Cryoablation inside the pulmonary vein after failure of radiofrequency antral isolation

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BACKGROUND Antral pulmonary vein (PV) ablation with radiofrequency (RF) energy has become widely used as a curative approach for the treatment of atrial fibrillation. In some patients, despite antral ablation, PV entry and exit conduction block (BDB) cannot be achieved with RF energy. Cryoablation inside the PV may be an effective method to achieve BDB.

OBJECTIVE This study sought to describe a strategy of cryoablation within the PV to produce BDB in patients in whom antral RF ablation has failed.

METHODS In 15 of 148 consecutive patients (57 ± 8.9 years old, 80% male) with atrial fibrillation (14 paroxysmal, 1 chronic) undergoing PV isolation cryoablation (CryoCath Technologies, Inc., Montreal, Canada) was performed 12 ± 2 mm inside the PV after RF antral isolation failed. Nine patients were undergoing a repeat PV isolation procedure. Procedural and follow-up data were recorded and collected.

RESULTS In these 15 patients, BDB could not be achieved in 23 veins (12 left superior PV) with antral or ostial ablation alone. After cryoablation inside the vein, all patients had documented PV BDB and were in normal sinus rhythm at the end of the procedure. The average PV diameter before and after the procedure was unchanged (1.77 ± 0.18 vs 1.74 ± 0.19, $P = .641$). The average fluoroscopic and procedure times were 57 ± 16 min and $5.3 + 1.2$ hours, respectively. At 1-year follow-up, 75% of patients remained in sinus rhythm off antiarrhythmic medication; 7 of 9 patients undergoing a repeat procedure were in sinus rhythm at 1 year off antiarrhythmics. None of the patients had clinical evidence of PV stenosis after cryoablation.

CONCLUSION Cryoablation inside the PV after failed antral isolation with RF is a safe and effective method to achieve acute BDB.

KEYWORDS Atrial fibrillation ablation; Cryoablation; Pulmonary veins

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Antral pulmonary vein (PV) ablation with radiofrequency (RF) energy has become widely used for the treatment of atrial fibrillation (AF).[1–8] The success rate for this procedure varies between 65% and 85% in patients without structural heart disease.[2,3] In many centers, the end point for ablation consists of the creation of PV entrance and exit block (BDB).[9,10]

In a small percentage of patients, despite diligent mapping and extensive antral and ostial ablation, BDB cannot be achieved with RF energy. This failure may be related to excessive tissue thickness at the antral and ostial position limiting the amount of conduction tissue destroyed with RF or because of limited RF power application for concern of causing ostial PV stenosis or esophageal fistula formation.

To achieve BDB in these situations, ablation at the ostium or inside the PV may need to be performed. Cryoablation does not seem to be associated with PV stenosis.[11] The purpose of this report is to describe a strategy of cryoablation within the PV to produce BDB in patients in whom antral RF ablation has failed.

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Methods

Procedure

Written informed consent was obtained from all patients before the procedure. Data from these procedures were entered into an established AF database approved by the Virginia Commonwealth University Institutional Review Board.

A transesophageal echocardiogram was performed before the procedure to rule out the presence of left atrial thrombus. Within 2 weeks before ablation, all patients underwent magnetic resonance imaging (MRI) to show preprocedure PV and left atrial anatomy on a 1.5-T magnet (Magnetom Avanto, Seimens Medical Solutions, Erlangen, Germany) with high-performance gradients.

Quadripolar catheters were placed in the right atrium, in the right ventricular apex, and across the septal tricuspid valve area to obtain a His recording. A decapolar catheter was placed in the coronary sinus. All patients underwent intracardiac echocardiography (ICE) using a 10F, 10.5-MHz phased array catheter (AcuNav Diagnostic Ultrasound Catheter, Acuson, Siemens, Mountain View, CA) imaging system introduced through an 11F venous sheath. The ICE catheter was fluoroscopically guided to the right atrium and oriented to visualize the left atrium.

A double transseptal puncture was performed using ICE and fluoroscopic guidance. Intravenous heparin was infused

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Table 1 Demographic characteristics of total patient population compared with those who underwent combined RFA and cryoablation

Energy source	RFA (N = 133)	RFA and cryoablation (N = 15)	*P* value
Age	56 ± 9	57 ± 9	NS
Male sex (%)	69	80	<.05
AF duration (years)	7.9 ± 6	7.8 ± 7	NS
Left atrial size (cm)	4.4 ± 0.9	4.2 ± 0.8	NS
Left ventricular ejection fraction (%)	60 ± 8	61 ± 6	NS
Structural heart disease N (%)	120 (9)	1 (7)	NS
Antiarrhythmic drugs (mean number)	2.4	2.25	NS
Paroxysmal AF N (%)	127 (95)	14 (93)	NS
Chronic AF N (%)	6 (5)	1 (7)	NS
Repeat ablation N (%)	24 (18)	9 (60)	<.05
Prior PV stenosis N (%)	1 (1)	2 (13)	<.05

AF = atrial fibrillation; PV = pulmonary vein; RFA = radiofrequency ablation.

to maintain an activated clotting time of at least 300 seconds. PV diameter was assessed using a combination of ICE and venograms performed under fluoroscopy after a bolus of adenosine (6 to 24 mg). ICE was also used to measure PV flow velocity with pulsed-wave Doppler at the beginning of the procedure and after each vein was isolated.

A circular mapping catheter (Lasso, Biosense-Webster, Diamond Bar, CA) was placed in the left atrium, and sequential mapping of the PVs using both ICE and fluoroscopic guidance was performed. Pacing from the distal coronary sinus was used to separate left atrial and PV signals from the left PVs, and pacing from the right atrium or proximal coronary sinus was used when isolating the right PVs ICE or venography was used to identify the antrum or border zone between the PV and the left atrium.[12]

Initially RF ablation around the PV and the poles of the Lasso catheter was performed with either a 7F, 8-mm-tip steerable radiofrequency ablation (RFA) catheter (Biosense-Webster) or an externally irrigated (with heparinized saline) 3.5-mm Thermacool catheter (Biosense-Webster). Contiguous applications of RF energy were delivered with the nonirrigated catheter with target temperature of 50°C and maximal power output 50 W for 20 to 40 seconds at each site. With the Thermacool catheter, the irrigation rate was set to 30 ml/min, the target temperature was <42°C, the maximal power output was 35 W, and lesion duration was on average 20 to 30 seconds at each site. If no change was noted by then, RFA was discontinued and mapping for a better site was performed. The power was limited to 25 W in the area of the left atrium where the esophagus was visualized by ICE or esophagram. The ablation was performed until all PV potentials were attenuated. During ablation with the 8-mm-tip catheter, the left atrium was monitored for microbubble formation during ablation.

Isolation of a PV was defined as eradication of all PV potentials and the presence of BDB when pacing from each bipolar pair of the 20-pole Lasso catheter positioned inside one or more PVs at 10 mA and 2 ms pulse width. When BDB could not be achieved with extensive RF ablation to the PV antrum or ostium, patients underwent cryoablation with either a 9F 8-mm Freezor Max or a 7F 6-mm Freezor Xtra (CryoCath Technologies, Inc., Montreal, Canada) inside the PV os. The target tip temperature was −75°C, and maximum lesion duration was 4 min per application. Repeat ICE and venograms with fluoroscopy after adenosine infusion were performed to reassess PV diameter after isolation.

Follow-up

Follow-up visits were scheduled at 3 months, 6 months, and 12 months after the procedure. All patients received 48-hour Holter monitors at the 3-month visit regardless of their symptoms. Patients with any symptom suggestive of arrhythmia recurrence also received an event monitor with automatic trigger to record asymptomatic episodes of AF.

Table 2 Number of PV isolations, presence, site, and percent PV stenosis after prior procedure; cryoablation site, catheter, number of lesions, and total time

Patient	PV isolations, no.	Presence/site (% PV stenosis)	PV cryoablation site	Cryoablation catheter	Cryoablation no.	Cryoablation time (min)
1	1	N	LS	9F, 8 mm	6	12.2
2	3	N	LS, RS, RI	9F, 8 mm	25	51.7
3	1	N	LS, LI	9F, 8 mm	4	8.0
4	1	N	LS, LI	9F, 8 mm	8	31.0
5	2	N	LS	9F, 8 mm	19	38.9
6	1	N	LS	9F, 8 mm	25	41.7
7	2	Y/RS (50%)	RS	9F, 8 mm	8	24.0
8	2	N	LS	9F, 8 mm	8	26.2
9	2	N	LS	9F, 8 mm	10	21.0
10	1	N	LS, LI	9F, 8 mm	7	28.0
11	2	Y/LS (20%)	LS, RS	7F, 6 mm	13	28.0
12	1	N	LS, LI	7F, 6 mm	24	53.8
13	2	N	LI	7F, 6 mm	12	44.0
14	2	N	LS	7F, 6 mm	9	27.8
15	2	N	RS, RI	9F, 8 mm	4	16.0

LI = left inferior; LS = left superior; PV = pulmonary vein; RI = right inferior; RS = right superior.

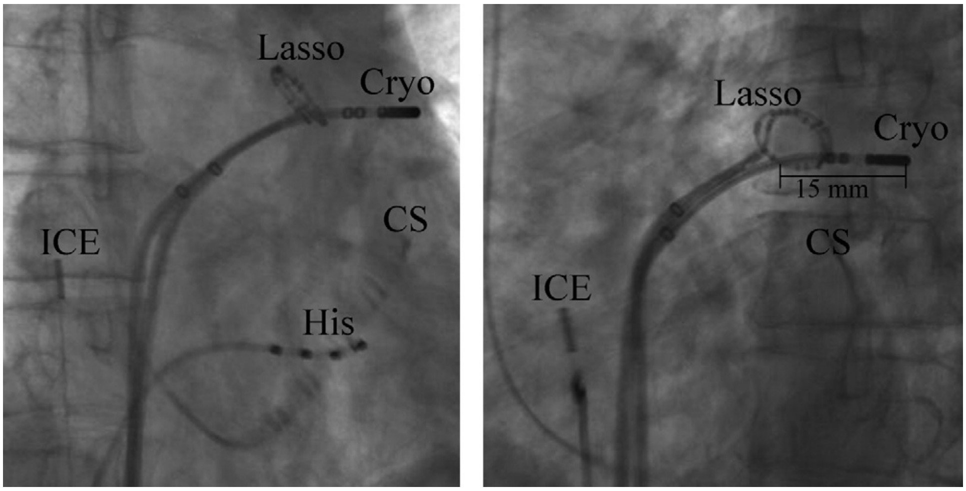

Figure 1 Cryoablation catheter positioned in the PV in the RAO (right) and LAO (left) projections. The Lasso catheter is positioned at the PV ostium. The coronary sinus (CS) and His bundle (His) catheters are in standard position. The ICE catheter is located in the right atrium. Note the cryoablation catheter 15 mm inside the PV ostium as defined by the Lasso catheter. Cryoablation was delivered here to isolate the PV. ICE = intracardiac echocardiography; PV = pulmonary vein.

Statistical analysis

SPSS version 10.0 (SPSS Inc., Chicago, IL) computer software was used for statistical analysis. Continuous variables were reported as mean ± SD as well as range, and comparisons between groups were based on a 2-sample *t* test. Comparisons between categorical variables were based on a χ^2 test. A *P* value ≤.05 was considered to be statistically significant.

Results

A total of 148 consecutive patients with a mean age of 57 ± 9 years old (68% male) underwent PV isolation for treatment of drug-refractory, symptomatic AF at our center between August 2005 and December 2006. In 15 of these patients (57 ± 9 years; 80% male) BDB, in 1 or more PVs, could not be achieved with antral or ostial isolation alone. Fourteen patients had paroxysmal and 1 had chronic AF. In these patients, cryoablation (CryoCath Technologies, Inc., Montreal, Canada) inside the PV was performed after failed antral and ostial RF ablation. The demographic characteristics of the total cohort of patients, as well as those undergoing combined RF and cryoablation, are presented in Table 1. Nine of 15 patients were undergoing a repeat procedure after recurrent AF. Two of the 15 patients had documented mild (<50%) PV stenosis from prior RF ablation.

In 133 of 148 (90%) patients and 569 of 592 (96%) PVs, entrance and exit block was achieved in all veins with RFA alone in the antrum or in the antrum and the ostium. In 15 of 148 (10%) patients and in 23 of 592 (3.8%) PVs undergoing antral or ostial isolation alone using RF, PV isolation was not achieved.

The demographic characteristics of the total patient population compared with those who underwent combined RF and cryoablation are presented in Table 1 and were statistically similar between groups, except that the percentage of female patients was slightly greater in the RF cohort versus the combined ablation modality group. The percentage of patients who were undergoing a repeat ablation attempt and those with prior PV stenosis were greater in the RF plus cryoablation group than in the RF ablation alone group (18% vs 60%, *P* <.05 and 1% vs 13%, *P* <.05, respectively).

The number of PV isolation procedures the patient had undergone; presence, site, and percent PV stenosis both after and before the procedure; site of cryoablation; cryoablation catheter type; number of cryoablation lesions; and total cryoablation time are listed in Table 2. Two patients who were undergoing combined RF plus cryoablation had prior PV stenosis diagnosed by comparing preprocedural MRIs. Neither of these patients had clinical manifestations of PV stenosis. Twelve patients had cryoablation in the left superior PV, 4 in the left inferior PV, 4 in the right superior PV, and 2 in the right inferior PV. Eleven patients underwent cryoablation with a 9F, 8-mm tip and four with a 7F, 6-mm catheter. Cryoablation was performed on average 12 ± 2 mm (range 8 to 15 mm) inside the PV, lesion number ranged from 4 to 25, and total time ranged from 8.0 to 53.8 min of cryoenergy delivery. Fluoroscopic images in the right anterior oblique and left anterior oblique projec-

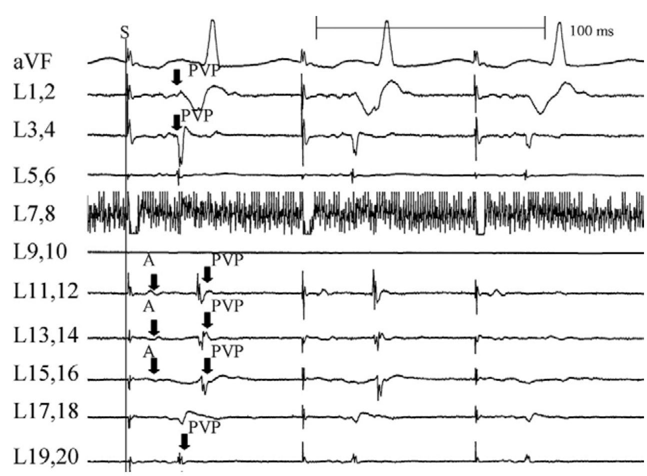

Figure 2 Electrograms recorded from a 20-pole Lasso (L1,2 [distal] to L19,20 [proximal]) catheter positioned at the PV antrum during cryoablation in the PV. Ten seconds elapsed from the time to reach target temperature until the disappearance of all the PV potentials (PVP) on the Lasso. The artifact from the cryoablation catheter is at L 7,8. A = atrial electrogram; PV = pulmonary vein.

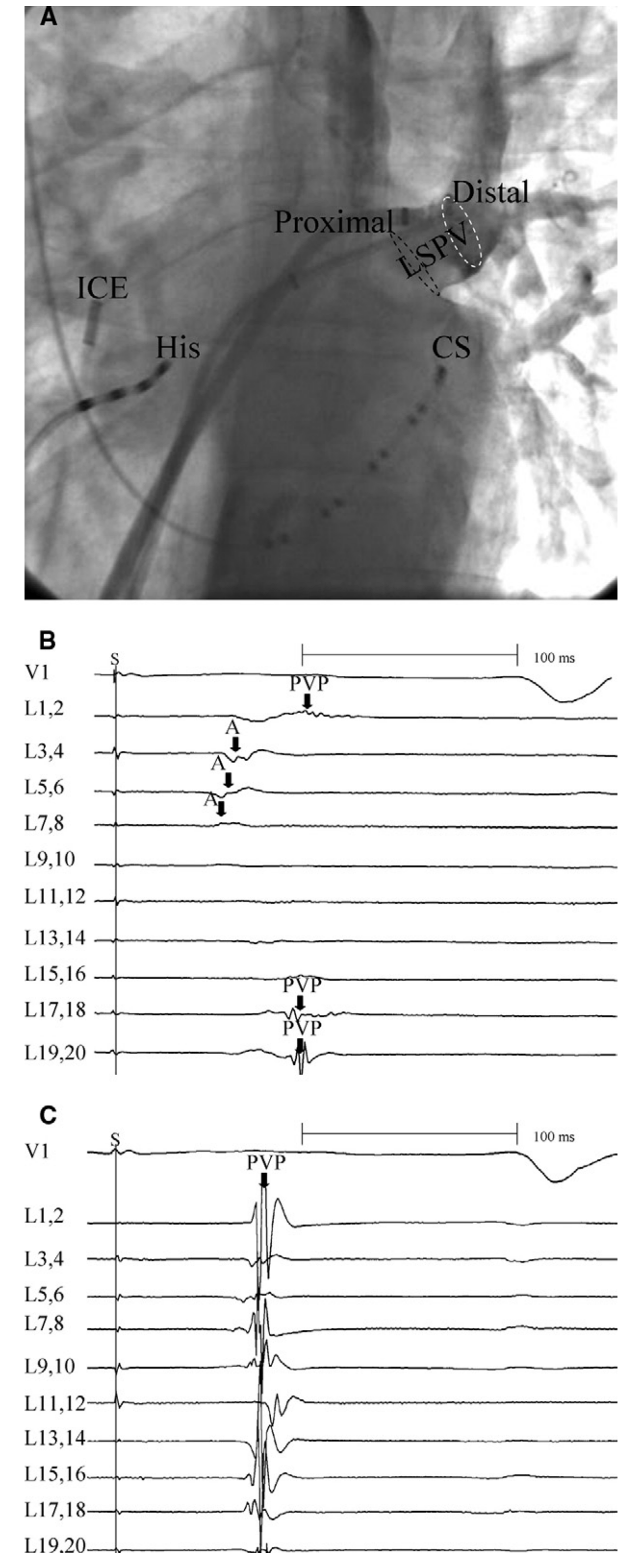

Figure 3 Venography of the LSPV in the LAO projection (**A**). The dotted black circle represents a Lasso positioned at the antrum after extensive ablation (Proximal), and the dotted white circle represents a Lasso positioned deep in the vein (Distal). The electrograms beneath the venogram represents Lasso recordings from a (**B**) distal position in the vein and proximally at the antrum (**C**). Note that deeper in the vein, the far field atrial electrogram is absent. A = atrium; CS = coronary sinus; ICE = intracardiac echocardiography; LSPV = left superior pulmonary vein; PVP = pulmonary vein potential; S = pacing stimulus.

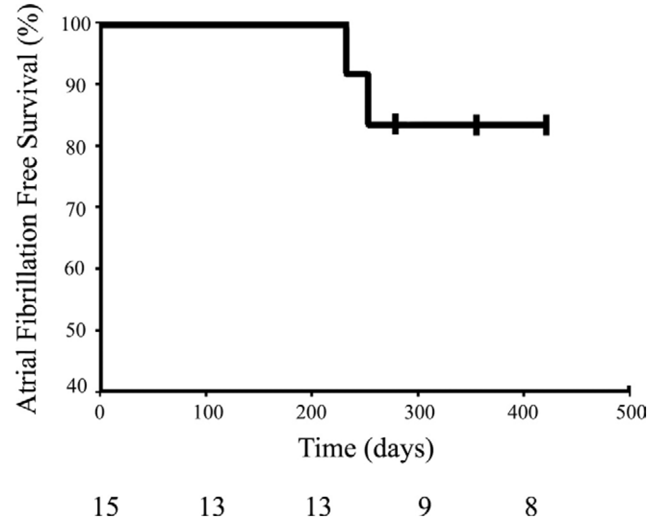

Figure 4 Kaplan-Meier curve of AF-free survival in 15 patients after combined cryoablation and RF. AF = atrial fibrillation; RF = radio frequency.

tions with the cryoablation catheter positioned inside the vein are shown in Figure 1.

An example of the achievement of entrance block recorded at 10 seconds after cryoablation onset from a Lasso positioned at the PV antrum is shown in Figure 2. A typical patient in whom entrance block was seen at the level of the antrum, but not deeper in the PVs where there was bidirectional conduction, is shown in Figure 3. This pattern was seen in all 15 patients. In this patient, the Lasso is positioned near the antrum, as defined by venography, and PV potentials remain present on only 2 sets of bipoles. After the Lasso is positioned slightly past the cardiac border, PV potentials are seen circumferentially around all poles.

Average fluoroscopic and procedure times were 57 ± 16 min and 5.3 ± 1.2 hours, respectively. The average fluoroscopic and procedure times for patients undergoing RF alone were 51 ± 14 min and 5.0 ± 1.1 hours, respectively. At 1-year follow-up (Figure 4), 83% of patients remained in sinus rhythm off antiarrhythmic medication; 7 of 9 (78%) patients undergoing a repeat procedure were in sinus rhythm at 1 year off antiarrhythmics.

The PV diameter and velocity before and after RF and cryoablation were compared in these patients for each PV

Table 3 Average pulmonary vein diameter before and after ablation and maximum pulmonary vein decrease

	Before ablation	After ablation	Maximal decrease
Left superior pulmonary vein diameter (cm)	1.7 ± 0.3	1.6 ± 0.2	0.7
Left inferior pulmonary vein diameter (cm)	1.6 ± 0.2	1.6 ± 0.2	0.7
Right superior pulmonary vein diameter (cm)	1.7 ± 0.3	1.7 ± 0.4	0.1
Right inferior pulmonary vein diameter (cm)	1.7 ± 0.2	1.6 ± 0.3	0.3

(Table 3). The average PV diameter before and after the procedure was unchanged (1.77 ± 0.18 vs 1.74 ± 0.19, $P = .641$) as determined by ICE or venography. None of the PVs had an increase in ICE velocity. At 1-year follow-up, none of the patients had clinical PV stenosis after cryoablation. Six patients had a follow-up MRI that showed no significant changes in PV diameter.

Discussion

Complete PV isolation has been shown to be an important goal in achieving improved efficacy of AF ablation.[9] PV isolation with RF delivered at the venous antrum and ostium is typically successful in achieving BDB in the PVs in the majority of patients.[3] In a small percentage of patients, combined antral and ostial isolation with RF is ineffective in achieving BDB in the PV. In these patients, when the Lasso is positioned in the antrum, electrical recordings suggest entrance block and PV isolation; however, it becomes apparent when the Lasso is placed deeper inside the PV that multiple connections between the PV and left atrium still exist. The reason for this is unclear. This may relate to the inability of the Lasso catheter to completely cover the inner surface of the PV wall. A second possibility relates to the hypothesis that PV automaticity stems from distinct serpiginous fibers that extend from deep in the vein out to the PV antrum where they arborize. The larger surface area and thicker tissue at the antrum makes complete and permanent destruction of this conductive tissue more difficult to complete at the antrum than inside the PV, where the tissue is thinner and the fibers are more densely arranged.

In patients in whom antral/ostial isolation of the PV with RF was ineffective in achieving BDB, instead of performing additional RF further inside the PV ostium or applying continued RF around the antrum and increasing the risk of PV stenosis or perforation and fistula,[13,14] we describe an approach using cryoablation inside the vein. After using this combined approach, all patients had documented BDB and sinus rhythm at the end of the procedure. Moreover, 83% of patients remained in sinus rhythm off antiarrhythmics after more than 1 year of follow-up.

When comparing the total patient cohort undergoing PV isolation with the 15 patients undergoing combined RF and cryoablation, the clinically significant features that differentiate these 2 groups were a history of PV narrowing from a prior procedure and undergoing a repeat ablation procedure. These 2 factors clearly relate to added concern about the cumulative effect of RF ablation on the PV and prompted the use of cryoablation. The presence of residual PV conduction is the most common reason for procedural failure and was the reason for an increased number of repeat procedures in the combined ablation group.

Our study supports prior reports of the safety of cryoablation.[11] In the 15 patients undergoing cryoablation in the PV, there was no significant change in PV diameter or Doppler velocity as assessed by ICE; there was no clinical occurrence of PV stenosis; and in the patients undergoing repeat MRI, there was no evidence of decreased PV diameter. This is in contrast to prior reports of RF ablation in the PV in which RF energy delivery inside the vein leads to decreased PV diameter, increased Doppler flow velocity in the vein, and a higher likelihood of clinical PV stenosis. One limitation in this study is the fact that not all of the patients had an MRI to assess for PV stenosis during follow-up.

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