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Usefulness of mean pulmonary artery pressure for predicting outcomes of transcatheter closure of atrial septal defect with pulmonary arterial hypertension

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Short Running Title: Transcatheter closure of ASD with PAH

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Wenzhi Pan, MD.

Abstract

Aims: This study aimed to provide a simple index for predicting the definite indication for transcatheter closure of atrial septal defect (ASD) with pulmonary arterial hypertension (PAH)

Methods and results: A positive response after attempted occlusion was defined as mean pulmonary artery pressure (MPAP) ≤ 30 mmHg or the decrement percentage of it ≥20% compared with the baseline. If a positive response was achieved, the occluder would be released, and the procedure was defined as successful. In 209 patients underwent successful procedure without PAH-specific medicine, there was a dramatic decrease in the percentage of patients with pulmonary arterial systolic pressure (PASP) ≥ 50 mmHg from baseline to the one-year follow-up (79.4% to 14.0%, P<0.001). The optimal cut-off value of MPAP to predict a positive response without PAH-specific medicine was 35.0 mmHg, with an area under the curve (AUC) of 0.919 (P <0.001). Administration of inhaled iloprost extended the cut-off point to 50.0 mmHg to reach a positive response, with an AUC of 0.774 (P=0.003).

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Conclusions: This large-scale study indicated that MPAP could be a simple but powerful index to predict benefit from closure in adult ASD patients with PAH.

Classifications and Keywords: atrial septal defect; pulmonary hypertension; clinical research

Condensed abstract

This study tested our proposed indication for closure and provided a simple index for predicting this indication in a large cohort of atrial septal defect (ASD) patients with pulmonary arterial hypertension (PAH). Most patients with a positive response undergoing permanent closure had a normal pulmonary artery pressure at the one-year follow-up. Mean pulmonary artery pressure (MPAP) less than 35.0 mmHg was a powerful index to predict positive response with a high area under the curve (AUC).

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Abbreviations :

ASD	atrial septal defect
PAH	pulmonary arterial hypertension
MPAP	mean pulmonary artery pressure
NYHA	New York Heart Association
PASP	pulmonary arterial systolic pressure
TR	tricuspid regurgitation

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Introduction

The development of pulmonary arterial hypertension (PAH) is frequent in adult patients with atrial septal defect (ASD). Approximately 6% to 35% patients with secundum ASD have PAH[1-3], and these patients are at higher risk of mortality, functional limitations and atrial tachyarrhythmias[4, 5]. Some reports observed that transcatheter closure of patients with secundum ASD and PAH could be associated with good outcomes[6, 7]. However, other studies found that PAH may still be progressive even after ASD device closure[3, 8]. For some patients, e.g. with R-L shunt and/or need for decompression, closure of ASD is even contraindicated. [9] There is consensus that some ASD patients with PAH will benefit from closure[9], but the definite indication for transcatheter closure of ASD with PAH remains controversial.

The Qp/Qs ratio and pulmonary vascular resistance are most important reference indices regarding indication for ASD closure of ASD closure in current guidelines. [9] But it is complicated to calculate and its evidences were old and poor. [3,9,10] Adult ASD patients with PAH is more common in developing country such as China.[11] We treated a large number of ASD patients with PAH in our center, and guessed that mean pulmonary artery pressure (MPAP) might be a simpler index regarding eligibility for ASD closure, based on our past clinical experience. This study aimed to test our proposed indication for permanent closure and give an optimal cut-off value of a simple index (MPAP) for predicting this indication in a large cohort of ASD patients combined with PAH.

Methods

Study Population

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The study retrospectively analyzed the data of patients with ASD and PAH who underwent attempted transcatheter closure between December 2013 and December 2016. During the period, there were 1956 consecutive patients with secundum ASD referred to our center for transcatheter closure. There were 408 patients with pulmonary hypertension, defined as MPAP ≥ 25 mmHg by catheterization. However, those patients were subsequently excluded if there were other coexisting congenital heart defects (N=54), residual shunt > 3 mm (N=15), failure to close because of anatomy (N=43), or identifiable causes for PAH (N=35), including mitral valve disease, a left ventricular ejection fraction <50%, pulmonary thromboembolic disease, severe lung disease with hypoxemia, portal hypertension, or obstructive sleep apnea. Thus, 261 ASD patients with PAH who underwent attempted transcatheter closure of ASD were enrolled in the primary analysis. Among the 261 patients, 7 patients who did not meet the positive response criterion (see the definition in the next paragraph) were closed, and closure was abandoned for 5 patients who met the positive response criterion. These 12 patients were excluded, and then 249 patients were included in the final analysis. The flowchart of patients selection was given in Figure 1. The study was conducted in accordance with the institutional Human Subjects Committee guidelines and approved by the local institutional review board. Because this was an observational study and all indices observed were commonly measured for all patients in our clinical practices, the need for written informed consent was waived by the review ethical review board.

Attempted Occlusion and Definition of a Positive Response

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Transcatheter ASD closure was performed under local anesthesia with fluoroscopic and transthoracic echocardiographic guidance. The procedures were conducted using Amplatzer-like domestic septal occluders (Lifetech, Shenzhen, China; SHSMA, Shanghai, China; or Star Way medical technology, Beijing, China). The flow chart of attempted occlusion is given in Figure 2**.** In our center, a positive response to attempted occlusion was defined as the absolute value of MPAP ≤30 mmHg or the decrement percentage of it ≥20% compared with the baseline immediately (5 minutes) after attempted occlusion, without a decrease of the mean peripheral blood pressure (<10%) or an increase in the ventricular end-diastolic pressure(<10%). If the positive response was achieved, the occluder would be released. Once a positive response was not reached (defined as a negative response) after attempted occlusion, inhaled iloprost was given. Inhaled iloprost was administered via a nebulizer (with a mouthpiece) at a cumulative dose of 20 ug for a total duration of 10 minutes. The MPAP was assessed again. If a positive response was attained, the patent's ASD would also be permanently closed. Otherwise, the closure would be abandoned. An increase in MPAP or right ventricular filling pressures or a drop in cardiac output suggests a low likelihood to benefit from permanent closure. Even if the MPAP declined but the percentage of decrement was less than 20% and MPAP ≥30 mmHg, permanent closure was still abandoned. In this study, if the positive response was achieved with or without inhaled ilopros, the ASD would be permanently closed, and the procedure was defined as successful. On the contrast, if the positive response could not be achieved even with inhaled iloprost, the closure would be abandoned, and the closure was defined as unsuccessful. Additionally, patients

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who had residual shunt > 3 mm and failed to close because of anatomy, had been excluded from the study, and thus they were not included in the unsuccessful closure definition.

Clinical Variables and Follow-Up

Data collection was obtained retrospectively. Baseline clinical data included age, gender, New York Heart Association (NYHA) functional class, history of atrial arrhythmia and associated comorbidities. Oral PAH-specific medicine was generally given for 3-6 month for the patients with successful closure with the inhaled iloprost. Transthoracic echocardiography was regularly performed in all ASD patients undergoing transcatheter closure before the procedure, before discharge and at 3 months and 1-year after the procedure. The maximum diameter of the ASD, pulmonary arterial systolic pressure (PASP), and degree of tricuspid regurgitation (TR) were assessed by transthoracic echocardiography. TR was quantified by color Doppler imaging. PASP was derived from right ventricular systolic pressure estimates using the tricuspid regurgitation velocity (V) and the Bernoulli equation as $4V^2$ + right atrial pressure[12]. A PASP measured by echocardiography ≥ 50 mmHg was regarded as PAH in this study according to the ESC guidelines[13].

Statistical Analysis

Continuous variables were expressed as the mean ± SD. Categorical variables were reported as the frequency and percentage. Normal distribution was assessed by the Kolmogorov-Smirnov test. Comparisons of continuous variables between different groups were performed by univariate analysis of variance, followed by a Bonferroni correction post hoc test when

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applicable. Comparisons of continuous variables between different time points within one group were performed with the paired Student's T test. Categorical variables were compared using the Chi-squared test. A receiver operating characteristic (ROC) methodology was used to analyze the optimal cut-off value of MPAP by catheterization in predicting a positive response without PAH-specific medicine for all enrolled patients. In addition, we performed the ROC analyses again for the patients who failed in attempted closure at first but then received inhaled iloprost to determine the optimal cut-off value of MPAP by catheterization. ROC analyses were expressed as curve plots and calculated area under the curve (AUC) with the confidence interval (CI) and the associated P value representing the likelihood of the null hypothesis (AUC = 0.5). A statistically derived value, based on the Youden index[14], maximizing the sum of the sensitivity and specificity was used to define the optimal cut-off value. A stepwise multivariate logistic regression was conducted to search the independent predictors of positive response. A criterion of $P < 0.05$ for entry and a $P \geq 0.10$ for removal was imposed in this procedure. All p values were 2-tailed. Statistical analyses were performed using SPSS version 19 (SPSS Inc., Chicago, IL).

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Results

Study Population and Baseline Characteristics

. Of the 249 patients who underwent attempted transcatheter ASD closure, 209 were successfully closed without PAH-specific medicine, 17 were successfully closed only after administration of inhaled iloprost, and 23 were

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failures, even combined with inhaled iloprost. Table 1 shows the main clinical and procedure data. PASP by echocardiography was significantly lower in the successful closure without iloprost group compared to the successful closure with inhaled iloprost group and the unsuccessful closure group (58.0±14.6 mmHg vs. 80.1±19.2mmHg and 93.0±28.6mmHg, respectively; both P<0.01). There were no differences in gender, age, history of systemic hypertension, history of atrial arrhythmia, NYHA functional class ≥ 3, ASD diameter and left ventricular ejection fraction (all P >0.05). The difference between mean left atria pressure and mean right atria pressure was higher in successful ASD closure without iloprost group (than the successful closure with inhaled iloprost group and the unsuccessful closure group (1.4±1.9 mmHg vs. 0.4± 0.9 mmHg and 0.4±1.6 mmHg, respectively; both P<0.01). This indicates the former group had more left-to-right shunts as compared with the latter two groups.

Echocardiographic Follow-Up after Transcatheter Closure

After discharge, 9.1% (19 cases) of patients who were successful-closure patients without inhaled iloprost and 76.4% (13 cases) of patients who were successful-closure patients with inhaled iloprost received the oral PAH-specific medicine. None of the followed up patients died. Among the first group, PASP by echocardiography was significantly decreased before discharge compared with the baseline (42.9±12.8 mmHg vs 58.0±14.6 mmHg; P < 0.00; N=209). At the 3-month (N=199) and 1-year follow-up (N=170), the improvements were stable (before discharge, 42.9±12.8 mmHg; 3-month follow-up, 40.8±10.6 mmHg; 1-year follow-up, 39.5±9.9 mmHg; P>0.05). There was a dramatic decrease in the percentage of patients with PASP ≥ 50 mmHg from the baseline to the one-year follow-up (79.4% to 14.0%, P<0.001). Before discharge, the left

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ventricular ejection fraction (LVEF) was increased (65.6±6.2% vs 67.8±5.2 %; P=0.001), and the pulmonary artery diameter (33.2±6.0 mm vs 32.8±5.9 mm, P<0.001) and percentage of moderate TR (21.5% vs 8.6%, P<0.001) were decreased compared with the baseline. These three indexes did not significantly change at the 3-month and 1-year follow-up (Table 2).

Among the 17 successful closure patients with inhaled iloprost, a decrease in PASP by echocardiography before discharge compared with the baseline was observed (59.4±14.4 mmHg vs 80.1±19.2 mmHg; P<0.001; N=17). Continued improvements occurred at the 3-month (53.3±11.6 mmHg, N=16) and 1-year (46.3±15.9 mmHg, N=12) follow-up (both P < 0.001 compared with discharge). There was a dramatic decrease in the percentage of patients with PASP ≥ 50 mmHg from the baseline to the one-year follow-up (96.4 % to 21.4 %, P<0.001). The pulmonary artery diameter, LVEF and percentage of TR did not change (all P>0.05) (Table 3).

ROC Curve Analyses of MPAP by Catheterization

The ROC curve analyses were performed twice. First, we pooled all the patients into the analysis to determine the optimal cut-off value of MPAP by catheterization in predicting a positive response without any PAH-specific medicine. The result of ROC curve analysis showed that the AUC of MPAP was 0.919 (CI: 0.873-0.966, P < 0.001, Figure 3). The optimal cut-off point of MPAP for predicting a positive response after attempting closure without any PAH-specific medicine was 35 mmHg. The sensitivity and specificity of this cut-off value were 79.9% and 95.0%. This means that 79.9% of patients with a positive response had MPAP≤35mmHg and 95.0% of patients with a negative response had MPAP > 35mmHg. Second, the ROC curve analysis was performed in

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patients who had received inhaled iloprost during the procedure to detect the optimal cut-off value of MPAP for predicting those who could not achieve a positive response, even when combined with PAH-specific medicine. The result of ROC curve analysis showed that the AUC was 0.774(CI:0.28-0.919, Figure 4). The optimal cut-off point of MPAP for predicting a negative response after attempted ASD occlusion combined with inhaled iloprost was 50 mmHg. The sensitivity and specificity of this cut-off value were 88.2% and 52.2%. A total of 88.2% of patients with a positive response had MPAP<50 mmHg (but ≥ 35mmHg) and 52.2% of patients with a negative response had MPAP ≥ 50 mmHg.

Multivariate analysis

The independent variables included in the multivariate logistic regression were the variables given in Table 1. If inhaled iloprost was not given, multivariate analysis found that only MPAP was the independent predictors of positive response (Exp(B)=0.811, P<0.001). If inhaled iloprost was applied to patients when necessary, multivariate analysis found that only MPAP was the independent predictors of positive response (Exp(B)=0.807, P<0.001).

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Discussion

To our best knowledge, this study included the largest series of ASD patients combined with PAH for closure. We confirmed the reliability of using our proposed indication (i.e., a positive response) for permanent closure in ASD patients with PAH. Most of patients with a positive response undergoing permanent closure had a normal PASP at the one-year follow-up. We found

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that MPAP could be a simple but powerful index to predict a positive response and thus an indication for closure. Multivariate analysis found that only MPAP was the independent predictors of positive response. The optimal cut-off value of MPAP to predict a positive response without PAH-specific medicine was 35.0 mmHg, with a sensitivity of 79.9% and a specificity of 95.0%. Administration of inhaled iloprost extended the cut-off point to 50.0 mmHg to reach a positive response. The sensitivity and specificity of this cut-off value were 88.2% and 52.2%, receptively.

Although current guidelines recommend that ASD patients with pulmonary vascular resistance ≥5 Wood units (WU) but <2/3 systemic vascular resistance or pulmonary arterial pressure <2/3 systemic pressure (baseline or when challenged with vasodilators, preferably nitric oxide, or after targeted PAH therapy) and evidence of net left–right shunt (Qp:Qs >1.5) may be considered for intervention (class ⅡB, level of evidence: C), this recommendation is based on poor evidence (9). The definitive indication for transcatheter closure of ASD with PAH remains controversial, and such studies either enrolled very few cases or were very old[3, 10, 15, 16].

Steele PM reported that all four surgically treated ASD patients with total pulmonary resistance greater than or equal to 15 U/m^2 were dead, while of the 22 surgically treated patients with total pulmonary resistance less than 15 U/m^2, 19 were alive with significant regression of symptoms[3]. Sánchez-Recalde A found that patients with a positive response (defined as a ≥ 25% reduction in PASP after occlusion, relative to the baseline level) had a good prognosis after closure, but their study just included 5 patients[10]. Attie F performed a large randomized controlled study and concluded that

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surgical closure was superior to medical treatment in patients > 40 years old with secundum ASD. However, they did not analyze the effectiveness of surgical closure in PAH subgroups and presented no implication about the indication for transcatheter closure of ASD with PAH. Huang ZW reported transcatheter closure for 7 ASD patients with PASP ≥60 mmHg and pulmonary vascular resistance ≥6 WU who had good short-term and medium-term outcomes [16].

In China, test-occlusion with balloon prior to closure is not generally used. The occluding device used in this study has three layers of isolation membrane. The vast majority of the patients would have no or very trivial residual shunt after attempted occlusion, based our clinical experience, as confirmed by the intra-operative echocardiograph. Additionally, if the patients still have large shunt (>3mm) by echocardiograph, this patients would be excluded (N=15). Therefore, direct test with occcluder device without balloon-test was equally informative. Because our center is an adult heart center, no children (< 12 years) were included in the study. The mean age of this cohort was approximately 45 years. In this study, a positive response to attempted occlusion was defined as MPAP ≤ 30 mmHg or the decrement percentage of it ≥20% compared with the baseline immediately after attempted occlusion, without a decrease in the aortic blood pressure or an increase in the ventricular end-diastolic pressure. We found that the PASP by echocardiography was significantly decreased before discharge and at the one-year follow-up. In previous studies, PASP measured by echocardiography ≥ 40 mmHg was regarded as PAH[7, 17]. However, this criterion was thought to be incorrect, and PAH is regarded as PASP by echocardiography ≥ 50 mmHg in the current ESC

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guidelines[13]. We adopted this criterion in this study. In patients with successful closure without inhaled iloprost, just 14.0% of patients did not reach normalization of PASP (<50 mmHg) at the one-year follow-up, while the percentage was 79.4% at baseline. In patients with successful closure with inhaled iloprost, only 21.4% of patients (96.4 % at baseline) did not reach normalization of PASP at the one-year follow-up. These results suggested that our proposed indication for permanent closure in ASD patients with PAH is reliable.

In the whole population, the optimal cut-off point of MPAP for predicting a positive response after attempted closure without any PAH-specific medicine was 35 mmHg. The AUC was 0.919.79.9% of patients with a positive response had MPAP≤35mmHg and 95.0% of patients with a negative response had MPAP > 35mmHg.In patients with a negative response after attempted occlusion, inhaled iloprost was then given, and MPAP was measured again. Administration of inhaled iloprost extended the cut-off point to 50.0 mmHg to reach a positive response. The sensitivity and specificity of this cut-off value were 88.2% and 52.2%, respectively. The high values of AUC, sensitivity and specificity in the above analyses supported our hypothesis that MPAP could be a simple but powerful index to predict a positive response and thus an indication for closure. Our results were consistent with the results reported by Yong et al., which showed that an independent predictor of normalization of PASP after transcatheter ASD closure was a lower baseline pulmonary pressure[16]. A large randomized controlled study found that patients with MPAP > 35 mmHg was an important predictor of adverse outcomes, regardless of surgical closure or

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medical treatment[15]. The optimal cut-off point of MPAP for predicting a positive response without any PAH-specific medicine was coincidentally 35 mmHg.

Limitations

Several limitations existed. First, this was a single center retrospective analysis and quite a large portion of patients (64/226) was lost at the one-year follow-up because the patient could not go back to our center. This may cause some bias of the analysis. However, the proportions of patents complete 3 months follow-up was high and just 11 patients was lost. The conclusions of our study could be also drawn from this short-term (3 months) follow-up. Some data were unavailable, such as Qp/Qs, cardiac output, and pulmonary vascular resistance, because these indices were not commonly collected in our clinical practice. However, we tried to simplify a hitherto more complex decision process regarding eligibility for ASD closure, beyond the traditional QP/QS and pulmonary resistance methods. Second, the term of follow-up was still short, and a longer follow-up is needed. Third, oral PAH-specific medicine was given for almost all the patients with successful ASD closure in the inhaled iloprost group. The analysis could be confounded by the effect of the medicine. However, the study still showed that transcatheter closure for these patients was reasonable, although oral PAH-specific medicine might be needed for these patients. Fourth, patients with a negative response, even after inhaling iloprost, did not undergo transcatheter closure. Whether this group was suitable for transcatheter closure is unknown. However, this group of patients was unlikely to have normalization of PASP because the percentage without normalization of PASP at the one-year follow-up in patients with successful closure with inhaled iloprost was up to 21.4%. Last, the patients in the study

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had not used pulmonary vasodilator agents before attempt occlusion, the conclusion of the study may not be applied to patients being pre-treated with such agents.

Conclusion

This large-scale study confirmed the reliability of our proposed indication for permanent closure in a large cohort of adult ASD patients with PAH. MPAP could be a simple but powerful index to predict benefit from closure in these patients. Large scale prospective studies are needed to confirm the encouraging results of our study.

Impact on daily practice

This study tested our proposed indication for closure and provided a simple index for predicting this indication in a large cohort of atrial septal defect (ASD) patients with pulmonary arterial hypertension (PAH).

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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Legend

Figure 1. The flow chart of patients selection. ASD, atrial septal defect; PAH, pulmonary arterial hypertension

Figure 2. The flow chart of attempted occlusion in our center.

Figure 3. ROC curve for MPAP in predicting a positive response after attempted closure without inhaled PAH-specific medicine. MPAP, mean pulmonary artery pressure; PAH, pulmonary arterial hypertension; ROC, receiver operating characteristic.

Figure 4. ROC curve for MPAP in predicting a positive response after attempted closure with inhaled PAH-specific medicine. MPAP, mean pulmonary artery pressure; PAH, pulmonary arterial hypertension; ROC, receiver operating characteristic.

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Table 1 Comparison of baseline characteristics and procedure data among different groups

	Successful ASD closure without iloprost N=209	**Successful ASD closure with iloprost N=17**	**Unsuccessful ASD closure N=23**	**p**
Age (years), mean ± SD	50.3±15.3	43.0±18.7	45.5±16.9	0.09
Female, n (%)	166 (79.4)	15 (88.2)	16 (69.6)	0.34
History of systemic hypertension, n (%)	37 (17.7)	2 (11.8)	2(8.7)	0.60
History of atrial arrhythmia, n (%)	35 (16.7)	2(11.8)	2(8.7)	0.61
NYHA functional class ≥ 3 class, n (%)	91 (43.5)	11(64.7)	15 (65.2)	0.10
Echocardiographic data				
ASD diameter (mm)	24.0±7.0	25.6±5.0	23.9±7.6	0.65
PASP (mmHg)	58.0±14.6	80.1±19.2	93.0±28.6	0.000
PASP≥50 mmHg (%)	146（69.9）	16（94.1）	23（100%）	0.009
PA diameter(mm)	33.2±6.0	32.3±3.1	36.4±7.8	0.047
Moderate TR, n (%)	45 (21.5)	6 (35.3)	7 (30.4)	0.30
Severe TR, n (%)	13 (6.2)	4(23.5)	6 (26.1)	0.001

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LVEF (%)	65.6±6.2	67.2±5.0	67.0±5.7	0.40
Hemodynamic data by cardiac catheterization				
MPAP (mmHg)	31.0±6.2	41.5±7.8	51.4±10.6	0.00
MRVP (mmHg)	19.2±8.1	21.1±12.5	25.4±15.3	0.01
MLAP(mmHg)	8.9±4.2	7.8± 5.2	6.3±4.8	0.16
MRAP(mmHg)	7.5 ±3.9	7.4± 5.3	5.9±4.6	0.01
(MLAP-MRAP) (mmHg)	1.4±1.9	0.4± 0.9	0.4±1.6	0.006

ASD, atrial septal defect; LVEF, left ventricular ejection fraction; MPAP, mean pulmonary artery pressure; MRVP, mean right ventricular pressure; NYHA, New York Heart Association; PA, pulmonary artery; PASP, pulmonary artery systolic pressure; TR, tricuspid valve regurgitation; MLAP, mean left atria pressure; MRAP, mean right atria pressure.

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Table 2 Echocardiographic changes at the baseline, before discharge and at the 3-month follow-up in the successful ASD closure without iloprost group.

	Baseline (N=209)	Before discharge (N=209)	3-month Follow-up (N=199)	1-year Follow-up (N=150)	P1 Before discharge vs. baseline	P2 3-month follow-up vs. before discharge	P3 1-year follow-up vs. 3-month Follow-up
PASP (mmHg)	58.0±14.6	42.9±12.8	40.8±10.6	39.5±9.9	0.000	0.002	0.24
PASP≥50 mmHg (%)	166 （79.4）	45(21.5)	37(18.6)	21(14.0)	0.000	0.27	0.10
PA diameter (mm),	33.2±6.0	32.8±5.9	31.4±4.3	30.8±2.9	0.001	0.22	0.30
Moderate TR, n (%)	45 (21.5)	18 (8.6)	11 (5.6)	9(6.0)	0.000	0.56	0.65
Severe TR, n (%)	13 (6.2)	4 (1.9)	4 (2.0)	4(2.7)	0.07	1.0	1.00
LVEF (%)	65.6±6.2	67.8±5.2	68.1±5.5	67.5±4.4	0.000	0.20	0.22

ASD, atrial septal defect; LVEF: left ventricular ejection fraction; PA, pulmonary artery; PASP, pulmonary artery systolic pressure; TR, tricuspid valve regurgitation.

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Table 3 Echocardiographic changes during at the baseline, before discharge and at the 3-month follow-up in the successful ASD closure with inhaled iloprost group

	Baseline (N=17)	Before discharge (N=17)	3-month follow-up (N=16)	1-year follow-up (N=12)	P1 Before discharge vs. baseline	P2 3-month follow-up vs. before discharge	P3 1-year follow-up vs. 3-month Follow-up
PASP (mmHg),	80.1±19.2	59.4±14.4	53.3±11.6	46.3±15.9	0.000	0.016	0.10
PASP≥50mmHg, n (%)	27 （96.4）	13(76.5)	11(68.8)	3(25.0)	0.05	0.86	0.000
PA diameter (mm)	32.3±3.1	30.9±2.2	33.0±4.6	33.3±2.7	0.18	0.15	0.74
Moderate TR, n (%)	6 (35.3)	6(35.3)	4(25.0)	4 (33.3)	0.55	0.73	1.00
Severe TR, n (%)	4(23.5)	3 (17.6)	3(18.8)	2(16.7)	0.71	1.0	1.00
LVEF (%)	67.2±5.0	68.4±6.5	67.0±4.3	65.6±6.1	0.65	0.54	0.60

ASD, atrial septal defect; PASP, pulmonary artery systolic pressure; PA, pulmonary artery; TR, tricuspid valve regurgitation; LVEF: left ventricular ejection fraction.

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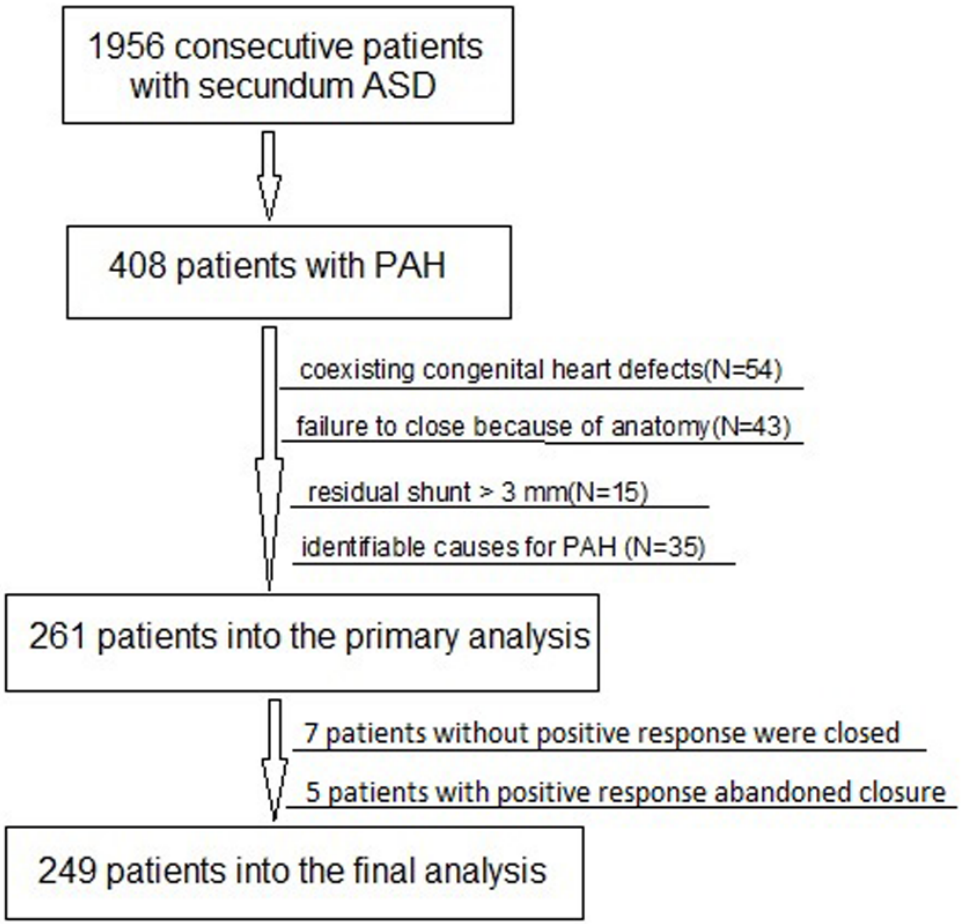

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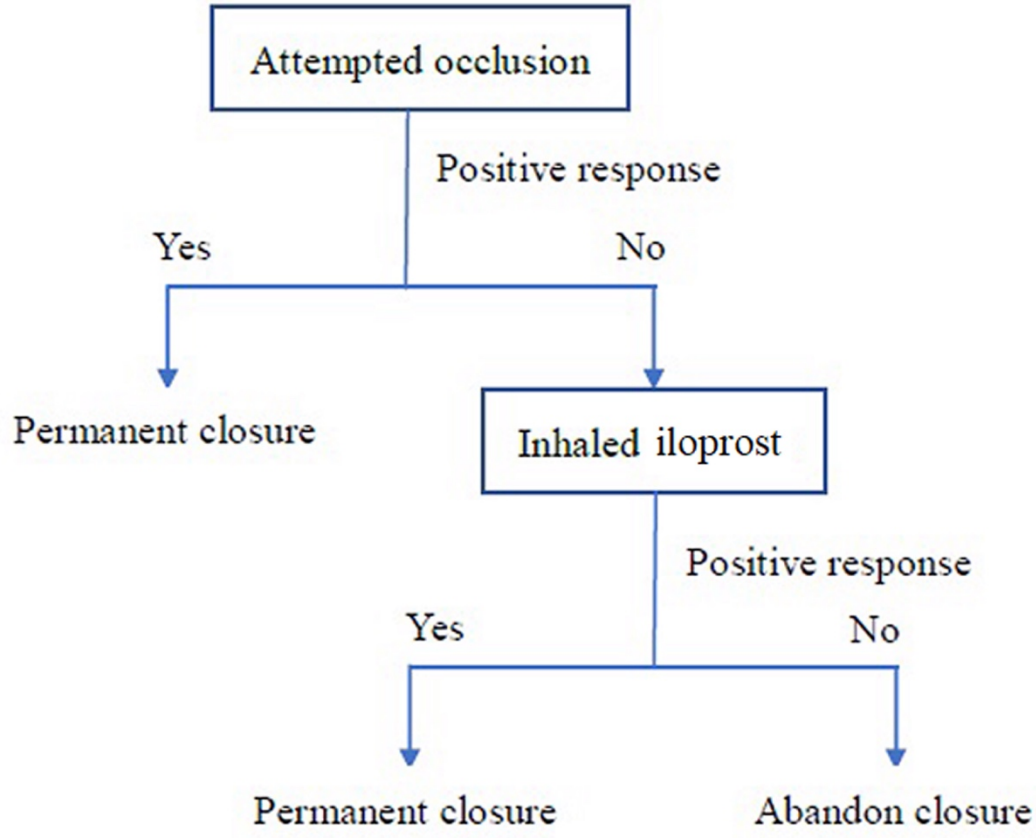

Positve response: MPAP<30mmHg or decrement percentage of MPAP≥20% after attempted occlusion

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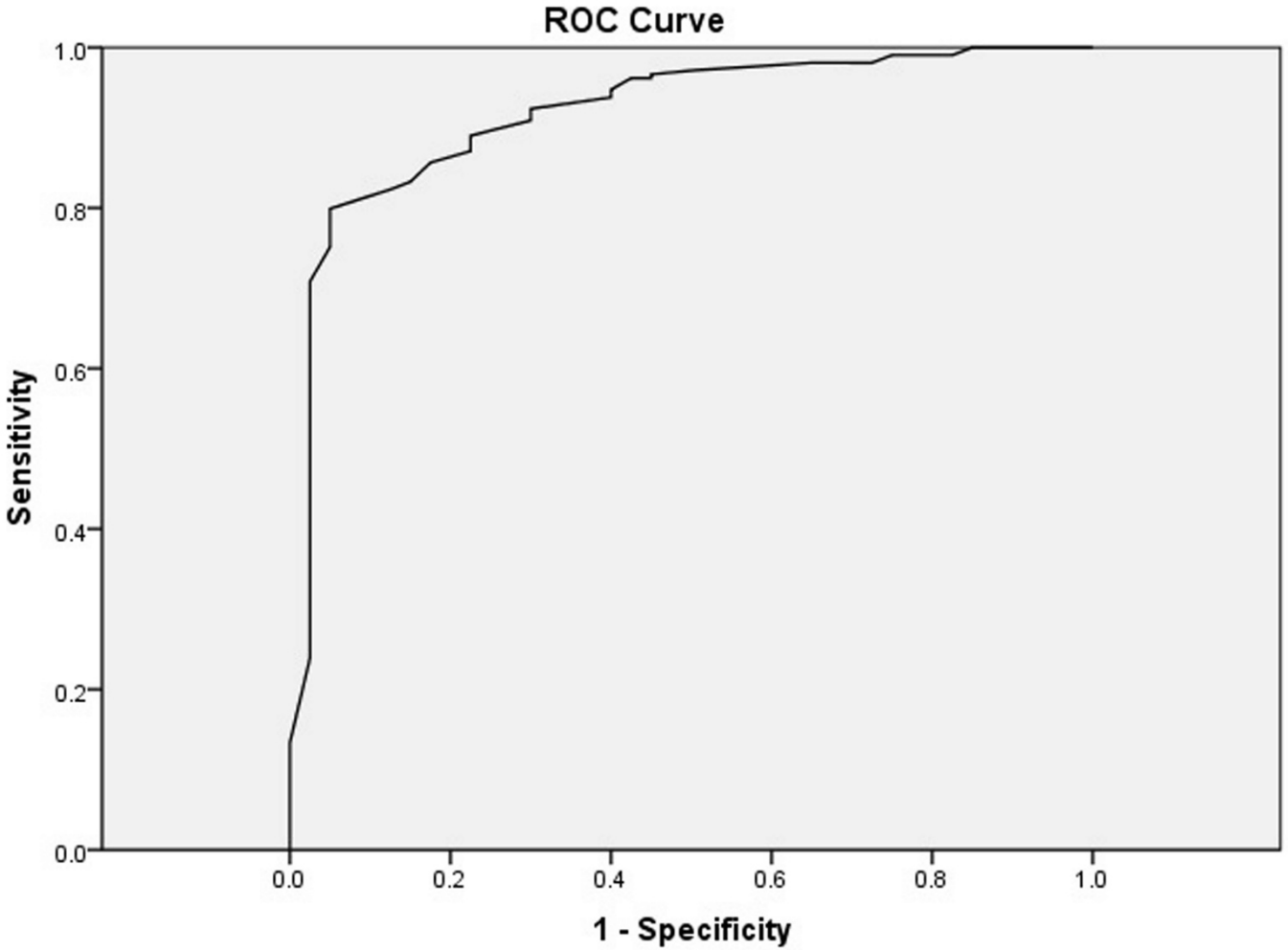

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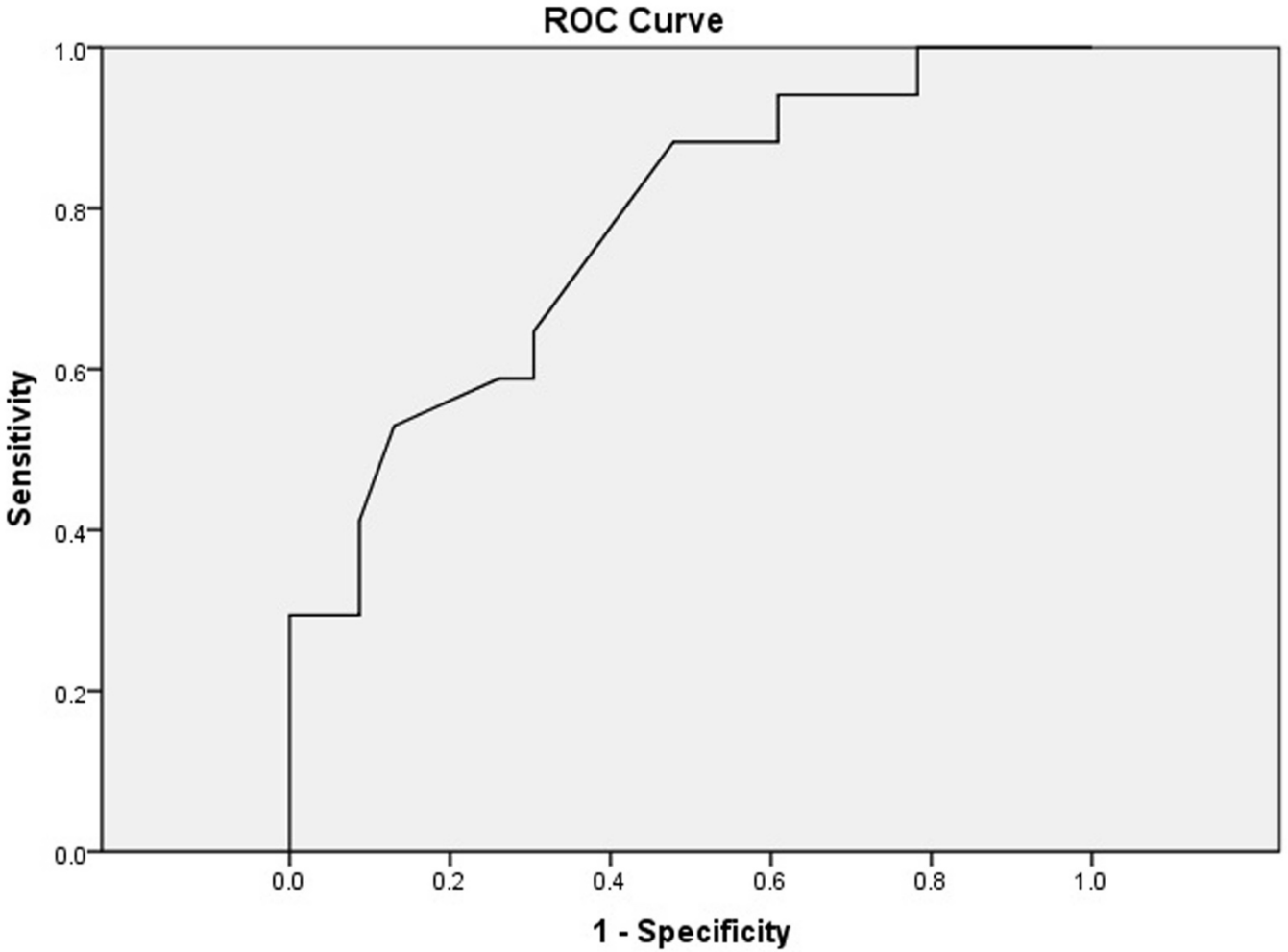

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