Simultaneous transcatheter intervention for atrial septal defect complicated with patent ductus arteriosus: A 13-year single institutional retrospective study

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ABSTRACT

Purpose: The feasibility and validity of simultaneous transcatheter interventions for patients with atrial septal defect (ASD) complicated with patent ductus arteriosus (PDA) has not been systematically evaluated.

Materials and Methods: A retrospective analysis was conducted in patients who received transcatheter procedures for ASD complicated with PDA concurrently. The indications and treatment protocols were in accordance with the current guidelines. The sequence of therapy for ASD complicated with PDA was determined by clinical experience. Patients were followed up for at least 6 months after therapy.

Results: Overall, 22 patients received simultaneous transcatheter interventional therapy, and the success rate was 100%. No severe complications transpired during the procedure or follow-up stage.

Conclusion: Simultaneous transcatheter intervention is feasible and effective for patients who have concurrent complications for both ASD and PDA.

Keywords: atrial septal defect; patent ductus arteriosus; transcatheter; interventional cardiology

INTRODUCTION

Transcatheter interventional therapy for congenital heart disease (CHD) has made tremendous strides in the past decades ever since the successful closure of a patent ductus arteriosus (PDA) in 1967 by Porstmann et al (1). With improvements in both interventional devices and procedural techniques, an increasing number of congenital cardiac defects have been treated by transcatheter interventional therapy (2). These minimally invasive treatment strategies have been proved effective and safe for most single defects of CHD, including both atrial septal defect (ASD) and PDA (3, 4). However, CHD is a complex clinical syndrome and a substantial proportion of CHD patients present more than one cardiac defect simultaneously, i.e., compound CHD, such as ASD complicated with PDA. Although surgical treatment has been considered a choice for therapy, transcatheter interventional procedures are much less invasive, less expensive, and less painful. Several case reports (5-9) and case series (10) have shown supportive opinions on the application of simultaneous transcatheter interventional strategies for compound CHD, however, a few studies relating to systematic experience have been reported. Therefore, in this study, we retrospectively analyzed 22 patient cases complicated with both ASD and PDA who received simultaneous transcatheter interventional treatment in our institution in the past 13 years. To the best of our knowledge, this study had the largest number of patients who received transcatheter intervention concurrently.

MATERIALS AND METHODS

Patients

22 patients diagnosed with ASD with concurrent PDA were retrospectively used in this study. Patient data was obtained from the Department of Congenital Heart Disease of General Hospital of Shenyang Military Command from June 2003 to September 2016. All patients were diagnosed with ASD complicated with PDA and were admitted from the outpatient department. Of the 22 patients, 7 were males and 15 were females. The age ranged from 3 to 51 years old (11.1 ± 13.5). Patient mean weight was 28.8 ± 18.1 kg ranging from 11 to 68 kg.

The study was approved by the ethics committee of the General Hospital of Shenyang Military Command. Before intervention, written informed consent was obtained from each patient or their guardians. All patients were diagnosed by comprehensive evaluation of their routine physical, radiological examinations, 2-dimensional doppler transthoracic echocardiographic examination (Philips IE33 Ultrasound Machine, Philips medical systems technologies ltd), and diagnostic catheterization and angiography.

The indications and contraindications for transcatheter interventional therapy were in accordance with the Chinese Guidelines of
Transcatheter Interventional Therapy for Patients with Congenital Heart Disease (11), ACC/AHA (12) and ESC (13) Guidelines for the Management of Adults with Congenital Heart Disease.

Inclusion criteria were as follows: (1) Age ≥ 3 years and weight ≥ 10 kg. (2) Diagnosed as ASD (foramen secundum type) complicated with PDA simultaneously. (3) ASD with a left to right shunt ≤ 36 mm. (4) Distance ≥ 5mm from the rim of ASD to the coronary sinus, superior and interior vena cava (IVC). (5) Distance ≥ 7 mm from the rim of the defect to the mitral or tricuspid valve. (6) Absence of other cardiac defects requiring surgical treatment.

Procedures

Anesthesia and Periprocedural Management

General anesthesia with intravenous injection of ketamine (1–2 mg/kg) was administered to patients aged less than 10 years old and local anesthesia with 5 mL 2% lidocaine was administered for patients older than 10 years of age. Procedures including percutaneous closures of ASD and PDA were performed following established methods routinely used in our institution (please see “Simultaneous Transcatheter Intervention Procedure”). For patients with pulmonary hypertension, right ventricular catheterization was performed to monitor pulmonary circulation, including total pulmonary resistance, the degree of shunt and the pulmonary to systemic flow ratio (Qp/Qs). Coronary angiography was also performed in patients over 50 years of age to exclude patients with coronary heart disease. Cefuroxime sodium (1.5 g bid for adults and 50 mg/kg bid for children who less than 12 years old) was administered preoperatively for prophylaxis of surgical infections. A loading dose of heparin (100 U/kg) was administered intravenously immediately prior to the procedure and one-quarter to one-third of the loading dose was administered hourly during the procedure. For patients undergoing percutaneous closure of ASD, low molecular heparin (0.01 ml/kg) was injected intramuscularly every 12 hours for the first 48 hours after procedure and aspirin (3-5 mg/kg was prescribed for 6 months after the procedure. All procedures were performed by experienced interventional physicians.

Simultaneous Transcatheter Intervention Procedure

Based on our institutional clinical experience, PDA is occluded first in most cases of transcatheter interventions in patients with ASD complicated with PDA. However, trial of ASD occlusion needs to be implemented prior to PDA occlusion if ASD is relatively too large or rims too short. Under such circumstances, a echocardiography evaluation is required to confirm the position of ASD occluder first; subsequently the PDA is occluded followed by release of ASD occluder. In the present study, only 1 case received ASD occlusion before PDA occlusion. Patients received arterio- and veni-puncture followed by lateral angiography of descending aortic arch to observe the morphology of PDA. The diameter and length of the aorta and pulmonary artery of the PDA was measured by radiograph. End-hole type catheter was guided from the right femoral vein to the pulmonary artery. After measurement of the pulmonary artery and right ventricle pressure, pathway was established by passing the 6F type catheter from the right femoral vein to the pulmonary artery and then from the PDA to the descending aorta. Subsequently, the delivering sheath was introduced and PDA occlusion was performed with the appropriate PDA occluder. Aorta and pulmonary artery pressure was monitored during procedure. Repeated descending aorta angiography was performed to observe the morphology of the occluder and residual shunts. The occluder was released when it was positioned appropriately and no residual shunts. Afterwards, ASD occlusion was initiated. A long, stiff guide wire was sequentially inserted through the IVC, right atrium, ASD, left atrium and into the left upper pulmonary vein, and then a sheath was introduced through the guidewire. An ASD occluder was attached to the delivery cable, pushed to the top of the sheath and opened after its correct location was confirmed by echocardiography (Fig. 1). During the procedure, echocardiography was used to observe the position of the ASD occluder, residual shunts and impact of the occluder on the surrounding structures.

Criteria for Procedural success: Simultaneous occlusion of both ASD and PDA were achieved and no adverse events were observed, such as, definite residual shunt, displacement or fall off of occluder, or any cardiovascular complications after the procedure.

Choice of the Device Size

The optimized size of the ASD occluder was 2-6 mm larger than the maximal diameter of the ASD as measured by echocardiography. FOR PDA, a mushroom occluder was a common choice, and the diameter of the occluder was 3-6 mm larger than the internal diameter of PDA narrowest defect as measured by X-ray after aortic angiograph. For PDA with small internal diameter and irregular shape, an ADO II occluder produced by AGA Medical Corporation was considered (Fig. 2).

Follow-up

Each patient was followed up using electrocardiograph (ECG), chest X-ray and echocardiographic examinations for at least 6 months after interventional treatment. Observations noted during follow-up included displacement or fall off of the occluder, pericardial effusion, arrhythmias and changes of internal diameter of the heart chambers. All patients received routine follow-ups, including chest radiographic, ECG and echocardiographic examination at 1, 3 and 6 months post-procedure.

Statistical Analysis

Continuous variables were expressed as means ± standard deviations (SDs). The differences between pulmonary valve gradients at baseline were assessed using paired value t-tests. A p-value < 0.05 was considered statistically significant. The statistical analysis was performed using SPSS 13.0 software.
**RESULTS**

**Baseline Data**

Among the 22 patients, 3 had a history of repeated respiratory tract infections, 12 had post-activity palpitations and panting, 15 presented continuous mechanical murmurs and 7 presented II-III class systolic ejection murmurs between the 2nd and 3rd intercostal on the left border of the sternum. Chest X-ray showed that the cardiothoracic (C/T) ratio ranged from 0.5 to 0.73 (0.56 ± 0.06). There was an increasing tendency of the C/T ratio for all 22 patients, where 13 patients had a significant increase in C/T. In addition, different degrees of pulmonary blood increase was observed in all 22 patients, of which 17 patients showed bulging pulmonary artery segments. For the pre-procedural ECG examination, 8 patients were normal, 6 showed incomplete right bundle branch block (IRBBB), 3 showed right ventricular preponderance, 3 showed left ventricular hypertrophy,
1 exhibited bi-ventricle enlargement and 1 was complicated with III° aurrículo-ventricular block (AVB) with junctional escape rhythm and right ventricle hypertrophy. With pre-procedural echocardiographic examination, all 22 patients were diagnosed with ASD complicated with PDA and with different degrees of pulmonary hypertension. Moreover, by echocardiographic measurement, 12 patients showed increased right atrial diameter (RAD), 14 showed increased right ventricle diameter (RVD), 10 showed increased left atrial diameter (LAD), 13 showed increased left ventricular end-systolic diameter (LVEDD) and left ventricular end-diastolic diameter (LVEDD).

Procedural Data

22 patients with ASD with concurrent PDA received interventional therapy, with a success rate of 100%. No complications occurred during the procedure. The whole procedure lasted between 30 to 120 (73.8 ± 26.7) min, and the X-ray exposure time ranged from 6.4 to 67.8 (24.7 ± 14.9) min. 20 cases at pre-procedure showed increased pulmonary artery pressure.

ASD occlusion outcomes

All 22 cases were categorized with foramen secundum ASD, with the size of defects ranging between 4 to 23 (9.6 ± 4.8) mm. There were 2 patients who received the ASD occluder produced by Amplatzer (USA) and the other 20 patients received the occluder produced by Shanghai Shape Memory Alloy (China). The waist diameter of the selected occluders ranged from 8 to 30 (14.2 ± 5.6) mm. No residual shunt was detected from the echocardiographic reexamination either performed immediately or on the second day post-procedure. The size of the ASD and choice of occluders for all the patients are shown in Table 1.

PDA occlusion outcomes

The narrowest diameters of PDA for all 22 patients shown by aortography ranged from 2-9 (3.3 ± 1.7) mm. Based on Krichenko classification, 8 patients were type A, 7 were type B, 1 was type C and the other 6 were type D. The occluders used in these patients had 2 from Amplatzer, 6 from ADO-II (among which each of size 4-4, 3-6 and 4-6 were in 2 cases), 12 from Shanghai Shape Memory Alloy (one patient had a symmetry ventricular septal defect occluder sized 4) and 2 from Beijing Starway Medical Technology. The waist diameter of the occluders ranged from 6 to 16 (9.3 ± 2.5) mm. No residual shunt was observed by aortography 5 min post-procedure. X-ray and choice of occluders for all patients are shown in Table 1.

The pulmonary artery pressure measured immediately post-procedure of all 22 patients with pulmonary hypertension were alleviated to different extents, of which there were still 16 cases that exceeded normal range, including 10 children (possibly associated with general anesthesia) and 6 adults (slightly higher than normal). ECG reexamination post-procedure showed 3 patients with IRBBB recovered to normal, 1 presented with sinus bradycardia and the other patients exhibited no significant changes.

Follow-up Data

Chest X-ray

Pulmonary blood flow for all patients returned back to normal at follow-up. Only 1 of the 13 patients with increased C/T ratio pre-procedure remained the same, while the other 12 patients had C/T ratios recover to normal levels. 2 of the 17 cases with bulging pulmonary artery segment at pre-procedure still remained bulged, but with a significantly lower level.

ECG

At the 3-month follow-up period, only 1 of the 6 patients with IRBBB at pre-procedure remained IRBBB, and was still the same after 6-month follow-up. The patient with right ventricular preponderance recovered to normal at the 3-month follow-up period. 2 of the 3 patients with left ventricular hypertrophy recovered to normal while the one patient still exhibited hypertrophy at the 6-month follow-up period. The patient with bi-ventricle enlargement displayed right ventricular enlargement at 3-month follow-up and still remained the same at 6-month follow-up. Patient with III°AVB complicated with junctional escape rhythm and right ventricular hypertrophy remained the same at 6-month follow-up without symptoms of syncope. The patient was advised to get an implant pacemaker but refused our suggestion. We suggested to the patient to come in for regular follow-up observations to monitor his condition.

Transsthoracic echocardiography

16 of the 22 cases with pulmonary hypertension at pre-procedure still remained higher than normal immediately after post-procedure, among which 3 patients were slightly higher at second day post-occlusion. At 6-month follow-up, the pulmonary artery pressure of all patients restored to normal levels. On the second day post-procedure, and at 1 and 3 month post-occlusion, RAD, RVD, LAD, LVESD and LVEDD measured by echocardiography showed declining tendency as compared with pre-procedural levels. At 3-month follow-up, there were still 10 patients with increased LAD, 13 patients with increased LVESD and LVEDD. At 6-month follow-up, all 12 patients that had increased RAD pre-procedure recovered to normal levels; only 1 of the 14 patients with increased RVD had slightly higher than normal levels; only 1 of the 10 patients with increased LAD had slightly higher than normal levels, and all the 13 patients with increased LVESD and LVEDD pre-procedure had levels restored to normal. Repeated measures of ANOVA showed that the procedure had significant effects on RAD, RVD, LAD, LVESD and LVEDD, and the changes to the data between pre-procedural and 6-month follow-up levels had statistical significance (P < 0.05, table 2).
Currently, both defects are amenable to transcatheter defects that usually do not occur concurrently. ASD and PDA are common congenital heart defects, which are rarely reported and only a small number of cases have been reported in limited case study reports. Our single center study retrospectively evaluated 22 patients diagnosed with both ASD and PDA. These patients received simultaneous transcatheter interventions. These simultaneous interventional procedures have been shown to be feasible and efficacious in these patients. In our retrospective study, no severe complications or recurrences of the treated disorders were detected during the 6-month follow-up period supporting the feasibility and efficacy of this approach. Taken together, the knowledge gained from the present study and two previous studies (14, 15), we determined that compared to resolving a single defect, simultaneous occlusion procedure of ASD complicated with PDA is much more complex and malformation diversity. Indications for interventional therapy for each single defect must be followed strictly. When implementing simultaneous interventional therapies, we need to be certain that the feasibility of performing both ASD and PDA

**DISCUSSION**

ASD and PDA are common congenital heart defects that usually do not occur concurrently. Currently, both defects are amenable to transcatheter closure, without the need for surgery. However, simultaneous transcatheter closure of both these two defects is rarely reported and only a small number of cases have been reported in limited case study reports.
occlusion by evaluating pre-procedural and intra-procedural examinations.

Taking the appropriate interventional treatment strategy is the key for successful therapy and for avoiding or reducing the occurrence of complications. Having a reasonable sequence of interventional treatment is significant for having a successful treatment strategy. The sequence of simultaneous interventional therapy for compound defects should follow the principles of "difficult first and easy second", "complex first and simple second" and "avoiding adverse effects of the second interventional therapy on the first therapy". For ASD complicated with PDA, the anatomical structure and defect diversity of ASD could interfere with the size and rim of the PDA. The indication for PDA occlusion under such circumstances is relatively more stringent, requiring careful echocardiography evaluation at pre-procedure or even transesophageal echocardiography to confirm the feasibility of interventional therapy. Because the trans-venous approach commonly used for PDA occlusion is introduced from right atrium to the right ventricle and even through PDA to the pulmonary artery, occlusion of PDA secondary to ASD occlusion would impose damaging effects on the closed ASD. Thus, pre-procedural evaluation of ASD/PDA compound defect should be mainly focused on ASD, with simultaneous interventional therapy starting with PDA occlusion followed by ASD occlusion, which is consistent with the procedure used by Ho CL's team (15). For ASD patients with uncertain feasibility of interventional therapy, a trial ASD occlusion needs to be conducted before PDA occlusion. If ASD has been confirmed feasible for occlusion, the ASD occlude should be held in position, then establish the contralateral intra-venous approach to close PDA and then release the ASD occluder after PDA is successfully occluded. Therefore, the effects of PDA occlusion on ASD occluder will be avoided. In this retrospective study, one patient received trial ASD occlusion prior to PDA occlusion.

Simultaneous interventional treatment for compound defects emphasizes individual therapy. Although the diagnosis of all patients in this study had ASD complicated with PDA, individual variations would lead to different shapes and sizes of ASD and PDA. With the development of interventional therapeutic instruments and diversity of the occluders, interventional therapy is gradually turning into individualized therapy. Selection of optimized occluders based on different anatomical subtypes is important for reducing complications and benefiting long-term outcomes. Based on the anatomical shunts and the age of the patient. The data from the atrium and ventricle diameter measurements collected by echocardiography clearly demonstrated this phenomenon, and the follow-up data further proved that ASD and PDA occlusion could gradually alleviate enlargement of the atrium and ventricles. Time required for restoration of the enlarged heart chambers mainly depends on the severity of the enlargement. Therefore, early intervention should be taken for patients with CHD suitable for intervention structures detected by aortography, PDA is typically classified using Krichenko classification system. For ASD, all patients were diagnosed with foramen secundum central type and the optimized occluder was selected individually based on the different sizes and rim of the defect. When necessary, transesophageal echocardiography should be performed to confirm the optimized occluder, avoiding insufficient endothelialization or adverse effects on the mitral and tricuspid valve and the aorta.

Due to the simultaneous diagnosis of ASD and PDA in this retrospective study, the left to right shunt from the two pathways could increase the pressure of the pulmonary artery, and in older patients, there is higher pulmonary artery pressure. With regards to pulmonary hypertension, strict recognition of its severity and property pre-procedures are essential. For resistant type pulmonary hypertension or pulmonary hypertension between resistant and dynamical type, PDA occlusion could be considered while noting changes to pulmonary artery pressure. If the pressure decreases significantly, ASD could be occluded simultaneously. If the pressure is stable, ASD needs to be maintained but not occluded, which could reduce the left to right shunt and relieve overload of the right heart system. In addition, patients with this condition are recommended to take targeted medication for pulmonary hypertension and receive follow-up observation post-procedure. The 22 patients in the present study exhibited different degrees of pulmonary hypertension, all of which fit the dynamical type, and showed decrease in hypertension immediately post-procedure. At 6 month follow-up, the pressure has been restored to normal levels.

In addition, ASD complicated with PDA could induce structural changes to the heart. Specifically, ASD typically induces the enlargement of the right atrium and ventricle. This is due to the left to right shunt from the left to right atrium, through the ASD and finally to right ventricle. Whereas, the haemodynamic changes of PDA induces the enlargement of the left atrium and ventricle. However, for ASD complicated with PDA, the enlargement of the right or left heart depends on the amount of shunt through the ASD and PDA. For example, the right heart enlargement dominants if ASD shunt is greater, while the left heart enlargement is more prominent when PDA shunt is greater. If the shunts through ASD and PDA are similar, the left and right heart enlargement could be induced simultaneously. The extent of enlargement is closely related with the size of the defects, the amount of therapy or surgical procedures.

In summary, simultaneous interventional therapy could correct concurrent ASD and PDA with a single transcatheter procedure. Compared with staged interventional therapy, simultaneous therapy is more acceptable, as it avoids repeating surgical punctures, general anesthesia and reducing the cost of therapy. Compared with cardiac surgery, interventional therapy is advantageous because of the small incisions, rapid recovery and avoidance of extracorporeal circulation.
or surgery-related complications and the occurrence of long-term arrhythmia post-surgery (16).

However, simultaneous transcatheter interventional therapy require greater technical expertise, thus, a thorough understanding of the heart structure and strictly following interventional therapy indications and correct evaluation of the whole procedure are essential for success.

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