LVH, left ventricular hypertrophy; BVH, bi-ventricular hypertrophy; LVIDd, left ventricular internal diameter at diastole by echocardiogram; SPAP, pulmonary arterial systolic pressure measured by echo-Doppler; L-to-R, left-to-right shunt; bidirectional (major: L-to-R), bidirectional shunt with left-to-right shunt greater than right-to-left shunt.

itive method, not even lung biopsy, that provides a definitive answer (*6*, *7*). It has recently been shown that trial balloon occlusion can be used cautiously in PDA with severe PH to evaluate the pulmonary vascular response in order to determine whether to proceed to permanent closure with Amplatzer occluder devices (*3*, *4*). In this report, we present our early experiences with and the short-term outcomes of closure of adult PDA with severe PH using Amplatzer occluder devices following trial balloon occlusion.

Methods

We reviewed the clinical, hemodynamic data and procedural details of PDA with severe PH in adults. The criterion for severe PH is basal pulmonary vascular resistance (PVR) >8 Wood units. From September 1999 to September 2005, there were 10 adult PDA patients with severe PH who underwent trial balloon occlusion, and nine cases subsequently underwent successful closure with Amplatzer occluder devices.

Patients

All patients were admitted at least 2 d before the procedure for clinical, laboratory, chest X-ray, ECG, and echocardiographic assessment. Basal clinical, chest X-ray, ECG, and echocardiographic findings for patients are shown in Table 1. There were eight female and two male patients, aged 20 to 54 years. Cyanosis after exercise was detected in only two patients, and resting cyanosis was found in none. The oxygen saturation of the right femoral artery ranged from 90 to 95% (93 ± 2%) (without supplemental oxygen inhalation). All patients were observed for cardiac enlargement in chest X-rays with the presence of either left or bi-ventricular hypertrophy in electrocardiograms. Echocardiograms demonstrated clinical pictures of the duct and of left ventricular volume overload in all patients, with an increase in left ventricular diastolic dimensions. Calcification of the duct was found in five patients and calcification of the nearby aorta in two patients. Aneurysmal dilation of the duct was found in case 7. Doppler echocardiography (echo-Doppler) revealed systemic pulmonary arterial pressure and a left to right, or bidirectional with predominantly left to right, shunt through the duct. There was no significant pulmonary regurgitation in these patients.

Procedures

Informed consent was obtained from the guardians of patients prior to the procedure.

The procedure was carried out under local anesthesia (30% FiO_2 was administered to patients suffering from depressed cardiac function or nervous tension in the test occlusion) with the help of digital subtraction angiography (DSA) (GE Advantx LCA DSA system; GE Medical System, Munich, Germany). After percutaneous puncture of the right femoral vein and artery, hemodynamic data (basal systemic pressure and basal pulmonary arterial pressure) were estimated, and Q_p/Q_s (pulmonary–systemic flow ratio) and basal pulmonary arterial resistance were calculated. A descending aortogram in the lateral projection was recorded using a 5 French (5F) pigtail catheter to define the shape and size of the PDA (*8*). The balloon catheter (Sorin arterial embolectomy catheter; COBE Cardiovascular, Inc., Arvada, USA) was introduced with a guildewire through a 6F arterial sheath and positioned at the duct. It was then slowly inflated by diluted contrast solution to the size required for duct occlusion. Another 5F multipurpose catheter was introduced from the femoral vein into the pulmonary artery for monitoring pulmonary arterial pressure. The sidearm of the same arterial sheath provided femoral arterial pressure (in general, we have used ascending aortic pressure for comparison, but only during balloon occlu-

Table 2. Hemodynamic Data of the Patients before and after Transient Balloon Occlusion

No.	Basal				30 min post-occlusion by balloon	
	BP (mmHg)	PAP (mmHg)	PVR (Wood units)	Q_p/Q_s	BP (mmHg)	PAP (mmHg)
1	130/75 (94)	122/69 (87)	9	2.53:1	125/78 (93)	70/35 (46)
2	150/85 (106)	135/71 (92)	11	2.32:1	140/81 (100)	90/52 (65)
3	116/71 (86)	110/72 (85)	14	1.51:1	118/76 (90)	100/68 (78)
4	135/70 (92)	134/64 (87)	12	1.75:1	127/70 (89)	78/ 54 (62)
5	108/65 (79)	95/58 (70)	13	1.65:1	115/60 (78)	67/40 (49)
6	120/50 (78)	111/51(76)	9	2.09:1	118/55 (76)	92/53 (66)
7	82/40 (54)	85/42 (56)	15	1.14:1	80/45 (56)	82/42 (55)
8	110/63 (79)	102/53 (69)	10	1.84:1	106/74 (85)	91/51 (64)
9	96/57 (70)	85/42 (56)	9	2.23:1	100/52 (68)	52/22 (32)
10	130/71 (91)	128/73 (91)	13	1.46:1	125/65 (85)	108/54 (71)

The number in parentheses is a value of mean pressure. BP, systemic blood pressure; PAP, pulmonary arterial pressure; PVR, pulmonary vascular resistance; Q_p/Q_s, pulmonary–systemic flow ratio.

sion of PDA has femoral arterial pressure been used to avoid additional arterial puncture; although this has some variances, they are probably acceptable) (*3*). Absolute occlusion of PDA by the balloon was ensured by the absence of a step-up in oxygen saturation between the right atrium and the pulmonary artery. The balloon occlusion lasted more than 30 min. During the procedure, ECG activity and femoral arterial and pulmonary arterial pressures were monitored continuously.

The decision to proceed to permanent closure of PDA with an Amplatzer occluder device was based on the following parameters: 1) no resting cyanosis; 2) no resting right-to-left shunt by echo-Doppler; 3) no abnormal whole-body responses (such as chest distress, shortness of breath, dyspnea, thoracalgia, dizziness, syncope, cyanosis of the lips, tachycardia, arrhythmia, bradycardia, or hypotension) during trial balloon occlusion, and 4) a decrease of more than 20 mmHg difference in the main pulmonary arterial pressure without a significant decrease in the systemic pressure during balloon occlusion. It was not essential to meet all of the criteria mentioned above, but the indication was based on the clinical findings and the overall data obtained.

If permanent closure of the PDA was indicated, the balloon catheter was withdrawn and a suitable Amplatzer PDA occluder device (ADO) (Aga Medical Corporation, Golden Valley, USA) was introduced into the delivery sheath and advanced from the femoral vein, under DSA fluoroscopic guidance, through the PDA into the descending aorta, where the retention disk was deployed. The introducing sheath was then withdrawn into the pulmonary artery to deploy the conical part of the ADO. With the device still attached to the cable, a descending aortogram was performed in the lateral projection to confirm the position of the device. When the proper position was confirmed, the device was released by rotating the delivery cable counterclockwise. A second descending aortogram was carried out 10 min after the release to check for residual shunting. Before the procedure was completed, pullback pressure measurements were obtained in the aortic arch and the pulmonary artery to check for stenosis. Prophylactic antibiotics were administered 30 min before the procedure.

In consideration of pulmonary arterial pressure near systemic pressure, an ADO larger than the smallest dimension of the PDA was chosen to prevent migration of the device. If the smallest dimension of the PDA exceeded 11 mm, an ADO was not used because the device is available only in sizes ranging from 6/4 mm to 14/12 mm (the larger measurement is that of the part used at the aortic site; the smaller refers to the pulmonary end). Instead, an Amplatzer atrial septal defect occluder (AMASDO) or Amplatzer ventricular septal defect occluder (AMVSDO) was used.

The procedures for closing the PDA were identical whether an ADO, AMASDO or AMVSDO was used.

Follow-Up

Patients were discharged within 3 d after this procedure. Those who underwent transcatheter occlusion of PDA were followed up clinically and with ECG, chest X-ray, and echo-Doppler 24 h, 1 month, and 6 months after successful closure.

Results

Hemodynamics

The hemodynamic data is shown in Table 2. Basal pulmonary arterial pressures were near systemic in all patients, with a mean PVR of 11.5±2.2 Wood units (range 9.0 to 15.0). The mean Q_p/Q_s ratio in the basal state was 1.85±0.44 (range 1.14 to 2.53). Thirty minutes after trial balloon occlusion, mean pulmonary arterial pressure decreased from 77±14 to 59±14 mmHg without significant change in mean systemic pressure. In six patients (cases 1, 2, 4, 5, 9, and 10), a decrease of more than 20 mmHg in the main pulmonary arterial pressure without a significant decrease in the systemic pressure was

Table 3. PDA Size, Shape, and Device Deployed

No.	Shape of PDA	Minimal dimension of PDA (mm)	Deployed device	Residual shunt
1	Krichenko A	15	20 mm AMASDO	trace
2	Krichenko C	8	12/10* mm ADO	n.d.
3	Krichenko A	12	16 mm AMVSDO	n.d.
4	Krichenko A	10	14/12* mm ADO	n.d.
5	Krichenko A	9.5	14/12* mm ADO	n.d.
6	Krichenko B	10	14/12* mm ADO	n.d.
7	Krichenko E	11	—	—
8	Krichenko A	5.5	10/8* mm ADO	n.d.
9	Krichenko C	8	12/10* mm ADO	n.d.
10	Krichenko A	14	20 mm AMASDO	trace

PDA, patent ductus arteriosus; AMASDO, Amplatzer atrial septal defect occlusion; AMVSDO, Amplatzer ventricular septal defect occlusion; ADO, Amplatzer PDA occluder. *Size of ADO used at the aortic site/plumonary end.

observed without abnormal whole-body responses during balloon occlusion, so we closed their PDAs with Amplatzer occluder devices. In three patients (cases 3, 6, and 8), the decrease in pulmonary arterial pressure was <10 mmHg, but we decided to close their PDAs in view of their overall data, including the absence of resting cyanosis, a basal Q_p/Q_s ratio of $>1.50:1$, an enlarged left ventricle, no right-to-left shunt on echo-Doppler and no abnormal whole-body responses during trial balloon occlusion. In contrast, on account of a basal Q_p/Q_s ratio of 1.14:1, occasional cyanosis, and no obvious shunt on echo-Doppler, it was ultimately decided not to proceed to closure in case 7, despite a hemodynamic response to the trial balloon occlusion similar to that in cases 3 and 8.

Closure of PDA

In this case series, the ADO was used in six patients, the AMASDO in two patients, and the AMVSDO in one patient. The sizes and shapes of the PDAs and the devices deployed are shown in Table 3.

Follow-Up (for Successful Closure)

No peri-operative complications were observed. No residual murmur was auscultated. A trace of residual shunting was detected by descending aortogram immediately after insertion of the Amplatzer occluder device in cases 1 and 10 (Table 3). The residual shunt, however, disappeared 24 h after the procedure, and no patient had a detectable residual shunt or pulmonary stenosis by color flow mapping, or any other complications, at the 6-month follow-up. Furthermore, to date, neither radiological evidence of device migration nor blood-test evidence of device-related hemolysis has been noted at follow-up. One patient (case 3) with a basal PVR of 14 Wood units underwent a re-catheterization 1 month after successful closure of PDA that revealed a decrease in the pulmonary arterial pressure to 65/34 mmHg and a PVR of 6.5 Wood units. All patients showed symptomatic improvement with regression of pulmonary arterial pressure, as assessed clinically and by ECG and echo-Doppler evaluation. Mean peak pulmonary arterial pressure assessed by echo-Doppler evaluation dropped to 38 ± 6 mmHg 6 months after the procedure and peak pulmonary arterial pressure was 38 mmHg for case 3, 42 mmHg for case 6, and 39 mmHg for case 8. No patient showed right ventricular hypertrophy on ECG. Echo-Doppler revealed no enlargement of right-sided chambers and normal motion of the interventricular septum with insignificant tricuspid and pulmonary regurgitation.

Discussion

The pathophysiology of PDA is the shunt of high-pressure and highly oxygenated blood from the aorta to the pulmonary artery. This abnormal shunt increases the preload of the left ventricle and exhausts the left ventricle reserve. The direct results of a long-term abnormal aorto-pulmonary shunt are PH and left ventricular dysfunction. In adult PDA with severe PH, possible responses after acute closure of the duct may include 1) acute elevation of PH, pulmonary hypertensive crisis, or even acute right heart failure or 2) sustained severe PH due to pulmonary vascular disease or possible migration of occluder devices (*4*). How can we correctly assess the operability of adult PDA with severe PH? Conventional surgical treatment of adult PDA with severe PH poses many difficulties and often requires the use of a cardiopulmonary or temporary bypass between the ascending aorta or aortic arch and the descending aorta or femoral artery, which leads to marked elevation of the inflammatory mediators or extensive surgical invasions and is apt to cause complications (such as hemorrhage, arrhythmia, crisis of PH, acute right ventricular failure, or even death). It was reported (*9*, *10*) that one of the main contraindications in surgical closure of PDA with severe PH was the presence of a bi-directional shunt with right-to-left shunt greater than left-to-right shunt that could be identified

by echo-Doppler. Another predictor of adverse prognosis was a rise in pulmonary arterial pressure and fall in systemic pressures upon clamping of PDA that could be identified by trial balloon occlusion of PDA. Those predictors explain the favorable outcome in our series. In addition, the non-surgical minimally invasive approach used for closure of PDA may also account for the favorable outcome.

In order to differentiate kinetic PH from obstructive PH and to evaluate the reversibility of pulmonary vascular disease in adult PDA with severe PH, we used a balloon catheter to tentatively occlude the patent duct before deciding whether to permanently implant the Amplatzer occluder. The decision to proceed to close PDA with an Amplatzer occluder device was based mainly on changes in hemodynamic data, especially the extent of the decrease in pulmonary arterial pressure, and on whole-body responses during PDA occlusion. Three results were caused by complete trial balloon occlusion of PDA with severe PH. First, when the main pulmonary arterial pressure dropped by more than one-fifth or 20 mmHg and the systemic arterial pressure did not decline relative to basal hemodynamic data, without abnormal whole-body responses, then kinetic PH and reversible pulmonary vascular disease were concluded, and the Amplatzer occluder devices could be implanted permanently. Conversely, when the main pulmonary arterial pressure rose and systemic arterial pressure fell with or without abnormal whole-body responses, then obstructive PH and irreversible pulmonary vascular disease were diagnosed, the balloon was withdrawn immediately, and advanced procedures were ruled out. Finally, when main pulmonary arterial pressure decreased slightly and systemic arterial pressure did not decline relative to basal hemodynamic data, without abnormal whole-body responses, then kinetic or obstructive PH could not be differentiated and permanent closure of PDA could be performed cautiously, based on an overall consideration of hemodynamic response during trial balloon occlusion of the PDA and other clinical data (such as cyanosis, blood-flow direction in the duct, and Q_p/Q_s). We ultimately decided to proceed to permanent closure of PDA in cases 3, 6, and 8, 1 h after balloon occlusion, and the pulmonary arterial pressure measured by echo-Doppler decreased significantly in all three patients at both 24 h and 6 months following the procedure. We inferred that the slight decrease in pulmonary arterial pressure during trial balloon occlusion in cases 3, 6, and 8 was probably correlated with pulmonary vascular spasm, without which pulmonary arterial pressure would decrease significantly during trial balloon occlusion.

Q_p/Q_s can reflect to some extent the severity of pulmonary vascular disease. Generally, the more serious the pulmonary vascular disease, the lower the value of Q_p/Q_s. However, the site at which the pulmonary arterial blood sample is obtained influences the value of Q_p/Q_s. Thus, although it is an important hemodynamic parameter and helps to evaluate the severity of PH and the reversibility of pulmonary vascular disease, Q_p/Q_s is not the key parameter for differentiating kinetic from obstructive PH or for diagnosing the reversibility of pulmonary vascular disease.

In order to differentiate kinetic PH from obstructive PH, a test with the PDA clamped in surgery that ordinarily lasts ordinarily 10 min is performed. Based on this test, we cautiously observe 30 min of trial balloon occlusion of the PDA. Generally speaking, observation as short as 30 min is sufficient. However, longer trial closure is better when neither significant hemodynamic change nor abnormal whole-body response is observed 30 min after the balloon occlusion.

Several changes in the shape of adult PDA with severe PH often prevent the introduction of the catheter from the femoral vein through the PDA into the descending aorta. We adopted alternative techniques; for example, the delivery sheath and occluder are advanced from the femoral artery or external iliac artery through the PDA into the pulmonary artery. If the PDA has a large internal duct diameter and the duct wall lacks flexibility, an occluder 2–4 mm larger than the smallest dimension of the PDA is chosen to reduce residual shunt. Conditions such as tachycardia and arrhythmia are caused by depressed cardiac function or nervous tension in adult PDA patients. Sufficient preparation, minimized operational time and proper intraoperative management make transcatheter occlusion of PDA safe and successful.

No patient in our series had a residual shunt detectable by color flow mapping or any other complications (such as device migration, hemolysis, or endocarditis) in the ensuing 6 months, and pulmonary arterial pressure assessed by echo-Doppler evaluation declined significantly 6 months after the procedure, which proved our methods to be safe and valid. A limitation of the study is that a follow-up catheterization was performed in only one patient. However, it was difficult for patients to accept recatheterization when they did well clinically and when their follow-up ECG and echocardiogram did not suggest residual shunt or sustained severe PH. Further follow-up is necessary to evaluate the medium- and long-term outcomes.

In conclusion, trial balloon occlusion can be used cautiously for adult PDA with severe PH, and it helps in determining the anticipated hemodynamics after occlusion of the duct and in making the decision whether to proceed to permanent closure of adult PDA with reversible but severe PH. Patients deemed to have reversible PH based on overall clinical and hemodynamic data have shown satisfactory immediate and short-term outcomes with closure of PDA using Amplatzer occluder devices after trial balloon occlusion.

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