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The efficacy, safety and clinical feasibility of a percutaneous atrial septal shunt device for pulmonary arterial hypertension: a single-center cohort study

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Abstract

Aim To evaluate the safety and efficacy of FreeFlow percutaneous atrial septal shunt device (manufactured by AOLIU Medical Technology Co., Ltd, Shanghai, China) in patients with refractory pulmonary arterial hypertension (PAH) for the first time.

Methods The study enrolled adult patients diagnosed with refractory pulmonary arterial hypertension (PAH) at the Department of Cardiology, Zhongshan Hospital, Fudan University, between Oct 2021 and Oct 2023. The patients were treated with the FreeFlow percutaneous atrial septal shunt device and underwent follow-up immediately after operation, as well as before and after discharge (at 1, 3, 6, 12 months post-operation). The primary endpoints of the study included the rate of major cardiovascular and cerebrovascular adverse events (MACCEs), serious adverse events (SAEs), and serious device-related adverse events (SADEs) within 12 months of shunt implantation. Data analysis was conducted using SAS 9.3.

Results A total of 12 patients were enrolled in the study and successfully completed the operation. 10 subjects had completed 12 months' follow-up after operation, while two subjects had died. The incidence of MACCE was 0%, and the incidence of SAEs was 33%, which was unrelated to the treatment with this device. No systemic or instrumental embolizations occurred during the follow-up period. All ten subjects exhibited a stable right-to-left shunt after the operation (100% success rate). Seven patients' New York Heart Association (NYHA) functional classification improved from grade III to grade II. The Short Form-36 (SF-36) score and the 6-minute walking distance (6MWD) at 12 months post-operation were significantly improved compared to baseline, with scores of 47.6 ± 19.5 versus 64.7 ± 24.6 ($P = 0.029$) and distances of 239.5 ± 137.8 m versus 401.7 ± 129.6 m ($P = 0.045$), respectively. Similarly, the levels of

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N-terminal pro-brain natriuretic peptide (NT-proBNP) and right heart diameter (RAD) also decreased significantly, from 3236 ± 1590.3 pg/mL to 1787.3 ± 703.7 pg/mL ($P = 0.039$) and from 59.1 ± 10.6 mm to 46.3 ± 7.5 mm ($P = 0.046$), respectively.

Conclusions The results of this clinical study demonstrate that the product can attain the anticipated performance under typical conditions of use. The risks associated with the product are deemed acceptable when weighed against its potential benefits. All preclinical and clinical evaluations have furnished definitive and rational scientific evidence supporting the safety and efficacy of the percutaneous atrial septal shunt.

Clinical trial number Not applicable.

Keywords Percutaneous atrial septal shunt, Refractory pulmonary arterial hypertension, Quality of life, Heart failure

Introduction

Pulmonary hypertension (PH) is a life-threatening cardiopulmonary vascular disease characterized by severe and detrimental manifestations. The most frequent complaints among patients with PH include shortness of breath, fatigue, dyspnea, hemoptysis, palpitations, hoarseness, and a substantial decline in quality of life (QoL [1, 2]. According to statistics, the incidence of PH in developed countries is approximately 1%. Among individuals aged over 65, the prevalence rises to 10% due to the coexistence of certain underlying heart and lung conditions [3]. However, for specific subtypes of PH, such as refractory pulmonary arterial hypertension (PAH), the incidence is exceptionally low, affecting only about 6 individuals per million adults [4]. Despite significant advancements in PH treatment over the past decade, a considerable proportion of patients still experience progressive worsening of symptoms, rendering lung transplantation as a final resort.

Balloon atrial septostomy (BAS) serves as an effective palliative measure for patients suffering from refractory pulmonary arterial hypertension (PAH) and other cardiovascular diseases that impose a significant burden on the right heart [5, 6]. By artificially creating a right-to-left shunt, BAS can alleviate the clinical manifestations of both acute and chronic right heart failure and augment left cardiac output in patients with PAH. However, spontaneous closure of the atrial septostomy may occur in approximately 25% of patients who undergo BAS [7]. While a larger atrial septostomy is less likely to undergo spontaneous closure, it does elevate the risk of acute severe hypoxia and potentially even fatal outcomes [8]. To date, several atrial septal shunt devices have been designed for the treatment of PAH or heart failure patients, including the transcatheter interatrial shunt device (IASD), the V-Wave device, and the Atrial Flow Regulator [9–13]. These devices are capable of effectively reducing atrial pressure, alleviating dyspnea, and improving hemodynamics and symptoms in the aforementioned patient populations.

In pursuit of therapeutic efficacy for the treatment of refractory pulmonary arterial hypertension (PAH), the FreeFlow percutaneous atrial septal shunt device (manufactured by Shanghai AOLIU Medical Technology Co., Ltd., as shown in Fig. 1) has been developed. This device is a derivative of the Amplatzer Septal Occluder and the Atrial Flow Regulator, specifically designed for the management of refractory PAH. Its potential use lies in further enhancing hemodynamics and alleviating symptoms in patients with PAH. The primary objective of this study was to assess, for the first time, the safety and efficacy of the FreeFlow percutaneous atrial septal shunt device in the treatment of refractory PAH. The findings from this study will inform decisions on whether and how to proceed with further clinical trials.

Methods

Study design and participants

This prospective single-center study aimed to assess the feasibility of utilizing a percutaneous atrial septal shunt device. Participants were treated with the FreeFlow percutaneous atrial septal shunt device manufactured by AOLIU Medical Technology Co., Ltd. (Shanghai, China) and underwent follow-up evaluations immediately post-operation, as well as before and after discharge at 1, 3, 6, 12 months post-surgery. The total duration of each participant's involvement in the trial spanned approximately 12 months.

Inclusion and exclusion criteria

Subjects were recruited if they were aged ≥ 18 years, had an $SpO_2 \geq 90\%$, were classified as New York Heart Association(NYHA) functional class III or IV, and had uncontrolled refractory heart failure/pulmonary artery hypertension (PAH; idiopathic, familial, connected to connective tissue disease, or drug-related) despite standardized drug therapy for ≥ 3 months or had experienced at least one hospitalization due to refractory heart failure/PAH. The exclusion criteria included local or systemic sepsis or other acute infection, thrombotic coagulation disorders, intolerance to contrast media or thrombosis treatment, pregnancy, severe restrictive or obstructive pulmonary disease, a mean right atrial pressure (mRAP) was > 20 mmHg, a left ventricular ejection

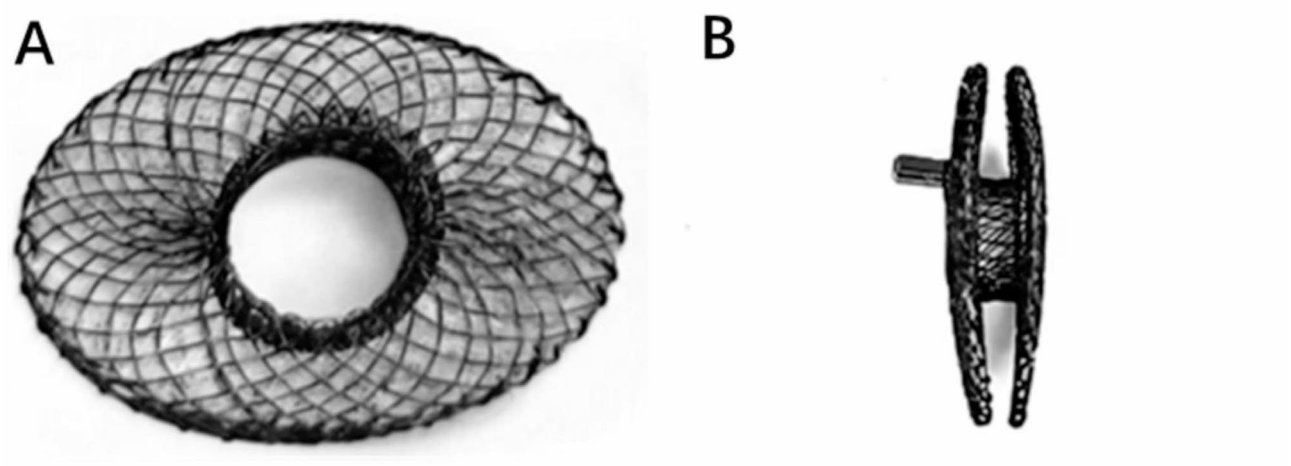

Fig. 1 Free flow atrial septal shunt device **A**: front view of the shunt device; **B**: side view of the shunt device

fraction (LVEF) < 40%, a tricuspid annular plane systolic excursion (TAPSE) < 10 mm, anatomic abnormalities that prevented shunt implantation across the atrial septum, and any other conditions deemed inappropriate by the investigators.

Percutaneous atrial septal shunt device implantation

After anesthetizing the subject, atrial septal puncture was performed via the right femoral vein under X-ray and transthoracic echocardiography (TTE) guidance. Following successful puncture, atrial septostomy was carried out using a 6–8 mm balloon. After creating the atrial septal stoma, the atrial septal shunt device was implanted using a technique analogous to that employed for atrial septal defect occlusion. An ultra-hard guidewire was introduced into the left upper pulmonary vein, along which a 9 F delivery sheath was advanced. After withdrawing the guidewire and sheath core, the left umbrella disk of the shunt device was deployed within the left atrium. The delivery sheath and device were then carefully withdrawn to the atrial septum. Using a fixed delivery cable, the right umbrella disk was deployed, securing the device on both sides of the atrial septum. A push-pull test confirmed the stability of the device, with TTE revealing a clear central shunt within the device. Finally, the shunt device was released, successfully completing the procedure.

Postoperative antithrombotic therapy

For individuals without indications for anticoagulation, the recommended postoperative regimen includes aspirin (100 mg) and clopidogrel (75 mg) daily for one month, followed by aspirin monotherapy for an additional five months. In contrast, patients with indications for anticoagulation—such as those with atrial fibrillation—are typically prescribed conventional anticoagulants, such as rivaroxaban (20 mg once daily), to mitigate thromboembolic risk after the procedure.

Baseline data collection and follow-ups

After reviewing the laboratory database through the hospital information management system, the following data were recorded: demographic information, laboratory measurements, electrocardiography (ECG) and transthoracic echocardiography (TTE) results, as well as details of the atrial septal shunt device implantation procedure. Prior to the operation and during follow-up visits, the following parameters were evaluated or documented: levels of N-terminal pro-brain natriuretic peptide (NT-proBNP), New York Heart Association Functional Classification (NYHA-FC), exercise capacity, quality of life (QoL), medications used, and any adverse events. Exercise capacity was assessed using the 6-minute walk distance (6MWD) test, while QoL was measured using the Short Form-36 (SF-36) questionnaire.

Efficacy and safety monitoring during the study

The primary endpoint of this study was to assess the rate of major adverse cardiovascular and cerebrovascular events (MACCEs) at 12 months post-operation, as well as the incidence of serious adverse events (SAEs), including death, systemic embolization, or instrumental embolization within 12 months of shunt implantation. The secondary objectives encompassed: 1, the rates of SAEs and serious adverse device events (SADEs) within 12 months of shunt implantation; 2, the success rate of shunt implantation defined as the proportion of cases where a stable intra-atrial right-to-left shunt was confirmed by echocardiography and/or digital subtraction angiography (DSA) within 12 months; 3, the improvement in movement ability measured by the 6-minute walking distance(6MWD) at 12 months post-operation; 4, the enhancement in quality of life at 12 months post-operation;5, the improvement in cardiac function at 12 months post-operation.

Statistical analysis

The data analysis was conducted using SAS 9.3 software. Continuous data was presented as the mean with standard deviation (SD), maximum and minimum values, or median with interquartile range (IQR). The Shapiro-Wilk test was employed to assess the normality of the data. Subsequently, either the Group T test or the Wilcoxon rank-sum test was utilized for comparisons between groups, depending on the data's normality. Categorical variables were reported as numbers and percentages, and comparisons among these variables were made using the continuity-corrected χ^2 test. In cases where more than 25% of cells had a theoretical frequency of less than 5, the Fisher's exact test was applied. All statistical analyses were conducted using two-sided tests, with a p-value < 0.05 considered statistically significant.

Results

Baseline characteristics of subject

A total of 12 patients were enrolled in the study. The first participant with pulmonary arterial hypertension (PAH) was enrolled in May 2022, and the 12th participant was enrolled in March 2023. As of the latest follow-up, ten subjects have completed the 12-month post-operative follow-up period. Unfortunately, two subjects passed away due to unrelated causes during the follow-up period. Prior to the operation, all patients were classified as NYHA functional class III. The average SF-36 QoL score was 47.6 ± 19.5, 6MWD was 239.5 ± 137.8 m and the NT-proBNP level was 3236 ± 1590.3 pg/mL(Table 1).

Interventional procedure and invasive cardiac parameters of subject

All patients successfully completed the operation. Intraoperatively, a decrease in mean pulmonary wedge pressure (mPCWP) and cardiac output (CO) was observed, along with an increase in mean right atrial pressure (mRAP) and mean pulmonary artery pressure (mPAP). Additionally, an average pulmonary-to-systemic blood flow ratio (Qp: Qs) of 0.8 ± 0.1 was observed intraoperatively. The average operation time for all patients was 23.57 ± 29.35 min. All patients underwent shunt implantation via right femoral vein approach. Specifically, three patients underwent intraoperative balloon dilation using a balloon with diameter of 6 mm, while nine patients underwent dilation with a balloon diameter of 8 mm. Consequently, three patients received shunt implants with a diameter of 5 mm, and nine patients received shunt implants with a diameter of 7 mm (Table 1).

Results of clinical follow up and endpoint evaluation

There were no major adverse cardiovascular and cerebrovascular events (MACCEs), systemic embolization or device embolization reported during the follow-up period. The incidence of SAEs was 33.3%, and these were unrelated to the treatment with the device. The 12-month mortality rate was 16.7% (2 subjects). Among the 10 subjects who completed the 12-month follow-up, the stable right-to-left shunt rate was 100%. Seven patients experienced an improvement in their NYHA functional class (FC), from Grade III to Grade II. Additionally, there was a significant improvement in both the SF-36 Quality of Life (QoL) score and the 6-Minute Walk Distance (6MWD): the SF-36 score increased from 47.6 ± 19.5 to 64.7 ± 24.6 (P = 0.029), and the 6MWD increased from 239.5 ± 137.8 m to 401.7 ± 129.6 m (P = 0.045). The levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) and right ventricular diameter(RVD) at 12 months post-operation was significantly lower than that at baseline, decreasing from 3236 ± 1590.3 pg/mL to 1787.3 ± 703.7 pg/mL (P = 0.039), 59.1 ± 10.6 mm vs. 46.3 ± 7.5 mm(P = 0.046), respectively(Table 1)(Fig. 2). Furthermore, all laboratory tests (including blood routine tests and coagulation tests) conducted during the follow-up period showed no device-related abnormalities.

Discussion

For patients with refractory PAH, the efficacy of current drug therapies remains suboptimal, ultimately leading to lung transplantation as the definitive treatment option [14]. However, due to various factors including the scarcity of lung donors, surgical complexity, appropriate timing for surgery, and the associated treatment costs, lung transplantation is only feasible for less than 3% of PAH patients [15]. In the absence of effective pharmacological interventions, the median survival time of patients with PAH is approximately 2.8 years [16]. Even after undergoing lung transplantation, patients often experience unsatisfactory quality of life (QoL) and survival outcomes. Right to left shunt creation is a crucial principle underlying the effectiveness of PAH treatment. BAS can serve as a bridging therapy for PAH patients with rapid clinical deterioration, despite maximal medical therapy [17]. By establishing a relatively stable right-to-left shunt, BAS can alleviate right heart pressure, mitigate symptoms of right heart failure, and reduce both clinical manifestations and mortality associated with PAH. This innovative technology holds promise as an economic, safe and efficacious treatment for heart failure, potentially revolutionizing the survival prospects of PAH patients in China.

A total of 12 patients enrolled in the study, and all successfully completed the operation. Out of these, 10 patients completed the entire 12-month follow-up period, with all (100%) demonstrating stable right-to-left shunt. Post-operatively, there was an improvement in the NYHA functional classification, 6-Minute Walk Distance (6MWD), and Short Form-36 (SF-36) Quality of Life (QoL) score for the patients. Furthermore,

Table 1 Baseline, Intraoperative, and latest follow-up information of all patients

Baseline information		
Demographics		
Males, n (%)		2 (28.6)
Age, y (mean ± SD)		46.86 ± 16.15
Heigh (cm)		164.86 ± 9.58
Weight (kg)		56.57 ± 11.54
Previous cardiovascular history, disease, medication history and surgical history		
Hypertension, n (%)		2 (16.7)
Type 2 diabetes, n (%)		1 (8.3)
Stroke, n (%)		1 (8.3)
CHD, n (%)		1 (8.3)
Myocardial infarction, n (%)		1 (8.3)
Atrial fibrillation, n (%)		1 (8.3)
History of using oral anticoagulant, n (%)		3 (25)
Previous heart operation, n (%)		5 (41.7)
Examinations		
NYHA function classification ≥ III, n (%)		12 (100)
SF-36 score		47.6 ± 19.5
6MWD (m)		239.5 ± 137.8
NT-ProBNP (pg/mL)		3236 ± 1590.3
Echocardiography		
LVEF (%)		58.7 ± 14.4
LAD (mm)		43.4 ± 8.9
LVEDD (mm)		46.2 ± 13.8
RAD (mm)		65.6 ± 13.7
RVD (mm)		59.1 ± 10.6
PASP (mmHg)		68.2 ± 24.9
Moderate to severe TR, n (%)		10 (83.3)
Intraoperative information		
	Before shunting	After shunting
mPCWP (mmHg)	10.1 ± 4.3	9.3 ± 2.3*
mRAP (mmHg)	8.9 ± 4.6	8.2 ± 5*
mPAP (mmHg)	40.5 ± 19.1	42.2 ± 21.7*
CO (L/min)	4.1 ± 1.4	3.9 ± 1.5*
Qp: Qs	1	0.8 ± 0.1*
Operative approach	Via the right femoral vein	12 (100.0%)
Balloon Diameter (mm)		
6		3 (25%)
8		9 (75%)
Shunt diameter (mm)		
5		3 (25%)
7		9 (75%)
latest follow-up information		
MACCEs, n (%)		0 (0)
SAEs, n (%)		4 (33.3)
SADEs, n (%)		0 (0)
right-to-left shunt, n (%)		10 (100)
6MWD		401.7 ± 129.6
SF-36 QoL		64.7 ± 24.6
NYHA function classification ≥ III, n (%)		3 (30)
RVD, (mm)		46.3 ± 7.4
LVEF (%)		61.4 ± 13.4
LAD (mm)		45.4 ± 9.2
LVEDD (mm)		48.1 ± 15.2

Table 1 (continued)

Baseline information	
RAD (mm)	59.1 ± 10.5
RVD (mm)	46.3 ± 7.5
PASP (mmHg)	68.8 ± 31.8
Moderate to severe TR, n (%)	5 (50)
NT-ProBNP, (pg/ml)	1787.3 ± 703.7

Abbreviations: CHD, coronary heart disease; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; LAD, Left atrial diameter; LVEDD, Left ventricular diastolic diameter; RAD, Right atrial diameter; RVD, Right ventricular diameter; PASP, pulmonary artery systolic pressure; TR, tricuspid regurgitation; SF-36, Short Form-36; 6MWD, 6-minute walking distance; NT-ProBNP, N-terminal pro-brain natriuretic peptide; mPCWP, mean pulmonary wedge pressure; mRAP, mean atrial pressure; mPAP, mean pulmonary arterial pressure; CO, cardiac output; Qp: Qs, pulmonary-to-systemic blood flow ratio, *: *P* value > 0.05

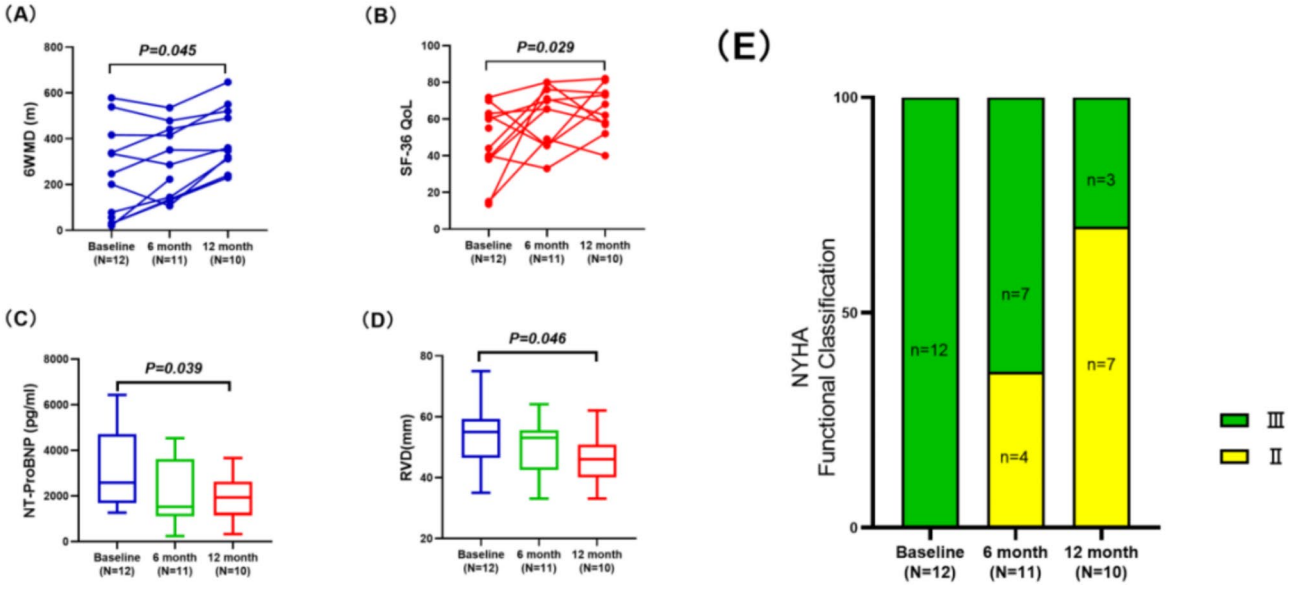

Fig. 2 Improvement in clinical parameters at baseline status, 6 months, and 12 months in patients after atrial septal shunt implantation: (**A**) Improvement of 6MWD; (**B**) Improvement of SF-36 QoL; (**C**) Improvement of NT-ProBNP; (**D**) Improvement of RVD; (**E**) Improvement of NYHA functional classification

compared to preoperative levels, there was a significant decrease in postoperative N-terminal pro-Brain Natriuretic Peptide (NT-proBNP) levels and right ventricular diameter (RVD), both of which are crucial indicators for assessing the clinical symptoms of patients with pulmonary arterial hypertension (PAH). Although four serious adverse events (SAEs) were reported in this study, the researchers assessed that these SAEs were unrelated to the use of this device. One patient was hospitalized due to fever and hypoxemia following acoronavirus disease 2019 (COVID-19) infection 4.5 months after the operation, unfortunately, this patient eventually passed away despite active rescue and treatment efforts. Another patient was admitted due to acute upper respiratory tract infection six months post-operation and was discharged after one week of treatment. The third patient died of syncope caused by a foreign body obstructing the respiratory tract after eating fruit ten months post-operation. Both deceased patients had severe pulmonary hypertension. After the shunt device was released, both surviving patients showed a slight increase in mPAP (Patient 1: 67 to 71 mmHg, Patient 3: 51 to 53 mmHg) and a decrease in CO (Patient 1: 2.3 to 1.9 mmHg, Patient 3: 3.2 L/min to 2.7 L/min), with no significant change in mRAP (Patient 1: 15 to 14 mmHg, Patient 3: 11 to 11 mmHg). The last SAE reported was paroxysmal atrial fibrillation occurring twelve months post-operation. The patient was treated with diuretics, cardiac function improvement therapies, and targeted drugs to reduce pulmonary pressure and heart rate. The patient's condition was stable and he was discharged.

The preliminary results of this study indicate that the device is well-tolerated and exhibits a promising short-term prognosis in PAH patients. Furthermore, these findings provide a certain degree of evidence for future multi-center clinical trials. However, it is important to acknowledge several limitations of this study. Firstly, the study represents a small single-center observational study. Secondly, due to the limited sample size and the number of participants who completed the follow-up, the 6MWD could not be statistically analyzed due to insufficient follow-up data. Similarly, the QoL and NT-proBNP

failed to reach statistical significance. Lastly, pulmonary hemodynamic parameters obtained during right heart catheterization (RHC) are crucial indicators for assessing the prognosis of PAH, and the inclusion of these data would strengthen the convincingness of the study results.

Compared with earlier devices, our atrial septal shunt device incorporates several advanced features. The device employs a polymer membrane that promotes rapid endothelialization, facilitating efficient physiological adaptation and recycling. Its unique oval disk design and compact implant volume ensure gentle engagement with atrial septal tissue, significantly minimizing the risk of atrial arrhythmia caused by tissue traction. To address diverse patient treatment needs, the device is available in multiple pore sizes—5 mm, 7 mm, 9 mm, and 11 mm—offering tailored solutions for effective intervention and enhanced patient comfort. This design provides a versatile and patient-centered approach to interventional procedures, setting a new standard in atrial septal shunt technology.

Conclusions

The results of this clinical study demonstrated that the product could attain the anticipated performance under typical usage conditions. When weighed against the anticipated benefits, the risks associated with the product are deemed acceptable. Comprehensive pre-clinical and clinical evaluations have yielded definitive and sound scientific evidence, confirming that the transcatheter atrial septal shunt manufactured by Shanghai AOLIU Medical Technology Co., Ltd. is both safe and effective.

Author contributions

Author Contributions: Ge JB, Zhou DX, and Guan LH presented the purpose of the study. Zhang L, Zhang XC, Pan WZ, Chen SS and Zhang Y collected the research data. Li MF, Chen DD, Fan JN and Tian D performed statistical analysis. All the authors wrote the main manuscript and reviewed the manuscript.

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Data availability

The data in the study can be obtained by contacting the corresponding author.

Declarations

Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The trial was conducted according to the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board (IRB) of Shanghai Zhongshan Hospital (NO.: B2021-630) and informed consent was obtained from each participant.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Xiong C, Yang B. Revising the hemodynamic criteria for pulmonary hypertension: A perspective from China [J]. J Transl Int Med, 2023;11(1):1–3.
2. He M, Jiang R, Fei S, et al. Cardiac magnetic resonance imaging-derived septum swing index detects pulmonary hypertension: A diagnostic study [J]. J Transl Int Med, 2023;11(4):459 – 67.
3. Hoeper M M, Humbert M, Souza R, et al. A global view of pulmonary hypertension [J]. Lancet Respir Med, 2016;4(4):306 – 22.
4. Leber L, Beaudet A, Muller A. Epidemiology of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: identification of the most accurate estimates from a systematic literature review [J]. Pulm Circ, 2021;11(1):2045894020977300.
5. Bauer A, Khalil M, Ludemann M, et al. Creation of a restrictive atrial communication in heart failure with preserved and mid-range ejection fraction: effective palliation of left atrial hypertension and pulmonary congestion [J]. Clin Res Cardiol, 2018;107(9):845 – 57.
6. Mlcek M, Meani P, Cotza M, et al. Atrial Septostomy for Left Ventricular Unloading During Extracorporeal Membrane Oxygenation for Cardiogenic Shock: Animal Model [J]. JACC Cardiovasc Interv, 2021;14(24):2698 – 707.
7. Sandoval J. Interventional Therapies in Pulmonary Hypertension [J]. Rev Esp Cardiol (Engl Ed), 2018;71(7):565 – 74.
8. Rothman A, Sklansky M S, Lucas V W, et al. Atrial septostomy as a bridge to lung transplantation in patients with severe pulmonary hypertension [J]. Am J Cardiol, 1999;84(6):682-6.
9. Paitazoglou C, Bergmann M W, Özdemir R, et al. One-year results of the first-in-man study investigating the Atrial Flow Regulator for left atrial shunting in symptomatic heart failure patients: the PRELIEVE study [J]. Eur J Heart Fail, 2021;23(5):800 – 10.
10. Hasenfuß G, Hayward C, Burkhoff D, et al. A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial [J]. Lancet, 2016;387(10025):1298 – 304.
11. Castaldi B, Cuppini E, Sirico D, et al. Feasibility, Safety, and Efficacy of the Atrial Flow Regulator in Pediatric Patients: A Single-Center Experience [J]. J Soc Cardiovasc Angiogr Interv, 2023;2(6Part B):101209.
12. Hansmann G, Sabiniewicz A, Sabiniewicz R. Atrial Flow Regulator for Post-capillary Pulmonary Hypertension: First-in-Human Transcatheter AFR Device Implantations in RCM [J]. JACC Case Rep, 2022;4(14):878 – 84.
13. Piccinelli E, Testa A, Butera G. Versatility of Atrial Flow Regulator Device in Congenital Heart Disease: A Case Series [J]. Pediatr Cardiol, 2024;45(6):1377-83.
14. Budev M M, Yun J J. Advanced Circulatory Support and Lung Transplantation in Pulmonary Hypertension [J]. Cardiol Clin, 2022;40(1):129 – 38.
15. Sultan S, Tseng S, Stanziola A A, et al. Pulmonary Hypertension: The Role of Lung Transplantation [J]. Heart Fail Clin, 2018;14(3):327 – 31.
16. D'alonzo G E, Barst R J, Ayres S M, et al. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry [J]. Ann Intern Med, 1991;115(5):343-9.
17. Lordan J L, Corris P A. Pulmonary arterial hypertension and lung transplantation [J]. Expert Rev Respir Med, 2011;5(3):441 – 54.

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