



Percutaneous endocardial septal radiofrequency ablation on syncope in patients with hypertrophic obstructive cardiomyopathy: a short-term safety and efficacy study

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Background: Syncope is a serious consequence in patients with hypertrophic obstructive cardiomyopathy (HOCM). Percutaneous endocardial septal radiofrequency ablation (PESA) has emerged as a promising intervention to alleviate symptoms and enhance the quality of life for HOCM patients. However, little is known about the effects of PESA on syncope in HOCM. The authors aimed to study the effects of PESA on syncope in patients with HOCM.

Materials and methods: Nineteen patients with HOCM and syncope were enrolled. The left ventricular outflow tract gradient (LVOTG) of the patients was more than 50 mmHg despite medication. The participants underwent PESA under the guidance of intracardiac echocardiography (ICE) combined with a three-dimensional electrophysiological mapping system. The patients were followed for 3 (3-5.5) months.

Results: The mean age of the patients was 54.8 ± 13.7 years. Out of the 19 participants, 7 (37%) were females. During the follow-up, the syncope was completely alleviated in 14 patients (73.7%) or the syncope episodes were reduced greater than or equal to 80% in 16 patients (84.2%). The mean NYHA functional class significantly improved from 2.2 ± 0.7 at baseline to 1.7 ± 0.6 during follow-up ($P=0.002$). The LVOTG and septal thickness showed a decreasing trend from baseline to follow-up (LVOTG: $P=0.083$, septal thickness: $P=0.086$).

Conclusion: The authors' investigation provides evidence supporting the effectiveness of PESA in reducing syncope episodes in patients with HOCM.

Keywords: hypertrophic obstructive cardiomyopathy, percutaneous endocardial septal radiofrequency ablation, syncope

Introduction

Hypertrophic obstructive cardiomyopathy (HOCM), a genetic heart disorder characterized by the thickening of the left ventricular wall, poses significant challenges to the patient quality of life^[1]. Apart from heart failure symptoms, syncope is the most serious consequences of HOCM^[2]. Spirito *et al.*^[3] investigated syncope and risk of sudden cardiac death (SCD) in 1511 consecutive patients with hypertrophic cardiomyopathy. They found that 14% of the population had experienced syncope, and

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HIGHLIGHTS

- Percutaneous endocardial septal radiofrequency ablation (PESA) could be an appealing alternative therapy of hypertrophic obstructive cardiomyopathy (HOCM) with syncope.
- PESA could safely improve the heart function and decrease left ventricular outflow tract gradient (LVOTG) in patients with HOCM.
- What's more, combining with intracardiac ultrasound, it can achieve accurate ablation of the obstruction area and avoid damage to key conduct fibers. PESA had a lower rate of permanent pacemaker (PPM) dependency than alcohol septal ablation (ASA) and septal myectomy (SM). Remarkably, no death occurred during PESA. Therefore, PESA could be superior to SM and ASA with regard to periprocedural safety.

demonstrated a recent syncope occurring within 6 months was associated with a five-fold increased risk of sudden death as compared to those who did not experience syncope. Syncope in HOCM patients is primarily attributed to the dynamic left ventricular outflow tract (LVOT) obstruction, atrial and ventricular tachy-arrhythmias, and abnormal cardiac and vascular reflexes^[4].

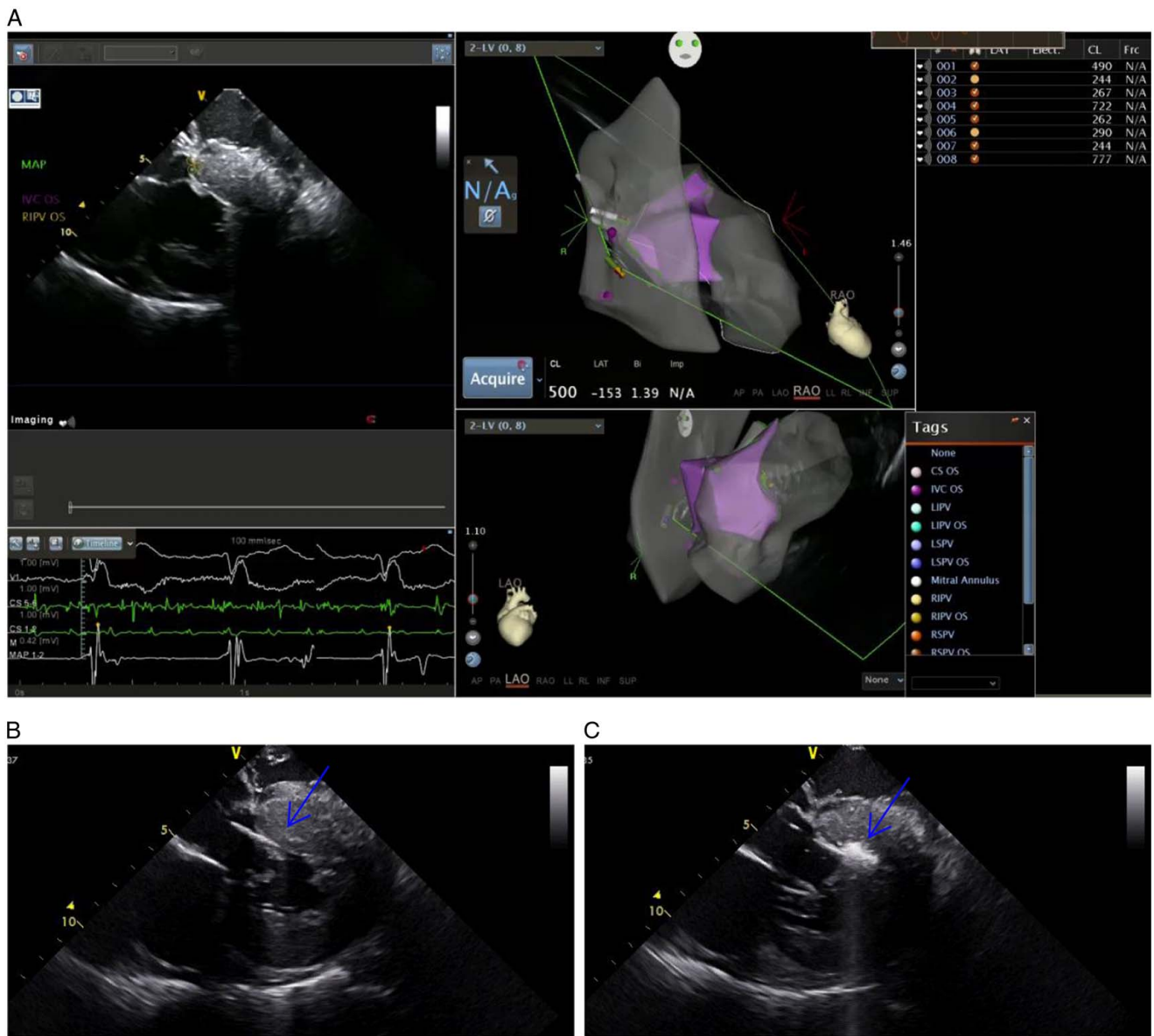


Figure 1. Representative images illustrating the PESA procedure. (A) PESA was performed utilizing a combination of a three-dimensional electrophysiological mapping system and ICE. The obstructive area, denoted in purple, was identified using this mapping system. Additionally, the His bundle, left branch, and Purkinje fibers were visualized with yellow, blue, and purple dots, respectively. (B) The image shows the hypertrophic septal wall and positioning of the catheter before ablation, indicated with a blue arrow. (C) The image demonstrates the occurrence of white septal edema during the ablation procedure, as indicated by the blue arrow. These images provide a visual representation of the steps and changes encountered during PESA, offering valuable insights into the technique and its impact on the septal wall. ICE, intracardiac echocardiography; PESA, percutaneous endocardial septal radiofrequency ablation.

To address this debilitating symptom, various treatment options have been explored, including pharmacological approaches and invasive techniques. Among these treatment measures, percutaneous endocardial septal radiofrequency ablation (PESA), a minimally invasive procedure, has emerged as a promising intervention to alleviate symptoms and enhance the quality of life for HOCM patients^[5]. It is well known that alcohol septal ablation (ASA) is an alternative to surgical septal myectomy (SM), particularly in patients who have a very high risk of surgical myectomy due to serious comorbidities or advanced age^[6]. However, ASA could not be performed in 10-15% of patients because of unsuitable coronary

artery anatomy^[7]. Besides, more pacemakers are implanted after ASA compared to SM^[8]. By contrast, the risk of conduction disorders could be controlled in PESA owing to the intracardiac electroanatomical mapping. In addition, the coronary arteries are unlikely be damaged during PESA. Hence, PESA is a safe invasive therapy. In a study of 19 patients with HOCM, Lawrenz *et al.*^[9] suggested that PESA was safe and effective in reducing LVOTG and improving cardiac function. Similarly, Kong *et al.*^[10] also showed PESA could achieve symptomatic improvement as well as reduction of the LVOTG in 25 patients. However, few studies have been performed to unravel the effect of PESA on syncope.

The objective of the current study is to evaluate the effect of PESA on syncope in patients with HOCM. By examining a cohort of HOCM patients with syncope who underwent PESA and comparing their pre- and post-procedure syncopal attack, our investigation aims to shed light on the effectiveness of this technique in managing syncope in this patient population. Given the limited data in this specific area, we expect that our findings will contribute valuable insights, paving the way for advancing treatment strategies for patients with HOCM concomitant syncope.

Methods

Study population

Thirty patients with HOCM who underwent PESA were enrolled from March 2017 to June 2023, consecutively. Syncope or pre-syncope was documented in 19 patients. The diagnosis of HOCM was based on a maximum LV wall thickness greater than or equal to 15 mm (or ≥ 13 mm with an unequivocal family history of HCM) in the absence of other cardiac or systemic diseases capable of producing comparable magnitude of hypertrophy, and peak LVOTG greater than or equal to 50 mm Hg at rest or during physiological provocation^[11]. Exclusion criteria were: age older than 80 years and less than 14 years, infectious disease or malignancy, moderate or severe hepatic impairment (Child-Pugh class B or C), severe renal failure (estimated glomerular filtration rate < 30 ml/min per 1.73 m²), and inability or unwillingness to adhere to standard treatment or to provide consent. Patient data from medical records were collected for analysis. Finally, 19

patients with syncope or pre-syncope were enrolled in the present study. Ethical approval was obtained from the Institutional Review Board of our Hospital. All participants provided their written informed consent in accordance with the Declaration of Helsinki. The work has been reported in line with the STROCSS criteria^[12]. This study has been registered into Chinese Clinical Trial Registry ChiCTR2400085244. <https://www.chictr.org.cn/> <https://www.chictr.org.cn/>.

PESA procedure

The pressure values of the left ventricular (LV) apex, the middle segment of the ventricular chamber, the sub-aortic valve, and the root of the aortic were measured respectively with a 6 F JR4.0 catheter via the right femoral artery. The pressure difference between the upper and lower sides of the obstruction area was LVOTG.

The PESA procedure was performed under the guidance of intracardiac echocardiography (ICE) combined with a three-dimensional electroanatomical mapping system. The ICE (Sound Star, Johnson & Johnson, Inc) was advanced to the right ventricle via the left femoral vein and used to construct the left ventricle. The ultrasound sector was integrated with the Carto Sound module (Bio sense Webster) of the Carto3 mapping system. The contact area between the interventricular septum and mitral valve at systolic phase, which is the obstructive area, was traced and marked with a cursor on the constructed three-dimensional structure map of the left ventricle.

Then the radiofrequency ablation catheter (56 holes, Thermocool Smart Touch, Johnson & Johnson) was advanced to the left ventricle through retrograde right femoral artery or atrial septal puncture via the right femoral vein. The key conduct fibers were mapped and marked (including His bundle, branch and Purkinje fibers). (Fig. 1) The nearest ablated point should be far away at least 8 mm away the key conducting fibers. The discharge would be stopped, and the catheter was moved to the nearby area to continue ablation if ventricular tachycardia or frequent ventricular premature beats persist for greater than or equal to 2 seconds during ablation. Radiofrequency energy was delivered using a power setting of 30–40 W with a saline irrigation of 17 ml/min at a temperature limit of 38–45°C.

When the thickness of the edema bright band detected by ICE in the ablation zone was greater than or equal to 5 mm and/or the ablated area accounted for greater than or equal to 1/2 of the obstructive area, again pressure measurement was performed. If LVOTG decreased by greater than or equal to 50% compared with that of before ablation, the ablation procedure could be terminated. If the pressure difference less than or equal to 50%, continue ablation until the pressure decreased by greater than or equal to 50%.

A temporary pacemaker electrode was placed at the apex of the right ventricle after the ablation. The pacing mode was ventricular on-demand inhibition (VVI), and the standby pacing frequency was 50 beats/min.

Follow-up

All the patients were scheduled for clinical follow-up at 3 and 6 months. During these visits, patients underwent a comprehensive evaluation, including a detailed assessment of syncope symptoms, ECG, echocardiography and cardiac function. We evaluate patient's cardiac function in accordance with NYHA

Table 1
Baseline characteristics of 19 patients with HOCM and syncope undergoing PESA

Variable	Value
Age (years)	54.8 ± 13.7
Female, <i>n</i> (%)	7 (37)
BMI (kg/m ²)	25.8 ± 3.4
NYHA functional class	2.2 ± 0.7
I, <i>n</i> (%)	3 (16)
II, <i>n</i> (%)	10 (53)
III, <i>n</i> (%)	6 (31)
Systolic blood pressure, mmHg	123.3 ± 11.5
Diastolic blood pressure, mmHg	72.0 ± 9.4
Atrial fibrillation, <i>n</i> (%)	5 (26)
Hypertension, <i>n</i> (%)	9 (47)
Diabetes mellitus, <i>n</i> (%)	4 (21)
β-Blockers, <i>n</i> (%)	11 (58)
Calcium channel blockers, <i>n</i> (%)	2 (11)
NT-proBNP (pmol/l)	815 (280–1491)
cTnI (ng/ml)	0.02 (0.014–0.129)
HbA1c (%)	6.4 ± 1.4
Echocardiography	
Septal thickness (mm)	20.3 ± 5.7
Left atrium diameter (mm)	43.4 ± 7.4
LV end-diastolic diameter (mm)	42.3 ± 5.7
LV ejection fraction (%)	65.2 ± 5.3
LVOTG at rest (mmHg)	67.6 ± 34.2

Data are expressed as mean ± SD, number (percentage), or median (interquartile range).

HOCM, hypertrophic obstructive cardiomyopathy; LV, left ventricular; LVOTG, LV outflow tract gradient; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PESA, percutaneous endocardial septal radiofrequency ablation.

Table 2
Procedural details of percutaneous endocardial septal radiofrequency ablation

Variable	Value
LV access	
Retrograde aortic, <i>n</i> (%)	7 (37)
Trans-septal approach, <i>n</i> (%)	10 (52)
Retrograde aortic and trans-septal approach, <i>n</i> (%)	2 (11)
Power (W)	37.4 ± 3.5
Temperature limit (°C)	43.3 ± 2.0
Real temperature (°C)	37.7 ± 4.3
Total ablation time (min)	20 (15.5–29)
Number of pluses of ablation	14 (9–23)
Synchronous ablation of AF, <i>n</i> (%)	2 (11)

Data are expressed as mean ± SD, number (percentage), or median (interquartile range). AF, atrial fibrillation; LV, left ventricle.

cardiac function classification criteria. No grade IV patients were enrolled in this cohort. The occurrence and frequency of syncope episodes, as well as any adverse events or complications, were recorded. If the syncope was completely alleviated or the syncope episodes were reduced greater than or equal to 80%, it was deemed responding well to PESA.

Statistical analysis

Descriptive statistics were used to summarize the study population characteristics and baseline data. The results were presented as mean ± standard deviation (SD) for continuous variables and percentages for categorical variables. Paired t-tests were utilized to compare pre- and post-procedure measurements. A *P* value of less than 0.05 was considered statistically significant. Statistical analysis was conducted with SPSS software (version 22.0, IBM Inc.) and Prism 5.0 (GraphPad Software Inc.).

Results

Baseline characteristics of patients with HOCM and syncope

The baseline characteristics of the study population in patients with HOCM and syncope is presented in Table 1. The mean age of the patients was 54.8 ± 13.7 years, out of the 19 participants, 7 (37%) were females. The baseline distribution of the NYHA functional class in the study population was as follows: 3 (16%) in Class I, 10 (53%) in Class II, and 6 (31%) in Class III. Atrial fibrillation was present in 5 (26%) patients. β-Blockers were taken in 11 (58%) patients. The baseline levels of NT-proBNP had a median value of 815 pmol/L (interquartile range: 280–1491 pmol/L). The mean septal thickness of the patients was 20.3 ± 5.7 mm. The mean LVOTG detected by transthoracic echocardiography was 67.6 ± 34.2 mmHg.

Table 3
Follow-up results of heart function, LVOTG, and septal thickness

Variable	Baseline	Follow-up	<i>P</i>
Syncope	19	4	
NYHA functional class	2.2 ± 0.7	1.7 ± 0.6	0.002
LVOTG at rest (mmHg)	67.6 ± 34.2	52.3 ± 45	0.083
Septal thickness (mm)	20.3 ± 5.7	19.1 ± 3.8	0.086

LVOTG, left ventricular outflow tract gradient; NYHA, New York Heart Association.

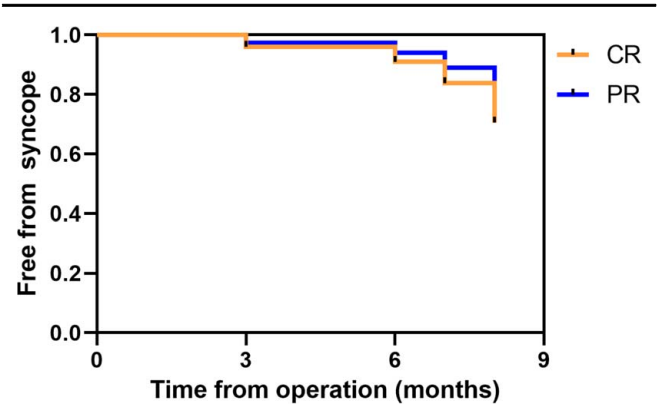


Figure 2. Kaplan–Meier Curve: Freedom from syncope during follow-up. Kaplan–Meier survival curve showing complete remission (CR) from syncope (73.7%) over the follow-up of the study, partial remission (PR) from syncope (84.2%) over the follow-up of the study.

Percutaneous endocardial septal radiofrequency ablation parameters

All ablations were performed at left ventricular septal endocardium. The PESA parameters and ablation pathways were shown in Table 2. 7 (37%) patients underwent the retrograde aortic approach alone, 10 (52%) underwent atrial septal puncture alone, and 2 (11%) underwent a combination of retrograde aortic and trans-septal approaches. The mean power used was 37.4 ± 3.5 watts, and the real temperature was 37.7 ± 4.3°C. The median number of pluses delivered during PESA was 14 (interquartile range: 9–23).

Follow-up results of syncope, heart function, LVOTG, and septal thickness

Syncope was completely alleviated in 14 (73.7%) patients or the syncope episodes were reduced greater than or equal to 80% in 16 (84.2%) patients after a follow-up of 3 (3–5.5) months (As shown in Table 3 and Fig. 2), suggesting that most of the patients with HOCM and syncope responded well to PESA. The mean NYHA functional class significantly improved from 2.2 ± 0.7 at baseline to 1.7 ± 0.6 during follow-up (*P* = 0.002). The LVOTG and septal thickness also showed a decreasing trend from baseline to follow-up, although statistical significance was not reached (LVOTG: *P* = 0.083, septal thickness: *P* = 0.086).

Discussion

Since PESA was proposed nearly 20 years ago, only a few related studies with short-term outcomes have been published, which were summarized in Table 4^[9,10,13–17]. Although syncope markedly dampens the quality of life in patients with HOCM, there are scarce data concerning the treatment of obstructive-related syncope. The present study aimed to evaluate the effect of endocardial radiofrequency ablation (PESA) on syncope in patients HOCM. Our study findings revealed a marked improvement in syncope-related symptoms in the majority of patients, indicating that PESA has a favorable effect on syncope in patients with HOCM.

Previous studies suggest that syncope in patients HOCM is caused by three principal mechanisms: arrhythmias, LVOT

Table 4
Comparison of published studies concerning PESA

Study	No. patients	Follow-up, months	Severe complications
Present study	25	37 ^a , 22 ^b	None
Guo <i>et al.</i> ^[12]	9	4	1 femoral pseudoaneurysms
Valdigem <i>et al.</i> ^[13]	12	12	1 arteriovenous fistula
Liu <i>et al.</i> ^[14]	20	6	None
Shelke <i>et al.</i> ^[15]	7	12	1 acute pulmonary edema
Crossen <i>et al.</i> ^[10]	11	12	2 PPM; 1 cardiac tamponade; 1 acute pulmonary edema
Cooper <i>et al.</i> ^[16]	5	6	1 death; 1 acute pulmonary edema
Lawrenz <i>et al.</i> ^[17]	19	6	4 PPM; 1 cardiac tamponade

PESA, percutaneous endocardial septal radiofrequency ablation; PPM, permanent pacemaker.

^aFollow-up for NYHA functional class.

^bFollow-up for transthoracic echocardiography.

obstruction, and abnormal blood pressure responses^[18]. Both supraventricular arrhythmias and ventricular arrhythmias are very common in HOCM. In a study of 26 patients with HCM by Schiavone *et al.*^[19] using 24-h Holter monitoring and electrophysiologic studies (EPS), supraventricular tachycardia was induced by EPS in 17 participants, among whom nine had symptomatic hypotension paralleling supraventricular tachycardia while lying supine. About one-third of HOCM patients have atrial fibrillation (AF) resulted from left atrial enlargement. Paroxysmal episodes of AF could lead to syncope or pre-syncope in that cardiac output is suddenly reduced due to increased ventricular rate and loss of effective atrial contraction. Currently, little is known about effects of catheter ablation of AF on syncope in patients with HCM. Of note, a recent observational multicenter study in 137 HCM patients reported that the recurrence rate of paroxysmal AF was 39.2% after 12-month period post-ablation, and 24 months after the ablation, 60% of those with paroxysmal AF recurred, and nearly all patients with persistent AF had relapsed^[20]. These observations implicated catheter ablation of AF may not be an effective therapeutic method for abolishing syncope.

Although non-sustained ventricular tachycardia (NSVT) is very common in patients with HCM, the NSVT is usually asymptomatic and benign^[21]. Sustained ventricular tachycardia (VT) is poorly tolerated in patients with HCM. Therefore, when sustained VT is detected, particularly along with other risk factors of SCD, an ICD implantation can effectively prevent SCD^[22].

Obstructive-related syncope is main cause of syncope in patients with HOCM. The syncope or pre-syncope may be induced by physical stress or drugs reducing preload and/or afterload, which can aggravate the LVOT obstruction. In a study of 239 patients with HOCM and syncope who had undergone surgical myectomy (SM), the authors found the recurrence rate of syncope was 11% in the SM patients and 40% in the medical group^[23]. Besides, Jensen and colleagues analyzed 531 patients with HOCM treated with alcohol septal ablation (ASA) from 5 Northern European centers. The proportion of patients with syncope decreased from 25 to 2% 0.6±0.6 years after ASA. These investigations implicated that septal reduction therapy may alleviate syncope by diminishing LVOT obstruction^[24].

Recently, some cardiac myosin inhibitors have been explored to treat HOCM by attenuating myocardial contractility, including mavacamten and afflicamten^[25]. Preliminary studies demonstrated that mavacamten and afflicamten could reduce LVOTG at rest and after provoking, as well as improving heart function^[26]. At present, little information about effects of myosin inhibitors on syncope is available.

Theoretically, the syncope in HOCM should be treated on the basis of corresponding etiology. Unfortunately, a probable mechanism of syncope can be identified in only a minority of patients. In more 80% of cases, no likely mechanism is found despite repeated examinations. In consequence, the syncope in HOCM is undertreated. There is still a great need to manage syncope in HOCM. Here our data unraveled that PESA could reduce recurrence of syncope. The observed improvement in syncope after PESA can be attributed to various mechanisms. Firstly, PESA targets the hypertrophied myocardium within the left ventricular outflow tract, thereby reducing the likelihood of obstruction during systole. This leads to improved blood flow dynamics and a subsequent decrease in syncope episodes. Secondly, the ablation procedure disrupts the abnormal electrical pathways responsible for ventricular arrhythmias, further contributing to better cardiovascular stability and a reduced risk of syncope. Overall, the combined impact of improved blood flow and stabilization of the myocardial electrical conduction system contributes to the alleviation of syncope symptoms.

Additionally, it is important to highlight that PESA has demonstrated a favorable safety profile in our study cohort. The procedure was associated with minimal complications, with no occurrences of major adverse events reported. This suggests that PESA can be considered as a safe intervention for managing syncope in patients with HOCM, offering potential benefits without substantial risks.

While our study suggests the positive effect of PESA on syncope in HOCM patients, there are certain limitations that should be acknowledged. Firstly, the sample size of our study cohort was relatively small, potentially limiting the generalizability of our findings. Future studies with larger cohorts are warranted to validate our results. Secondly, the study design was retrospective, which can introduce bias and confounding variables. Prospective studies with randomized control groups may provide more robust evidence for the effectiveness of PESA. Additionally, the follow-up period of our study was relatively short. Long-term monitoring of patients undergoing PESA would provide a more comprehensive understanding of its sustained effects on syncope.

Conclusion

In conclusion, our investigation provides evidence supporting the effectiveness of endocardial radiofrequency ablation in reducing syncope episodes in patients with HOCM. The procedure demonstrates a favorable safety profile, suggesting its potential as a treatment option for HOCM patients suffering from syncope. Further research is required to validate these findings and explore the long-term outcomes and cost-effectiveness of PESA compared to other treatment modalities. Ultimately, enhancing our understanding of the effect of PESA on syncope in HOCM contributes to improving patient care and optimizing therapeutic strategies for this specific patient population.

Ethics approval

Ethical approval was obtained from the Institutional Review Board of Fuwai Hospital. All participants provided their written informed consent in accordance with the Declaration of Helsinki.

Consent to participate

Written informed consent was obtained from the patient for publication and any accompanying images.

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Author contribution

All authors contributed to the research and/or preparation of the manuscript. Y.J., and J.L., and X.G. participated in the study design and performed the PESA operation; T.Z. collected and processed the data finalized the manuscript. P.F., and M.T. participated in the study design, K.C., and Y.Y. reviewed the manuscript. A.T. performed the statistical analyses and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

This study is a retrospective analysis and there is currently no clinical study registration number available. However, we are currently undergoing a retrospective study registration process and believe that we will soon be able to obtain a clinical study registration number.

Guarantor

Yuhe Jia.

Data availability statement

The data related to this study can be made public, and if necessary, the corresponding author can be contacted.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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