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Original research

First in-human modified atrial septostomy combining radiofrequency ablation and balloon dilation

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ABSTRACT

Objective Preclinical research suggests that the combined use of radiofrequency ablation and balloon dilation (CURB) could create stable interatrial communications without device implantation. This study examined the first in-human use of CURB for modified atrial septostomy in patients with severe pulmonary arterial hypertension (PAH).

Methods Between July 2018 and October 2021, CURB was performed in 19 patients with severe PAH (age: 31.5±9.1 years; mean pulmonary artery pressure: 73 mm Hg (IQR: 66–92); pulmonary vascular resistance: 18.7 Wood units (IQR: 17.8–23.3)). Under guidance of intracardiac echocardiography and three-dimensional location system, (1) fossae ovalis was reconstructed and ablated point-by-point with radiofrequency; (2) then graded balloon dilation was performed after transseptal puncture and the optimal size was determined according to the level of arterial oxygen saturation ($SatO_2$); (3) radiofrequency ablation was repeated around the rims of the created fenestration. The interatrial fenestrations were followed-up serially.

Results After CURB, the immediate fenestration size was 4.4 mm (IQR: 4.1–5.1) with intracardiac echocardiography, systolic aortic pressure increased by 10.2±6.9 mm Hg, cardiac index increased by 0.7±0.3 L/min/m^2 and room-air resting SatO2 decreased by 6.2±1.9% (p<0.001). One patient experienced increased pericardiac effusion postoperatively; the others had no complications. On follow-up (median: 15.5 months), all interatrial communications were patent with stable size (intraclass correlation coefficient=0.96, 95%CI:0.89 to 0.99). The WHO functional class increased by 1 (IQR: 1–2) (p<0.001) with improvement of exercise capacity (+159.5 m, P<0.001).

Conclusion The interatrial communications created with CURB in patients with severe PAH were stable and the mid-term outcomes were satisfactory.

Trial registration number NCT03554330.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Although balloon atrial septostomy has beneficial effects on circulatory decompression in multiple cardiovascular diseases, the high rate of spontaneous closure limits its clinical utilisation. Preclinical research suggests that the combined use of radiofrequency ablation and balloon dilation (CURB) could create stable interatrial communications.

WHAT THIS STUDY ADDS

⇒ CURB was found to have the potential to produce personalised interatrial communications in patients with severe pulmonary arterial hypertension, according to the haemodynamic parameters, and the fenestration size was stable during the mid-term follow-up.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ CURB can create personalised and stable interatrial communications without device implantation. Further research is required to evaluate its application for heart failure with preserved ejection fraction.

INTRODUCTION

Atrial septostomy is an important palliative therapy for patients with refractory pulmonary arterial hypertension (PAH), heart failure with preserved ejection fraction and multiple forms of other cardiovascular diseases.[1–14] Although graded balloon atrial septostomy is widely used, the frequency of spontaneous closure is high, thus limiting its clinical utilisation.[2–5 13 14] To reduce spontaneous closure, the applications of different specialty devices have been reported; however, the usefulness of these approaches remains to be proven.[15–25] Additionally, potential complications secondary to device implantation might occur, and their long-term safety is still unknown.[16–24]

Our preclinical study suggested that the combined use of radiofrequency ablation and balloon dilation (CURB) could create stable interatrial communications without device implantation.[26] Radiofrequency catheter ablation (RFA) on the fossae ovalis can reduce the elastic recoil of local tissue, thereby contributing to a transseptal puncture and creating the desired interatrial fenestration with balloon dilation. Around the rims of the fenestration created with balloon dilation, additionally, RFA has the potential to cause irreversible damage, which prevents the re-adhesion of the septal remnants. This study was performed to investigate the first in-human use of CURB for modified atrial septostomy in patients with severe PAH.

METHODS

Study design and Participants

This prospective single-centre study was conducted to evaluate the feasibility of modified atrial septostomy with CURB, and the primary outcome

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measures included the stability of created fenestration (patency and size change of communication) and the exercise tolerance (6 min walk distance). Between July 2018 and October 2021, a total of 19 patients (age: 31.5±9.1 years; 3 male patients and 16 female patients) fulfilled the inclusion criteria and were referred for atrial septostomy with CURB. All patients were part of the study group registered at clinicaltrials.gov and had right heart failure refractory to medical therapy. All patients underwent chest radiography, electrocardiography and transthoracic Doppler echocardiography (TTE). Furthermore, multi-slice CT was performed preoperatively to evaluate the morphology and exclude cardiovascular malformations and coronary artery disease. The level of N-terminal pro-brain natriuretic peptide was measured, and the exercise capacity was evaluated using the 6 min walk distance.

All patients underwent routine right and left heart catheterisation to assess the haemodynamics without discontinuation of targeted medical therapy. Then, CURB was performed. Based on the levels of resting arterial oxygen saturation ($SatO_2$) and left ventricular end diastolic pressure, the optimal size of interatrial communication was achieved with graded balloon dilation. After CURB, the immediate haemodynamic parameters were measured, and the created fenestration was evaluated with intracardiac echocardiography (ICE) and TTE. Anticoagulation was commenced postoperatively, and the size of the interatrial fenestration was followed-up serially with TTE.

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of the research.

Inclusion and exclusion criteria

The inclusion criteria were: (1) severe idiopathic PAH or severe PAH related to repaired congenital heart diseases; (2) WHO functional class III or IV with right heart failure refractory to medical therapy; (3) mean pulmonary artery pressure (MPAP) >50 mm Hg and pulmonary vascular resistance (PVR) >12 Wood units with targeted medical therapy.

The exclusion criteria were: (1) severe right heart failure with cardiorespiratory support; (2) presence of deep vein thrombosis or pulmonary embolism; (3) presence of cardiovascular malformations, patent foramen ovale or coronary artery disease; (4) presence of implanted cardiac devices; (5) echocardiographic evidence of intracardiac thrombus, mass, tumour or vegetation; (6) mean right atrial pressure >20 mm Hg; (7) room-air resting $SatO_2$ <88%; (8) left ventricular end diastolic pressure ≥18 mm Hg; (9) indexed PVR>5.5 Wood units/m^2.

CURB Procedure

Preparation

Under local anaesthesia, percutaneous punctures of the femoral vein were performed and two intravenous introducers were inserted (one 8F introducer and one 11F introducer; Cordis, Cashel, Ireland) (online supplemental figure 1). All patients underwent right heart catheterisation using a 6F multipurpose diagnostic catheter (Cordis, Miami, Florida, USA).[27] After percutaneous puncture of the right femoral artery or radial artery, a 5F pigtail catheter (Terumo Medical, Somerset, New Jersey, USA) was introduced to perform left heart catheterisation. Complete haemodynamic data and blood samples were obtained. Haemodynamic parameters included right atrial pressure, right ventricular pressure, pulmonary artery pressure (PAP), aortic pressure and left ventricular pressure (online supplemental figure 2). Cardiac output (systemic blood flow), cardiac index (cardiac output/body surface area) and PVR ([MPAP−left ventricular end diastolic pressure]/cardiac output) were calculated using Fick's oximetric principle.

Reconstruction of fossae ovalis

Under fluoroscopic guidance, a ThermoCool SmartTouch SF Bi-Directional Navigation catheter (Biosense Webster, Diamond Bar, California, USA) was introduced into the right atrium, and

Table 1 Baseline characteristics of patients with severe PAH (n=19)

Age (years)	31.5±9.1
Female, No (%)	16 (84.2)
Body mass index, kg/m^2*	21.5±3.0
Aetiology of PAH, No (%)	
Idiopathic PAH	10 (52.6)
PAH related to repaired CHD	9 (47.4)
Symptoms, No (%)	
Exertional dyspnoea	19 (100)
Syncope	11 (57.9)
Lower limb oedema	14 (73.7)
WHO functional class, median (IQR)†	3 (3, 4)
III, No (%)	11 (57.9)
IV, No (%)	8 (42.1)
6MWD (metre)	252.9±98.3
NT-proBNP (pg/mL), median (IQR)†	1478 (859, 2331)
Haemoglobin (g/dL)	14.9±2.0
Cardiothoracic ratio (%)	56.4±4.4
Electrocardiography	
Heart rate (beats/min)	84.9±12.3
Atrial tachycardia, No (%)	2 (10.5)
Paroxysmal atrial flutter, No (%)	1 (5.3)
First-degree atrioventricular block, No (%)	1 (5.3)
TTE	
RAD (mm)	56.0±7.9
RVD (mm)	43.4±6.4
LAD (mm)	28.1±4.0
LVD (mm)	33.2±4.7
LVEF (%)	65.4±4.2
TAPSE (mm)	17.7±3.1
Tricuspid regurgitation (moderate/severe), No (%)	14 (73.7)
Pericardial effusion, No (%)	8 (42.1)
Targeted medical therapy, No (%)	
Ambrisentan	14 (73.7)
Tadalafil	16 (82.1)
Bosentan	3 (15.8)
Sildenafil	3 (15.8)
Macitentan	2 (10.5)
Subcutaneous treprostinil	5 (26.3)
History of balloon atrial septostomy, No (%)	3 (15.8)

Values expressed as mean±SD for normally distributed variables, median (IQR) for non-normally distributed variables and No (%) for categorical variable.
*Calculated as weight in kilograms divided by height in meters squared.
†Non-normally distributed variables.
‡Thirteen patients performed the 6-minute walk test before the procedure.
CHD, congenital heart disease; LAD, left atrial dimension; LVD, left ventricular dimension; LVEF, left ventricular ejection fraction; 6MWD, 6 min walk distance; NT-proBNP, N-terminal pro–brain natriuretic peptide; PAH, pulmonary arterial hypertension; RAD, right atrial dimension; RVD, right ventricular dimension; TAPSE, tricuspid annular plane systolic excursion; TTE, transthoracic Doppler echocardiography.

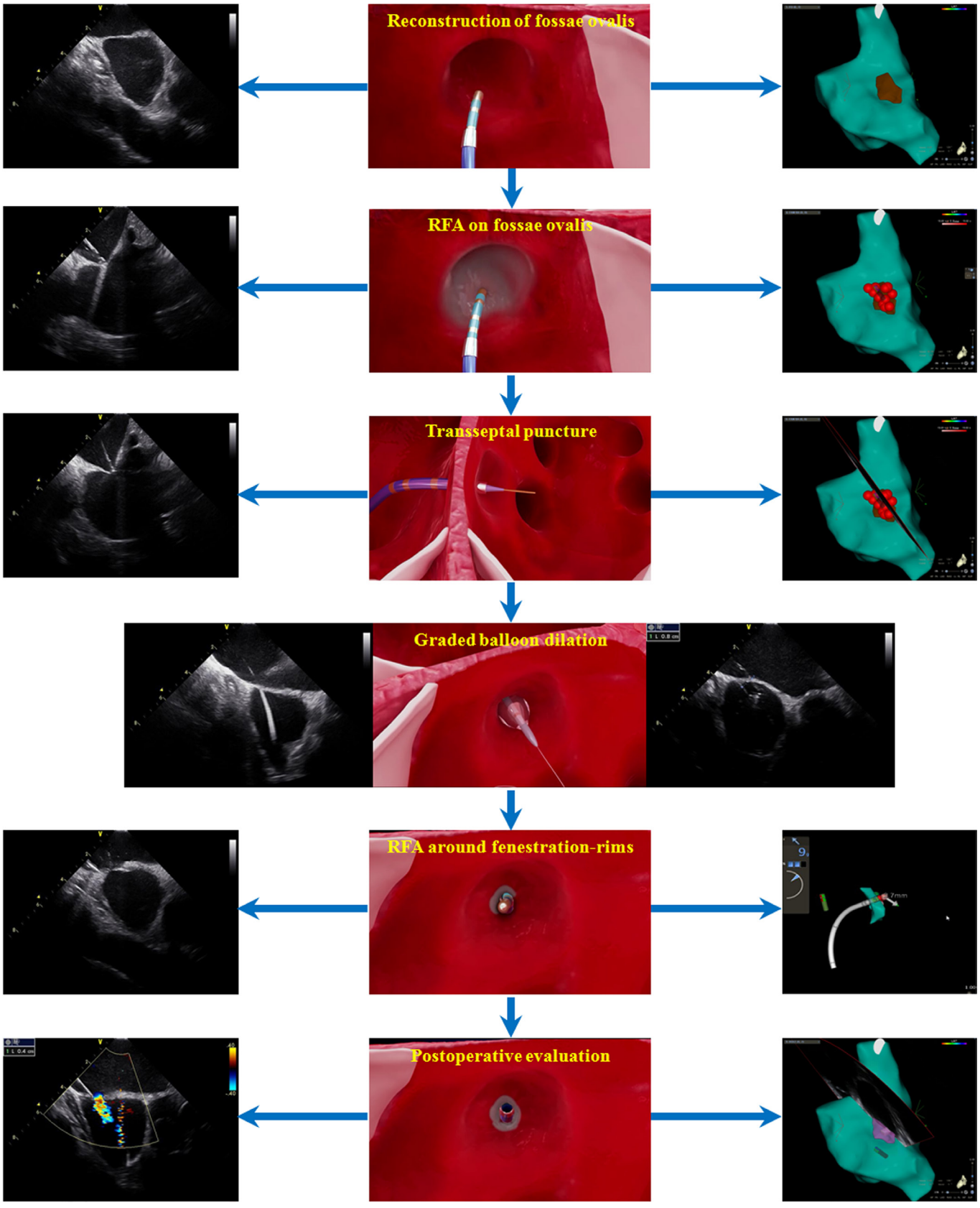

Figure 1 Modified atrial septostomy with combined use of radiofrequency ablation and balloon dilation (CURB). Under the guidance of intracardiac echocardiography (left panel) and a three-dimensional location system (right panel), the fossae ovalis was delineated and reconstructed. On the region of the fossae ovalis, radiofrequency catheter ablation (RFA) was conducted point-by-point to reduce the elastic recoil of local tissue and facilitate transseptal puncture and balloon dilation. After transseptal puncture, graded balloon dilation was performed. RFA was repeated around the rims of the created fenestration to cause irreversible damage and prevent spontaneous closure. Finally, the interatrial created fenestration was evaluated with intracardiac echocardiography.

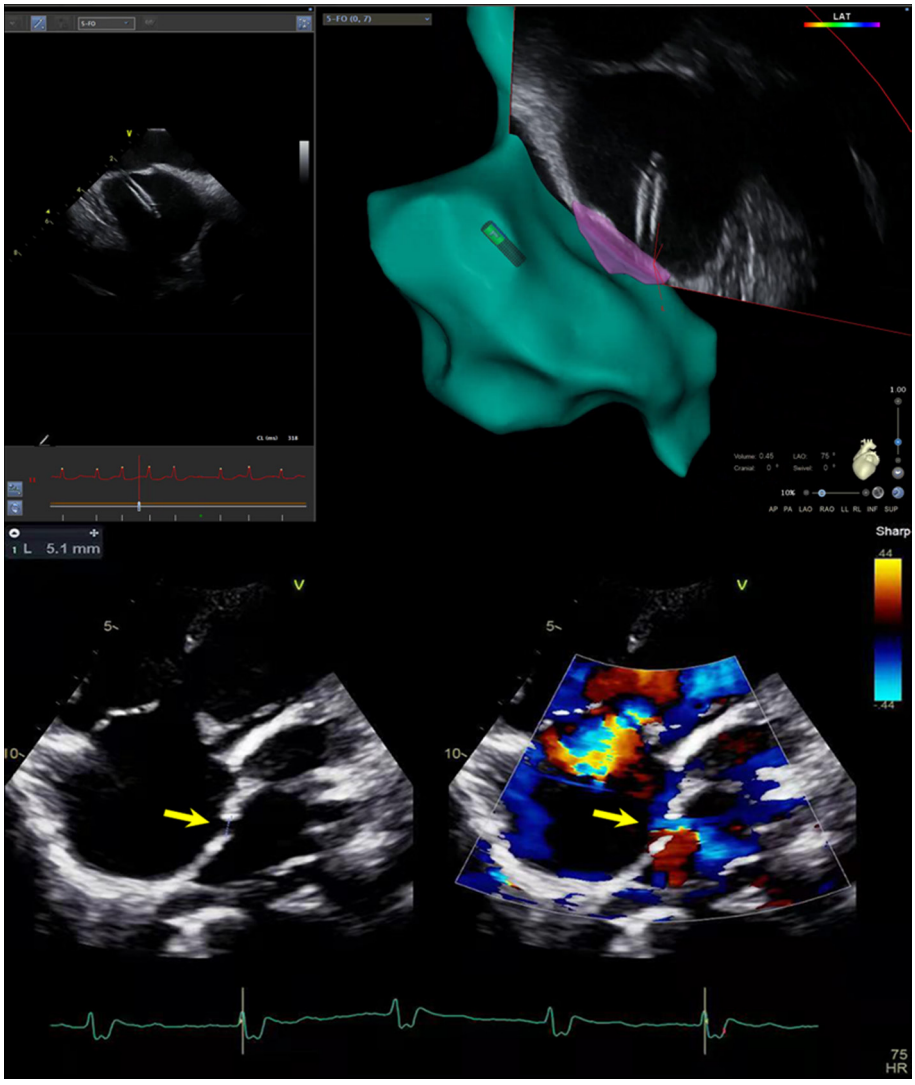

Figure 2 Accurate transseptal puncture assisted with intracardiac echocardiography. The accurate transseptal puncture site and position of the long sheath were confirmed with intracardiac echocardiography (upper left panel) and a three-dimensional location system (upper right panel). The exact location of the interatrial communication (arrow) was demonstrated with transthoracic Doppler echocardiography (lower panels). The fenestration size was 5.1 mm with continuous shunting from right to left (1 year after the procedure).

fast anatomic mapping was performed to reconstruct the right atrium. Then, an ICE Catheter (SoundStar; Biosense Webster) was advanced intravenously into the right atrium, and images of the atrial septum were obtained using the GE Vivid i System. Under the guidance of ICE, the fossae ovalis was delineated and reconstructed (online supplemental video 1), and the thickness of fossae ovalis was measured.

RFA on fossae ovalis

The SmartTouch SF catheter was introduced into the right atrium. Calibration of the contact force and respiratory gating were performed in the right atrium. Then, the steerable SmartTouch SF catheter was deflected and advanced until it touched the region of the fossae ovalis. Under the guidance of ICE and a three-dimensional location system (Carto3 system; Biosense Webster), point-by-point RFA was performed on the fossae ovalis (online supplemental video 2) using a compatible SmartAblate RFA generator (Biosense Webster) in the power-controlled mode (without ramping). The maximum interlesion distance between two neighbouring lesions was ≤6 mm to ensure the contiguity of the lesion undergoing RFA. The following parameters were used: RFA power, 40 W; cut-off temperature, 43°C; heparin saline irrigation flow rate, 17 mL/min; contact force, 5–25 g; and application time, 20 s.

Transseptal puncture and balloon dilation

Under the guidance of fluoroscopy and ICE, transseptal puncture of the central area of the fossae ovalis was performed using the Brockenbrough transseptal needle, a Mullins transseptal dilator and an 8.5F sheath (Medtronic, Minneapolis, Minnesota, USA); the transseptal needle was preshaped to facilitate puncture. Then, the needle and dilator were slowly withdrawn and blood was aspirated from the sheath. After transseptal puncture, all patients were administered 100 units/kg of intravenous heparin. The positioning of the sheath was confirmed to be in the left atrium with manual contrast injection. Using the sheath, a 6F multipurpose diagnostic catheter was introduced and manipulated deep into a left superior pulmonary vein with the aid of a 0.035-inch, 150 cm hydrophilic guidewire (Terumo Medical). Then, it was exchanged for a 0.035-inch, 260 cm guidewire (Cordis). Over the fixed guidewire, the catheter was withdrawn and graded dilation of the atrial septum was performed using

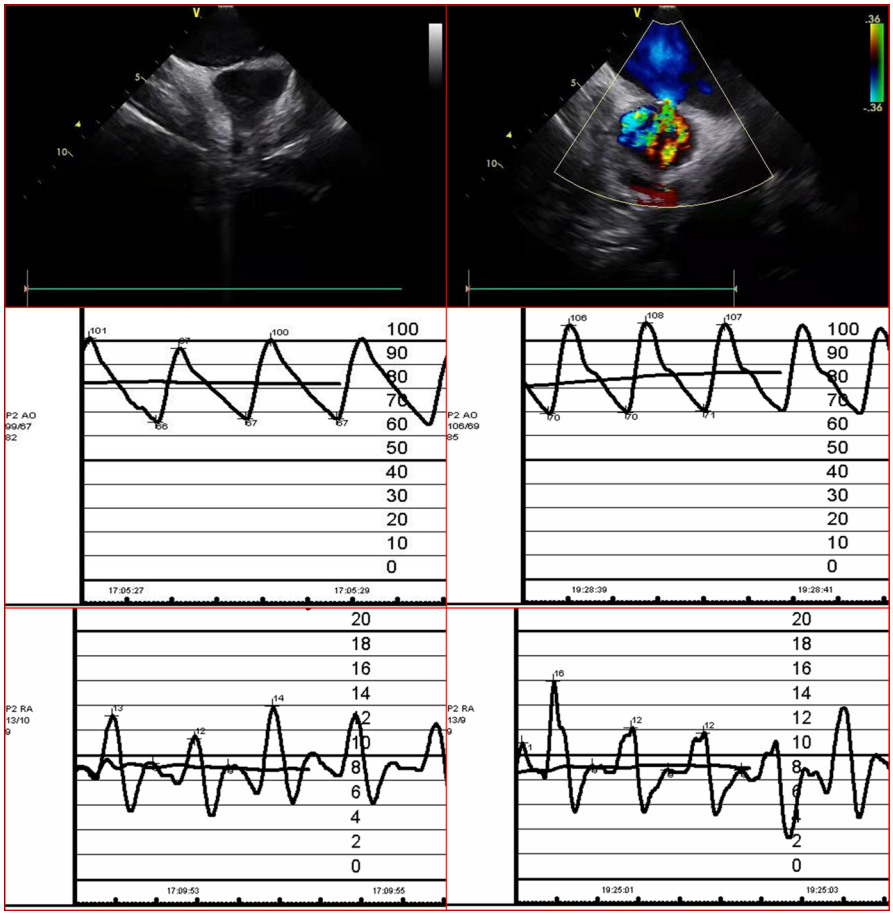

Figure 3 Aortic pressure before and after combined use of radiofrequency ablation and balloon dilation (CURB). An appropriate interatrial communication was created successfully with CURB, and a right-to-left shunt was detected (left panel, before CURB; right panel, after CURB). The immediate systolic aortic pressure increased from 99 to 106 mm Hg, and there was no significant change in the mean right atrial pressure. Furthermore, the symptoms improved immediately. AO, aorta; RA, right atrium.

a 6 mm diameter balloon in increments of 2 mm until 12 mm was reached (Mustang balloon; Boston Scientific, Marlborough, Massachusetts, USA). Five minutes after each dilation of the atrial septum, room-air resting $SatO_2$, left ventricular pressure and aortic pressure were measured. The endpoints were a postoperative level of resting $SatO_2$ ranging from 85% to 88% and left ventricular end diastolic pressure <18 mmHg.

Table 2 Haemodynamicparameters before and after CURB (n=18*)

	Pre-CURB	Post-CURB	P value
SAOP (mm Hg)	102.2±11.6	112.4±6.5	<0.001
SPAP (mm Hg), median (IQR)†	116.5 (101.0–134.0)	110.5 (98.0–127.0)	<0.001
SPAP/SAOP	1.2±0.2	1.0±0.2	<0.001
MPAP (mm Hg), median (IQR)†	72.5 (66.0–92.0)	71.0 (65.0–91.0)	<0.001
MRAP (mm Hg)	12.6±2.0	10.1±1.4	<0.001
LVEDP (mm Hg)	9.5±2.1	10.7±1.9	<0.001
CI (L/min/m^2)	2.1±0.3	2.8±0.2	<0.001
PVR (Wood unit)	21.1±6.8	21.1±6.7	0.666
Room-air resting $SatO_2$ (%)	93.4±1.9	87.2±0.8	<0.001

Values expressed as mean±SD for normally distributed variables and median (IQR) for non-normally distributed variables.
*The patient who had increased pericardiac effusion postoperatively was excluded.
†Non-normally distributed variables.
.CI, cardiac index; CURB, combined use of radiofrequency ablation and balloon dilation; LVEDP, left ventricular end diastolic pressure; MPAP, mean pulmonary artery pressure; MRAP, mean right atrial pressure; PVR, pulmonary vascular resistance; SAOP, systolic aortic pressure; $SatO_2$, arterial oxygen saturation; SPAP, systolic pulmonary artery pressure.

RFA around the rims of interatrial fenestration

Through the interatrial created communication, the SmartTouch SF catheter was advanced into the left atrium. Under the guidance of the three-dimensional location system, the curved SmartTouch catheter was dragged slowly from the left atrium to the right atrium until the desired contact force was recorded. The correct position of the electrode tip was determined with continuously recorded contact force (5–25 g) and ICE images, in which the electrode tip overrode and touched the fenestration rim, and the microbubbles of irritating saline from the electrode tip were identified simultaneously in both atria (online supplemental video 3). Then, RFA was performed and the related parameters were identical to those of fossae ovalis ablation. The SmartTouch catheter deflected and/or rotated slightly to change the vector of contact force to four different desired directions, upper, lower, anterior and posterior, around the fenestration rim, and RFA was conducted at the four target sites (one RFA site per quadrant). After the procedure, the interatrial fenestration was evaluated with ICE (online supplemental video 4) and TTE. Right and left heart catheterisation were repeated, and the postoperative cardiac index was calculated.

Transthoracic Doppler echocardiography

For each patient, TTE was performed before CURB (online supplemental figure 3) and during follow-up. The interatrial fenestration size was defined as the largest dimension observed

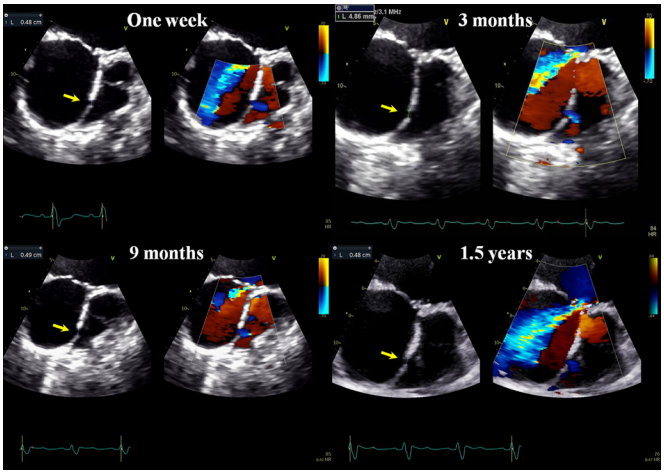

Figure 4 Follow-up with transthoracic Doppler echocardiograghy. During follow-up, the interatrial communication (arrows) was patent with a right-to-left shunt. The interatrial fenestration was 4.80 mm at 1 week, 4.86 mm at 3 months, 4.90 mm at 9 months and 4.80 mm at 1.5 years.

from the parasternal short-axis view, parasternal four-chamber view or subcostal view.[27] Additionally, the direction of shunting was determined using Doppler echocardiography. In the apical four-chamber view, the end diastolic right ventricular dimension and left ventricular dimension were measured, and tricuspid annular plane systolic excursion was measured by M-mode echocardiography with the cursor optimally aligned along the direction of the tricuspid lateral annulus. All echocardiographic data were averaged over three beats.

Follow-up

For each patient, chest radiography, electrocardiography and TTE were recorded serially at 1 week, 1 month and 3-month to 6 month intervals. The patency and size of the interatrial fenestration were evaluated with TTE. Additionally, clinic visits included an evaluation of the WHO functional class and 6 min walk distance. At 3 to 6 months after the procedure, repeated multi-slice CT was suggested to evaluate the interatrial fenestration and cardiac remodelling. At 1 year after the procedure, repeat right heart catheterisation was suggested to evaluate the haemodynamic parameters and patency of the interatrial fenestration.

Statistical analysis

Based on previous studies,[2–5 13 14] the probability of spontaneous closure for balloon atrial septostomy was estimated to be 30%. For CURB, a sample size of 13 cases was required to achieve 80% power to detect a 25% reduction in spontaneous closure. The characteristics of the patients are expressed as mean±SD or median and IQR for normally distributed variables and non-normally distributed variables, respectively; categorical variables are expressed as the number and percentage. To determine the clinical efficacy of CURB, we compared the differences in aortic pressure, PAP, mean right atrial pressure, left ventricular end diastolic pressure, cardiac index, PVR, $SatO_2$, WHO functional class and 6 min walk distance before and after CURB using the paired t-test for normally distributed variables and the Wilcoxon signed-rank test for non-normally distributed variables. Intraclass correlation coefficient (ICC) (two-way mixed absolute agreement) and its 95% CI were used to assess the concordance of fenestration size across follow-up, and ICC >0.75 was considered as good concordance. All tests were two-tailed, and $p<0.05$ was considered statistically significant. All analyses were performed using SAS software (V.9.4; SAS Institute).

RESULTS

Baseline characteristics

Among 19 patients, 10 patients had idiopathic PAH and 9 had PAH related to repaired congenital heart disease (surgical repair of a ventricular septal defect in 5 patients and transcatheter closure of the patent ductus arteriosus in 4 patients). All patients underwent targeted medical therapy (two or more pulmonary vasodilators), and the clinical baseline characteristics of the enrolled patients are presented in table 1. There were 11 patients with syncope and 14 patients with peripheral oedema. Six patients were unable to perform the 6 min walk test. The right atrium (56.0±7.9 mm) and right ventricle (43.4±6.4 mm) in all patients were greatly enlarged and had concurrent opposite changes in the markedly diminished left atrium (28.1±4.0 mm) and left ventricle (33.2±4.7 mm). Moderate to severe tricuspid insufficiency was identified in 14 patients, and mild pericardiac effusion was observed in 8 patients. Additionally, the tricuspid annular plane systolic excursion was 17.7±3.1 mm. There were three patients with a history of balloon atrial septostomy alone who had spontaneous closure confirmed at 2 weeks, 2 weeks and 1 month, respectively.

Combined use of radiofrequency ablation and balloon dilation

Right heart catheterisation showed that MPAP was 73 mm Hg (IQR: 66–92) and PVR was 18.7 Wood units (IQR: 17.8–23.3) with targeted medical therapy. Systolic PAP at baseline was 118.7±18.7 mm Hg and systolic aortic pressure at baseline was 102.6±11.4 mm Hg. Furthermore, systolic PAP was suprasystemic in 16 patients (online supplemental figure 4) and near-systemic in three patients. CURB was performed successfully in all patients (figure 1). The thickness of fossae ovalis was 2.1±0.7 mm (online supplemental figure 5), and the intended transseptal puncture sites of the fossae ovalis were confirmed with ICE and the three-dimensional location system (figure 2; online supplemental figure 6). The maximum balloon diameter was 10 mm (IQR: 10–12), and the immediate fenestration size was 4.4 mm (IQR: 4.1–5.1) according to ICE. Postoperatively, the systolic aortic pressure increased by 10.2±6.9 mmHg, cardiac index increased by 0.7±0.3 L/min/m^2 and room-air resting $SatO_2$ decreased by 6.2%±1.9% ($p<0.001$) (figure 3 and table 2). Additionally, the mean right atrial pressure decreased by 2.5±1.8 mm Hg (online supplemental figure 7). After the procedure, one patient had increased pericardiac effusion (effusion thickness posterior to the left ventricular posterior wall increased from 5 mm preoperatively to 11 mm postoperatively). Subsequently, pericardiocentesis was performed. The patient underwent thoracotomy exploration later and a tiny perforation of the left atrial wall was detected, which might have been secondary to the guidewire. No complications were observed in the other patients. The procedural time was 113.2±30.3 min.

During follow-up (median: 15.5 months; range: 2–39 months; n=18), all interatrial communications were patent and the fenestration size was stable (ICC=0.96, 95% CI: 0.89 to 0.99; Figures 4 and 5). Symptomatic improvement was observed in all patients. The WHO functional class increased by 1 (IQR: 1–2) ($p<0.001$) and the exercise capacity improved significantly (+159.5 m, $p<0.001$). Repeat multi-slice CT was performed

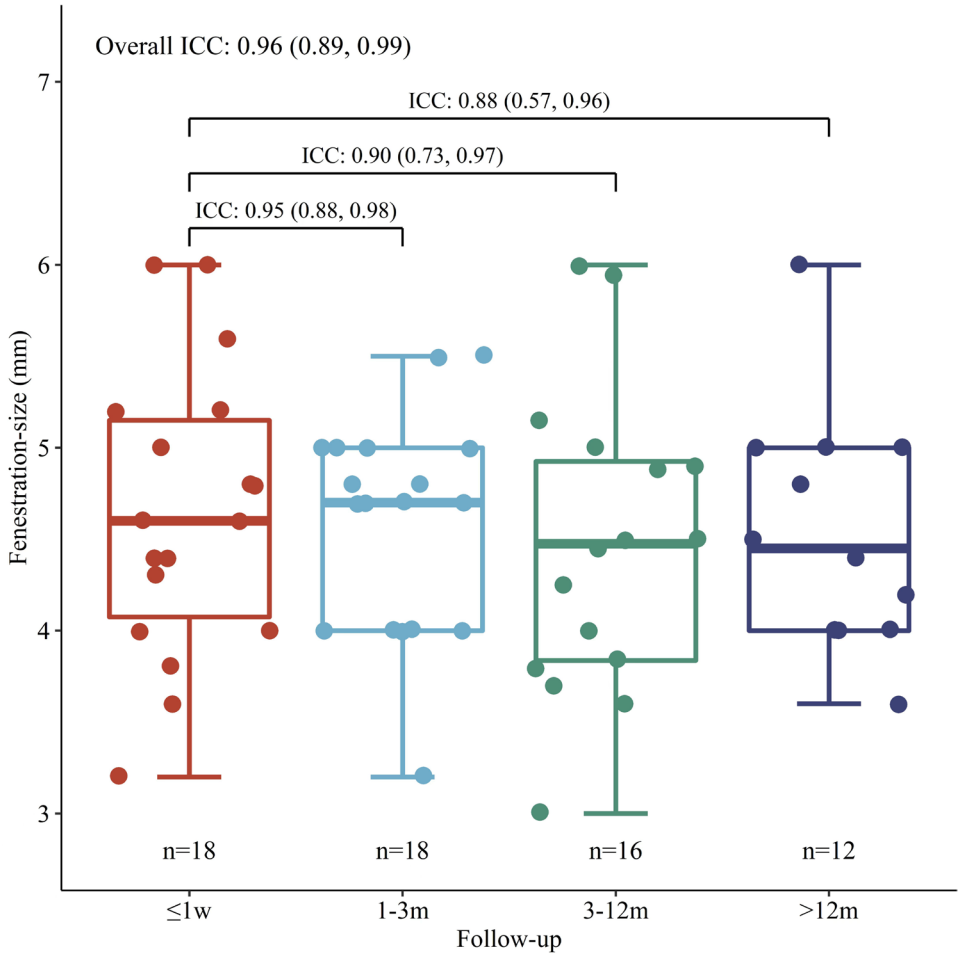

Figure 5 Serial follow-up of fenestration size. All interatrial communications were patent and the fenestration size was stable (within 1 week, at 1–3 months, at 3–12 months and at more than 12 months; intraclass correlation coefficient (ICC)=0.96). ICC (two-way mixed with absolute agreement) was used to assess the concordance across the four visits, and the ICCs between the fenestration-size within 1 week and other phases were also calculated.

in nine patients, and patent fenestrations were confirmed with favourable cardiac remodelling (figure 6, online supplemental figure 8,9). Twelve patients participated in more than 1 year of follow-up. Right heart catheterisation was performed in two patients whose fenestrations were confirmed to be patent with the passage of the catheter and angiography (online supplemental video 5).

DISCUSSION

For patients with severe PAH, CURB has the potential to create stable interatrial communications without device implantation. During the follow-up, all communications were patent and there was no significant change in the fenestration size. This work describes the first in-human use of CURB for modified atrial septostomy, and the mid-term outcomes were satisfactory with improvement of symptoms and exercise capacity.

During the follow-up, the size of the fenestration created with CURB was stable. With balloon atrial septostomy alone, spontaneous closure was common (nearly 30%), which mainly occurred within 1 year.[2–5 13 14] In comparison, all fenestrations created with CURB were patent on mid-term follow-up. In this study, the combination of RFA and balloon dilation exhibited complementary advantages that produced a personalised interatrial fenestration with a stable size. Because RFA and balloon dilation are mature clinical techniques with satisfactory safety, CURB might become an alternative procedure for atrial septostomy. The stability of the created fenestration with CURB was demonstrated in patients with severe PAH. Further research is ongoing to investigate the clinical application of this approach for heart failure with preserved ejection fraction (ClinicalTrials.gov ID: NCT04573166).

Based on the levels of $SatO_2$ and left ventricular end diastolic pressure, CURB has the potential to produce personalised interatrial communications. To improve the shunt patency, different types of specialty devices have been designed and applied for atrial septostomy. Because of the fixed size of the fenestration with these devices, they make it difficult to create personalised interatrial communications. Additionally, their long-term safety is still unknown, and the potential risks related to such devices have to be considered, such as device embolisation, device-associated thrombus, spontaneous closure, among others.[16–24] During the current study, CURB was demonstrated to be a reliable procedure for personalised atrial septostomy without device implantation. According to the haemodynamic parameters, the optimal size of the fenestration was determined with graded balloon dilation, and fenestration stability was achieved with RFA. Furthermore, the effectiveness and safety of CURB were confirmed by the improvement of symptoms and haemodynamic parameters with an acceptable level of resting $SatO_2$.

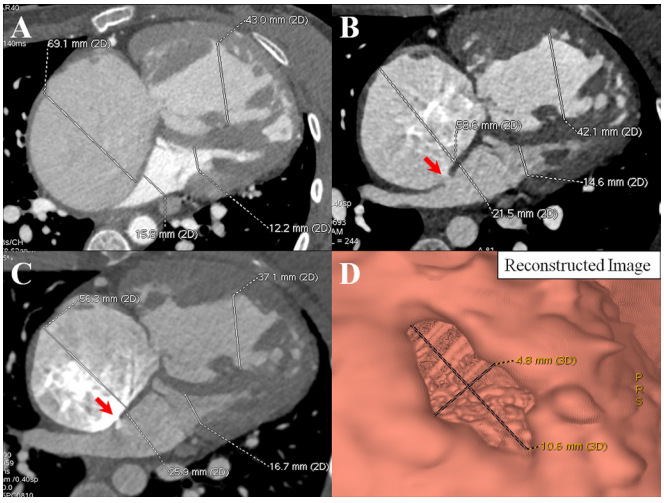

Figure 6 Follow-up with multi-slice CT. Before combined use of radiofrequency ablation and balloon dilation (CURB) (A), the right atrium and right ventricle were greatly enlarged with a concurrent opposite change in the markedly diminished left atrium and left ventricle. At (B) 3 months after CURB and (C) 1 year after CURB, the sizes of right atrium and right ventricle were alleviated with the increase of the left atrium and left ventricle. The interatrial fenestration (arrows) was patent and approximately oval. It was 10.6 mm × 4.8 mm (D). The reconstructed image is based on the 3month multi-slice CT results and the maximum balloon size was 12 mm in this patient.

Accurate RFA of the target site is crucial to ensure the stability of the interatrial fenestration, and a double RFA strategy was used during this study. The first RFA procedure was conducted to cause irreversible damage to the fossae ovalis. The second RFA procedure further ensured contiguous lesions of the fenestration rims. Considering the balloon size (≤12 mm) and maximum surface diameter of the lesion that underwent RFA (>7.5 mm),[28] four RFA sites were designed around the rims of the fenestration. The correct position of the electrode tip was determined with the aid of ICE, three-dimensional location system and contact force recording, which increased the complexity and time of CURB. Further research is required to simplify the procedure with new methods, such as radiofrequency hot balloon and cryoballoon ablation.[25 29 30] Although the fenestration size at 1–3 months seemed to be larger than that within 1 week, the difference was not significant, in contrast to reports of preclinical research (the fenestration created with double RFA tends to increase within 2 months and remains stable subsequently).[26] This discrepancy might be due to the tough/thick atrial septum, the small sample size of our study, and other factors.

Study limitations

The major limitation of this preliminary study is the small sample size, which limits the generalisability of the results. However, the enrolment of appropriate patients is ongoing. Although the mid-term patency of the created fenestration has been confirmed in this study, its long-term outcomes are still unclear. During the follow-up, the stability of the fenestration was evaluated only by measuring its size (not the area), which represents another limitation of this study. Further studies are required to compare the patency and stability of the fenestrations created using CURB with the patency and stability of those created using balloon atrial septostomy alone or device implantation.

CONCLUSIONS

For patients with severe PAH, CURB is a reliable procedure that can create personalised and stable interatrial communications. Mid-term outcomes were satisfactory with clinical improvements. Further research is required to investigate the clinical application of CURB in a large population.

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Contributors CY conceptualised and designed the study. CY have full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. L Wan, HL, CW, TG, HN, SL, PY, L Wang and WF collected data and analysed the data. Additionally, L Wang and WF provided clinical advice. All authors approved the final submitted research manuscript and agree to be personally accountable for their contribution and for the academic integrity of the work. CY accepts full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Ethics Committee of Fuwai Hospital (reference number: 2018-K20-1), and written informed consent was obtained from each patient. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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Online Supplement

Title: *First in-human modified atrial septostomy combining radiofrequency ablation and balloon dilation*

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Legends for the Videos

Video 1: Delineation of Fossae Ovalis With Intracardiac Echocardiography. Under the guidance of intracardiac echocardiography, the fossae ovalis was delineated and reconstructed.

Video 2: Radiofrequency Catheter Ablation on Fossae Ovalis. The SmartTouch SF catheter touched the region of the fossae ovalis, and radiofrequency ablation was performed point-by-point to cover the fossae ovalis.

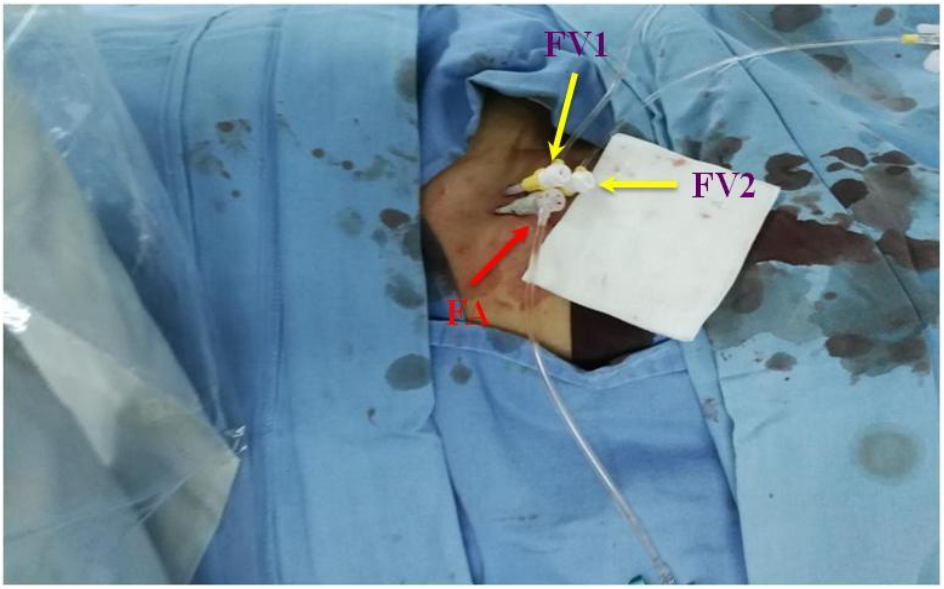
Video 3: Radiofrequency Catheter Ablation Around Fenestration-rims. From a series of holes at the very distal tip of SmartTouch SF catheter, microbubbles of irritating saline were identified simultaneously in the left atrium and right atrium. The contact force was continuously recorded, which ensured the correct position of the electrode tip.

Video 4: Postoperative Evaluation With Intracardiac Echocardiography. After the procedure, the fenestration was evaluated with intracardiac echocardiography. There was continuous right-to-left shunting through the interatrial fenestration.

Video 5: Repeated Right Heart Catheterization and Atrial Angiography. At 1 year after the procedure, a 6F multipurpose diagnostic catheter was advanced into the left atrium transvenously via the interatrial fenestration. Atrial angiography was performed during the withdrawal of the catheter, and the patency of the interatrial communication was confirmed in the left anterior oblique view. *Note: The patient underwent surgical repair of a ventricular septal defect ten years ago*.

Yan C, *et al. Heart* 2022;0:1–9. doi: 10.1136/heartjnl-2022-321212

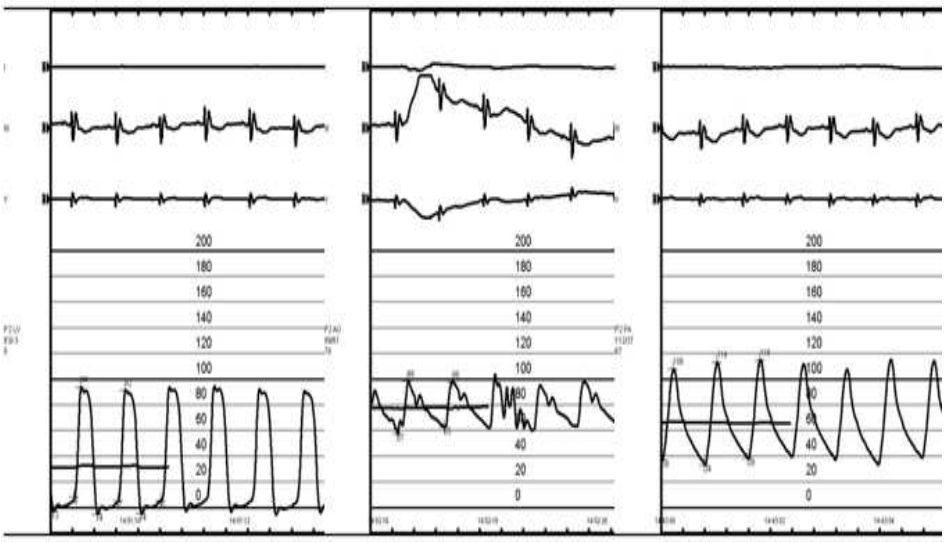
Supplemental Figure 1



Legend: After percutaneous punctures of right femoral vein and artery, two intravenous introducers (8F and 11F) and one arterial introducer (5F) were inserted, respectively. *Note: FV, femoral vein; FA, femoral artery.*

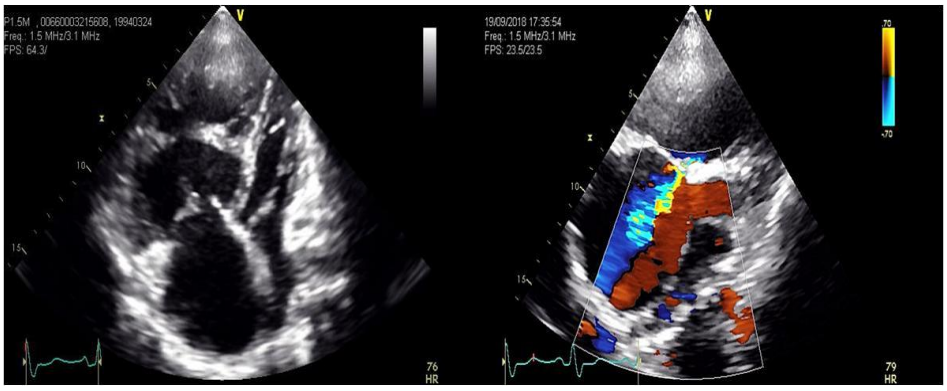
Yan C, *et al*. *Heart* 2022;0:1–9. doi: 10.1136/heartjnl-2022-321212

Supplemental Figure 2



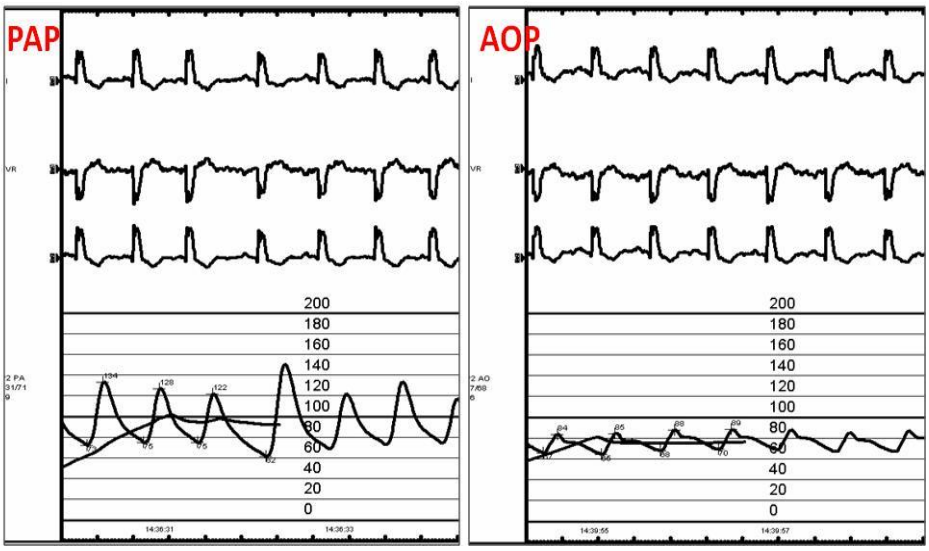
Legend: Left and right heart catheterization was conducted, and left ventricular pressure, aortic pressure and pulmonary artery pressure were recorded. *Note: LV, left ventricle; AO, aorta; PA, pulmonary artery.*

Supplemental Figure 3



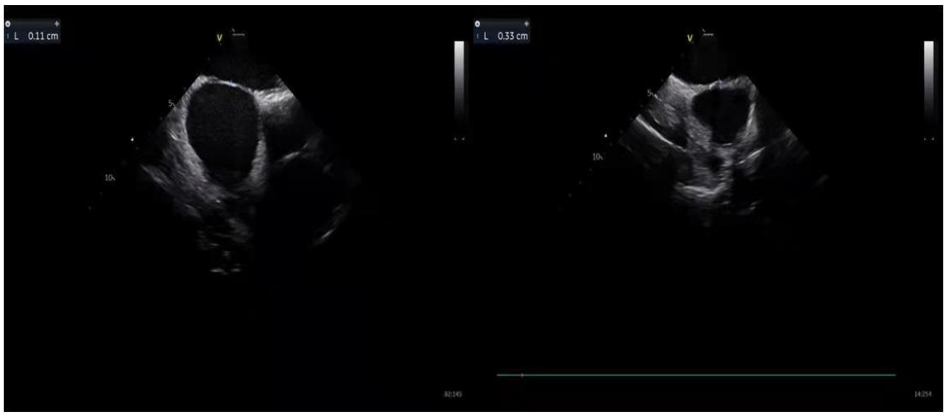
Legend: Preoperative transthoracic Doppler echocardiography showed a markedly dilated right atrium and right ventricle and compressed left atrium and left ventricle.

Supplemental Figure 4



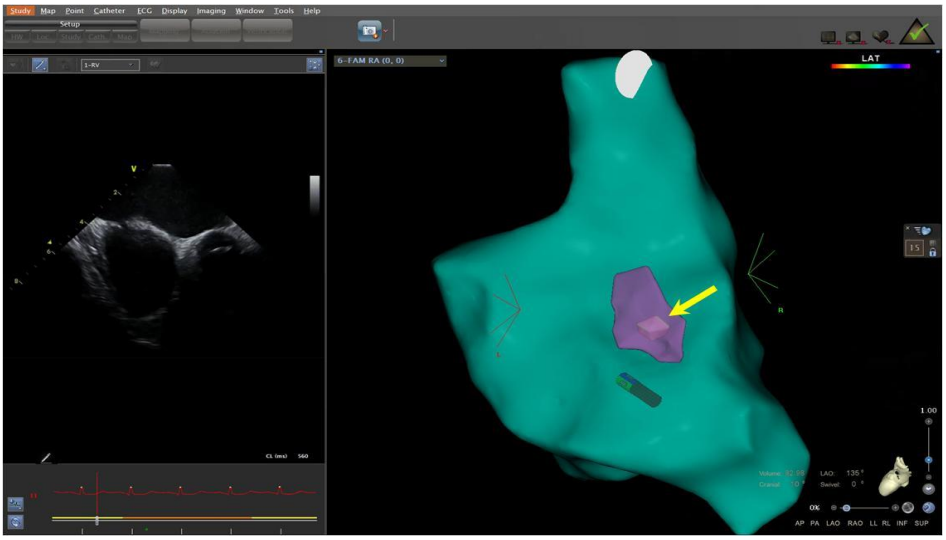
Legend: In most patients, pulmonary artery pressure was supra-systemic. *Note: PAP, pulmonary artery pressure; AOP, aortic pressure.*

Supplemental Figure 5



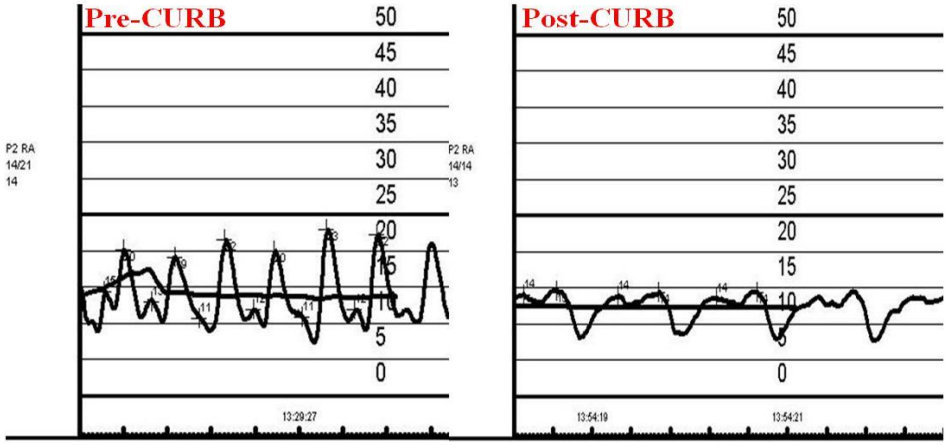
Legend: The thickness of fossae ovalis varied greatly in patients with severe PAH. *Note: left panel, the thickness was 1.1mm; right panel, the thickness was 3.3mm.*

Supplemental Figure 6

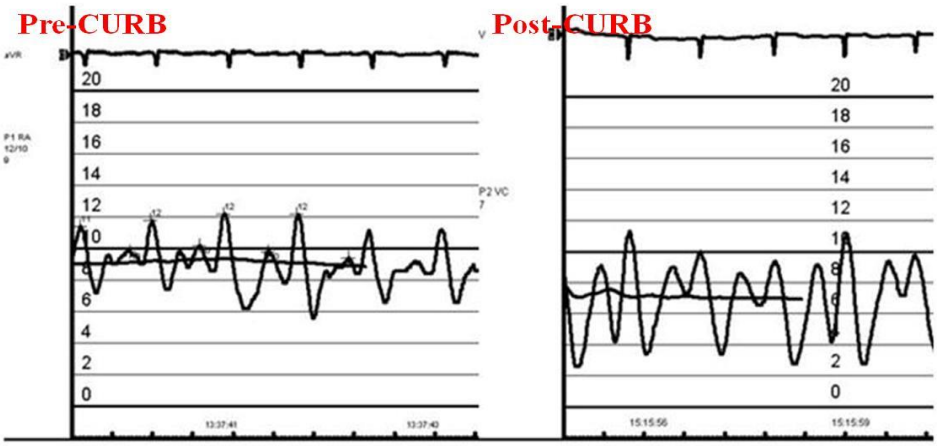


Legend: The created-fenestration (white area indicated by yellow arrow) was located in the central area of fossae ovalis (purple area).

Supplemental Figure 7
Case-1

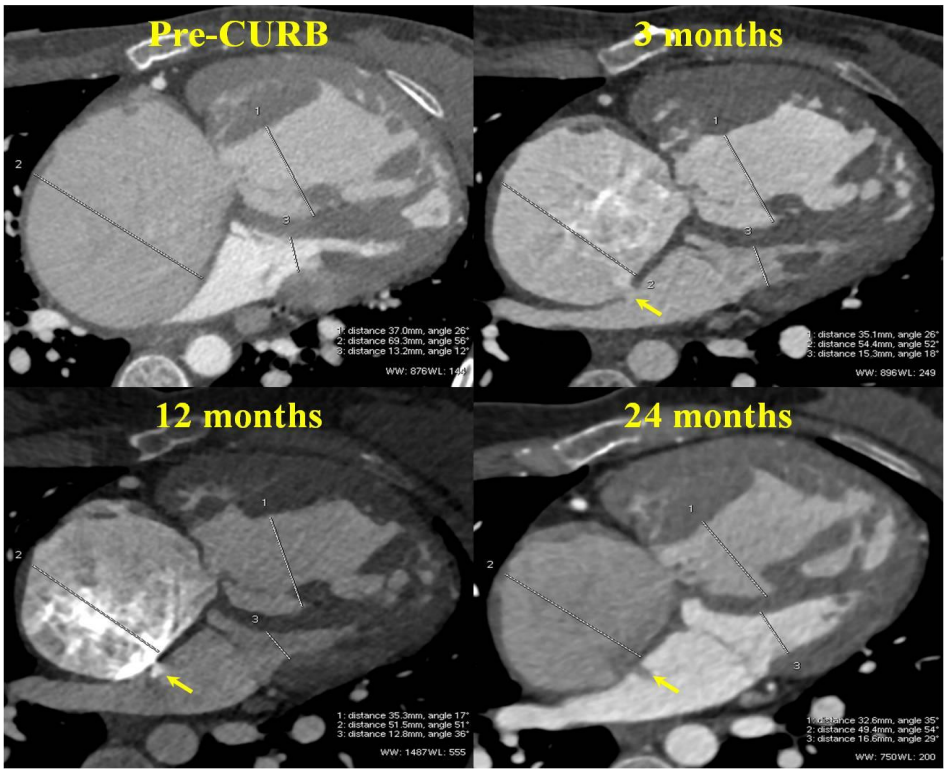


Case-2



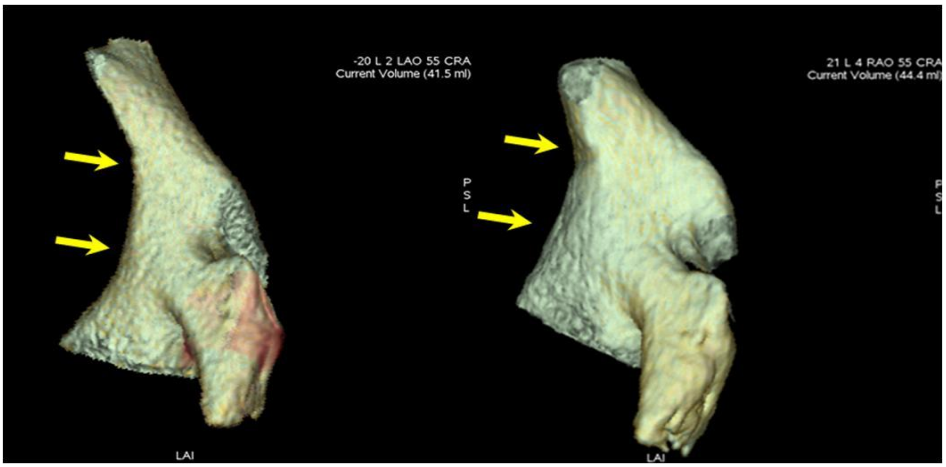
Legend: After CURB, right atrial pressure decreased in most patients. *Note: RA, right atrium; VC, vena cava.*

Supplemental Figure 8



Legend: Serial follow-up with multi-slice computed tomography showed that the created-fenestration was patent (arrows). Right to left shunting can be detected.

Supplemental Figure 9



Legend: After CURB, multi-slice computed tomography showed that the compressed left atrium was alleviated with the increase of left atrial volume from 41.5 ml to 44.4 ml. *Note: Left panel, pre-CURB; Right panel, post-CURB; Arrows, atrial septum.*