A modified endocardial radiofrequency ablation approach for hypertrophic obstructive cardiomyopathy guided by transthoracic echocardiography: a case series

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Background: A series of studies showed that endocardial radiofrequency ablation (ERFA) could reduce the left ventricular outflow tract (LVOT) gradient in patients with septal hypertrophy. This study aimed to determine the safety and efficacy of a modified ERFA approach guided by transthoracic echocardiography (TTE) as an alternative to ablation performed under a three-dimensional (3D) electroanatomical system or intracardiac echocardiography (ICE).

Methods: Twenty-five patients with hypertrophic obstructive cardiomyopathy (HOCM) underwent ERFA of septal hypertrophy, guided by echocardiography. The LVOT gradient, left ventricular ejection fraction (LVEF), LV thickness, New York Heart Association (NYHA) class, and biochemical laboratory values were recorded before ablation and during follow-up.

Results: The patients' peak and stress-induced LVOT gradients were significantly reduced after 12 months of follow-up (resting gradient: from 123.2±17.7 to 15.7±7.8 mmHg, P<0.05; provocative gradient: from 140.2±20.8 to 18.4±8.0 mmHg, P<0.05). Compared with baseline, the septal diameter was reduced slightly after 12 months, but the difference was not significant (24.8±3.5 *vs.* 24.2±3.4 mm, P>0.05). The reduction in LVOT gradient was associated with an improvement in NYHA functional classification (from 3.0±0.0 to 1.6±0.7, P<0.05), the 6-minute walking distance (413±129 m at baseline; 458±108 m immediately after ERFA; 471±139 m after 12 months, P<0.05), and pro B-type natriuretic peptide levels (from 924.00±139 to 137.45 ±75.73 pg/mL, P<0.05). After the procedure, the patients showed no worsening of LVEF compared with baseline (64%±5.3%), and no cases of bundle branch block nor complete heart block occurred.

Conclusions: ERFA guided by TTE provides a new treatment option for HOCM which can achieve symptomatic improvement as well as a significant and sustained reduction of the LVOT gradient. Moreover, by avoiding the use of the 3D electroanatomical system or ICE, this treatment has an acceptable cost.

Keywords: Radiofrequency ablation; echocardiography; hypertrophic obstructive cardiomyopathy (HOCM); left ventricular outflow tract (LVOT)

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Introduction

Hypertrophic obstructive cardiomyopathy (HOCM) is an inherited disease that is transmitted in an autosomal dominant pattern. It presents with variable penetrance and increased left ventricular outflow tract (LVOT) gradients (1). Hypertrophic cardiomyopathy has a prevalence of approximately 1/500, and the prevalence of obstruction may be as high as 70% with provocation maneuvers (2). It is the most common causes of cardiac sudden death in young, especially in the competitive athletes. HOCM also constitutes a risk for myocardial ischemia, mitral regurgitation, leading to chronic heart failure.

Symptoms caused by LVOT obstruction is reversible by septal reduction, including Morrow procedure or alcohol septal ablation. While, the long-term risk such as arrhythmogenicity and sudden death associated with septal reduction remains unresolved.

In addition to substantial improvement in the quality of life, endocardial radiofrequency ablation (ERFA) of septal hypertrophy is regarded as a feasible and effective approach to alleviating LVOT gradients via the mechanism of discrete septal hypokinesia. As a therapeutic catheter-based approach, it provides a surgical option for patients with HOCM (3). However, several studies performed ablation under a three-dimensional (3D) electroanatomical system or intracardiac echocardiography (ICE), which may result in skyrocketing medical costs and a high cost of health insurance.

Therefore, as an alternative treatment strategy for patients with HOCM, we designed a modified approach based on guidance by transthoracic echocardiography (TTE). In the present study, we aimed to appraise the immediate and long-term safety and efficacy of this modified procedure. We present the study in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/atm-21-2783)

Methods

This retrospective study involved patients with HOCM undergoing ERFA for septal hypertrophy. Patient data were retrospectively retrieved from archived medical records. All aspects of the study involving human participants adhered to the Declaration of Helsinki (as revised in 2013) and were approved by the Institutional Review Board of Fudan University (No. ZHSH-LL-201810210061). Written informed consent was obtained from each participant before their inclusion in the study.

Patients

Twenty-five patients with HOCM who had an LVOT gradient >50 mmHg at rest or after provocation were enrolled (Figures S1-S4). All of the patients were suffering from severe symptoms (including chest pain, dyspnea, syncope) despite taking medication. Patients were inrolled for the ERFA procedure after signing a written informed consent form (*Table 1*).

Ablation technique

The patients were placed under sedation and local anesthesia for the procedure, which was performed under the guidance of TTE (iE33, Philips Medical System, Netherlands). A retrograde transaortic approach was adopted for septal hypertrophy ablation in all patients. A 4-mm irrigated-tip ablation catheter (CoolFlow Irrigation Pump, Biosense Webster, California), with the flow speed of 30 mL/min was used in the ERFA procedure. In order to reduce LVOT obstruction, each lesions were ablated for 60–120 s, with a power setting of 40–60 W. The radiofrequency energy was delivered strictly to the most proximal parts of the septum in the immediate vicinity of the LVOT. To obviate complete heart block, the tip of the ablation catheter was navigated away from the His bundle region as far as possible. Real-time TTE imaging was used to monitor the catheter location and its stable contact with the left ventricular (LV) septum (*Figure 1*).

ERFA was delivered to each site for 60–180 seconds with a power setting of 40–60 W. To maintain an activated clotting time of 300–350 seconds during the procedure, patients also received adjusted doses of heparin. LVOT gradients were measured by TTE at baseline and after the procedure.

A gradient reduction of >50% was regarded as the endpoint for ERFA.

Patient evaluation and follow-up

Comprehensive TTE was performed at baseline and at each follow-up. Patients' left ventricular ejection fraction (LVEF), LV thickness, New York Heart Association (NYHA) class, and biochemical laboratory values were assessed at baseline and each follow-up, held 3 days, and 1, 6, and 12 months after the procedure. The LVOT gradients were measured at rest or after provocation (bicycle exercise, 75 W, for

Table 1 Patient characteristics

Patient[#]	Age, yrs	Septal diameter at baseline, mm	LVOT gradients, mmHg		Ablation site, N	Ablation time, min	Maximum power, W
			Rest	Provocation			
1	54	30	100	140	16	32	60
2	34	32	125	130	10	20	55
3	42	20	137	137	16	32	60
4	31	22	99	110	10	23	50
5	42	24	97	100	12	25	60
6	49	28	89	129	10	20	60
7	69	27	134	134	9	37	50
8	64	27	111	111	9	25	55
9	24	26	120	120	14	34	55
10	65	22	127	145	12	32	60
11	26	20	133	133	9	27	50
12	30	22	120	169	14	25	50
13	34	24	150	150	17	34	50
14	37	25	118	164	11	23	45
15	41	24	127	157	13	30	60
16	37	28	138	138	12	31	60
17	60	21	165	184	10	28	55
18	36	20	108	117	9	27	55
19	44	27	133	133	16	37	50
20	34	30	131	145	14	28	50
21	54	20	129	122	15	43	50
22	57	21	110	146	10	30	45
23	27	30	108	168	11	27	55
24	19	23	120	173	12	30	50
25	20	28	150	150	13	29	50

5 minutes), and the maximum gradients were recorded for analysis. All parameters were evaluated by two experts, who were blinded to the clinical details.

Patients were monitored by electrocardiogram from immediately after the ERFA procedure until discharge, and during each follow-up. The 6-minute walking distance was also measured at each follow-up.

Statistical analysis

Paired data were analyzed using the Wilcoxon signed-rank test, while unpaired data were analyzed with the Mann-Whitney U test. SPSS Statistics for Windows (version 21.0, IBM Corp., Armonk, NY, USA) was used for all data analyses. Statistical significance was defined as $P<0.05$.

Results

Twenty-five patients with HOCM underwent ERFA. The patients had a mean age of 41.2±14.1 years (range, 19–69 years), and 17 of them were male (68%). At baseline, the mean LVOT gradient was 123.2±17.7 mmHg at rest

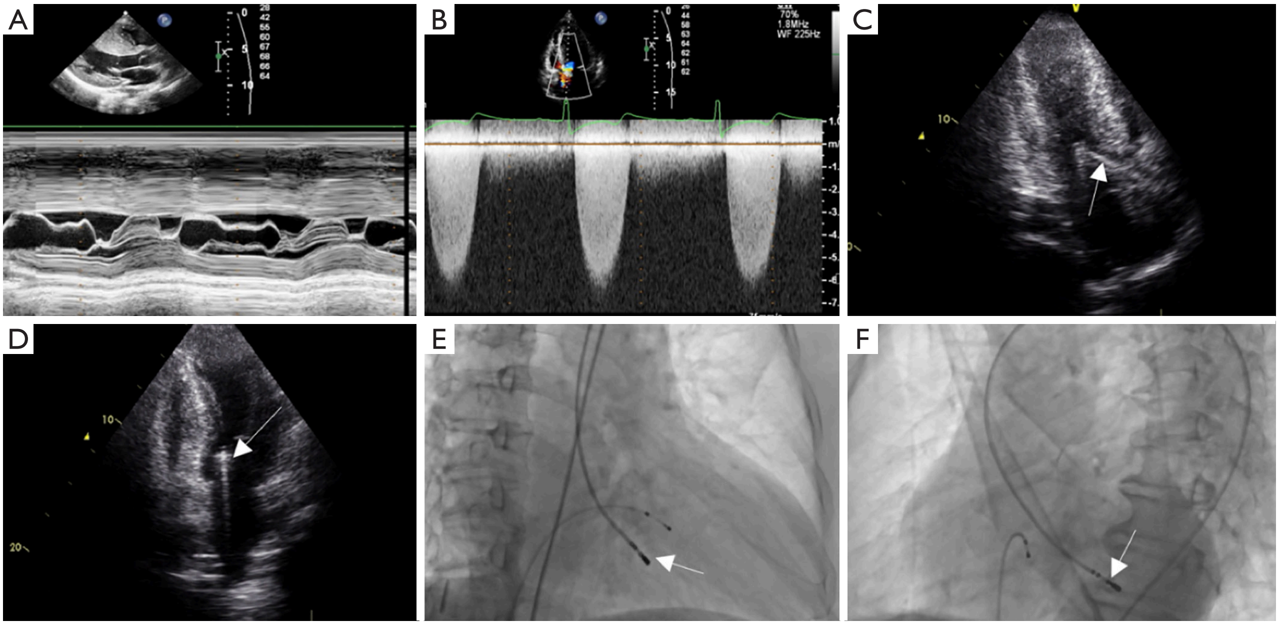

Figure 1 Preoperative and intraoperative imaging. (A,B) HOCM examination before ERFA; (C,D) the catheter location (arrow) was monitored under real-time TTE imaging; (E,F) fluoroscopy was also used for guidance. HOCM, hypertrophic obstructive cardiomyopathy; ERFA, endocardial radiofrequency ablation; TTE, transthoracic echocardiography.

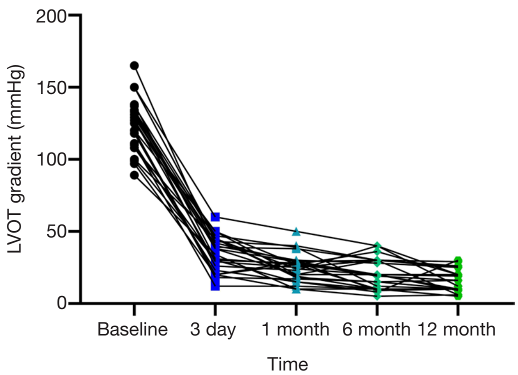

Figure 2 Reduced LVOT obstruction at rest. LVOT, left ventricular outflow tract.

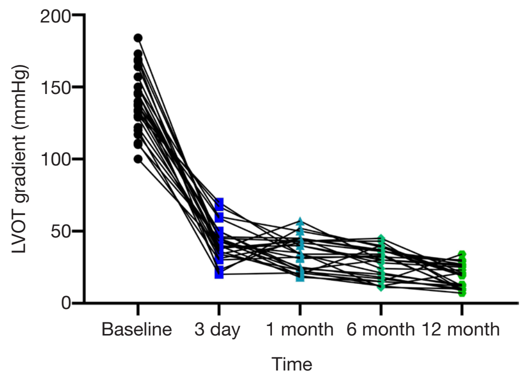

Figure 3 Reduced LVOT obstruction after provocation. LVOT, left ventricular outflow tract.

and 140.2±20.8 mmHg after provocation. In all patients, a decrease was seen in the echocardiographic gradient immediately after the procedure, and further reductions were observed at each follow-up (*Figures 2-5*). After the procedure, there was no worsening of the LVEF compared with baseline (64%±5.3%).

After 12 months of follow-up, the peak and stress-induced LVOT gradients displayed significant sustained reductions in patients (resting gradient reduced to 15.7±7.8 mm Hg; P<0.05 and provocative gradient reduced to 18.4±8.0 mmHg; P<0.05). The data revealed a mild decrease in interventricular septal thickness after the procedure, although the difference was not significant (24.8±3.5 *vs.* 24.2±3.4 mm, P>0.05).

The reduction in the LVOT gradient was also associated with an improvement in NYHA functional classification (from 3.0±0.0 to 1.6±0.7, P<0.05), 6-minute walking distance (413±129 m at baseline; 458±108 m immediately after ERFA; 471±139 m after 12 months, P<0.05), and pro B-type natriuretic peptide levels [from 924.00±139 to

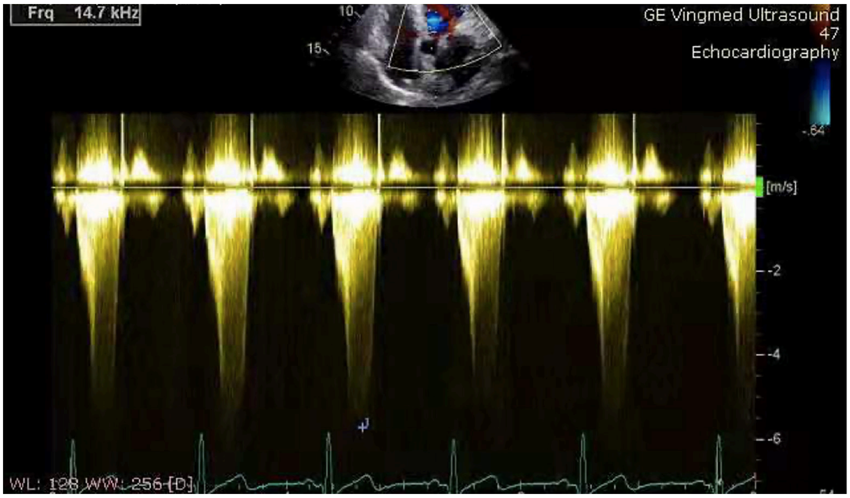

Figure 4 LVOT obstruction before ablation. LVOT, left ventricular outflow tract.

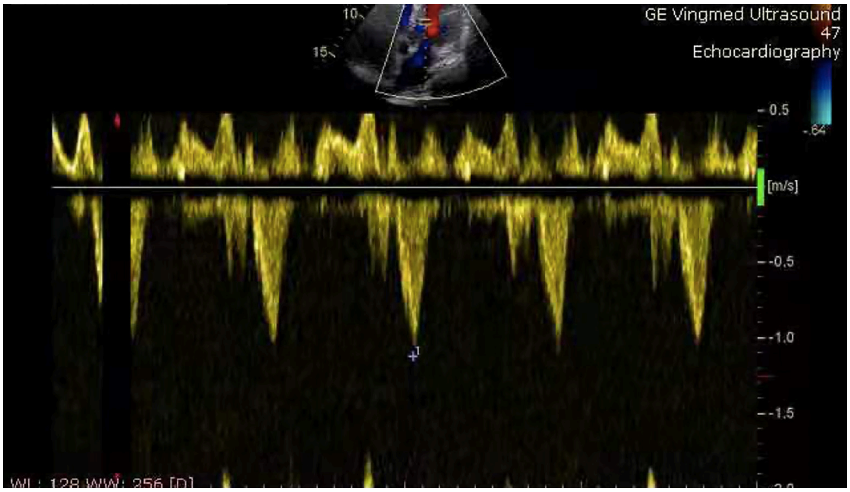

Figure 5 The LVOT gradients of the patients reduced to normal after ablation. LVOT, left ventricular outflow tract.

137.45±75.73 pg/mL; P<0.05).

Serial electrocardiograms revealed no cases of bundle branch block or complete heart block among the patients in this study.

Discussion

On the basis of extensive worldwide guidelines and expert consensus recommendations, septal myectomy and percutaneous transluminal septal myocardial ablation have been recommend as the preferred option for patients with severe drug-refractory symptoms (4). While quite a few patients cannot tolerate the septal reduction due to heart failure.

The narrowing of the LVOT by asymmetric septal hypertrophy is typically aggravated by contact between the anterior mitral valve leaflet and the interventricular septum caused by systolic anterior motion (SAM). All relevant literature results show that ERFA may create a localized myocardial scar on the SAM-interventricular septum contact point. R wave amplitude decreased, transient ST segment elevation and peaked T waves were found on V1 and V2 intraoperatively, indicating the focal myocardial injury in the septum. This scar tissue caused by the ablation can interrupt the SAM-septal feedback mechanism and subsequently reduce the LVOT gradient (4,5). Thus, we hypothesized that the localized septal hypokinesis induced by ERFA in HOCM also resulted in a reduced mitral regurgitation and LVOT gradient.

Different techniques have been used to localize the contact point of the anterior mitral leaflet and the interventricular septum, including fluoroscopy, ICE, and the CARTO system. Lawrenz *et al.* (6). reported the first three septal ablation procedures via LV approach under the guidance of fluoroscopy. In 2011, Lawrenz *et al.* (7). discussed the outcomes of ERFA in 19 adult patients with HOCM. They mapped the atrioventricular node, bundle brunch conduction sites, and SAM-interventricular septum contact point using the electrode catheter in the CARTO (Biosense Webster) system. In their study, Riedlbauchová *et al.* used ICE and electroanatomic CARTO mapping to identify the target site (8).

Studies have suggested that localized ablation of the interventricular septum can attain an intraventricular pressure gradient reduction during the treatment session and a post-intervention gradient reduction during cycle exercise, as assessed by Doppler echocardiography, in addition to a reduction in septal thickness (8-10). However, the investigators in those studies usually used ICE or the CARTO system to obtain high-quality images, and currently, the medical expenses related to these procedures are high.

As an alternative, TTE may provide images of a sufficient quality to enable precise lesion location of the patient undergoing ERFA (11,12). To detect the SAM-septum contact area, the present study used the parasternal long-axis view, the parasternal short-axis view, and the apical five-chamber view of intraoperative TTE (*Video S1*). The three orthogonal planes were useful in monitoring the catheter location and its stable contact with the LV septum.

Compared with that at baseline, the septal thickness of our patients showed a minor reduction after 12 months (*Videos S2,S3*). During follow-up, we also observed subaortic septal hypokinesia, enlargement of the LVOT, and an increase in the patients' exercise capacity. Therefore, we can infer that ERFA produced localized hypokinesis of endomyocardial tissue. The ineffective contraction in the treated segment subsequently resulted in a decrease in pressure gradient across the LVOT (Figures S5-S7). Our results show that the reduction in gradient and the relief of symptoms were sustained until 1 year after the procedure.

Inadvertent block is the major complication of ablation (13). Therefore, in this study, ablation was delivered primarily using steerable catheters with 4- or 5-mm tip electrodes and conventional irrigated energy application (14). At moderate temperatures (target temperature, 55 ℃) and with a maximal power output of 50 to 60 W, ERFA is considered to be safe and effective (15); the duration of energy application should also exceed 60 seconds. Real-time TTE imaging enables precise catheter placement and preservation of movement during the procedure.

Study limitations

This study has some limitations that should be addressed. First, although this is the first report regarding the use of this novel approach, the number of cases was small, a larger prospective, multicenter study is needed to establish further safety and efficacy. Second, the follow-up period was short, we did not measure maximum oxygen consumption. Finally, the study was non-randomized and retrospective in nature.

Conclusions

Although ERFA has previously been reported, our study is the first to document the safety and efficacy of ERFA performed with invasive TTE guidance. This approach can reduce the LVOT gradient of patients significantly and sustainably; thus, it may be an alternative treatment option for patients with HOCM by avoiding the use of the 3D electroanatomical system or ICE.

Acknowledgments

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/atm-21-2783

Data Sharing Statement: Available at https://dx.doi.org/10.21037/atm-21-2783

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/atm-21-2783). The authors have no conflicts of interest to declare.

Ethical Statement: 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. All aspects of the study involving human participants adhered to the Declaration of Helsinki (as revised in 2013) and were approved by the Institutional Review Board of Fudan University (No. ZHSH-LL-201810210061). Written informed consent was obtained from each participant before their inclusion in the study.

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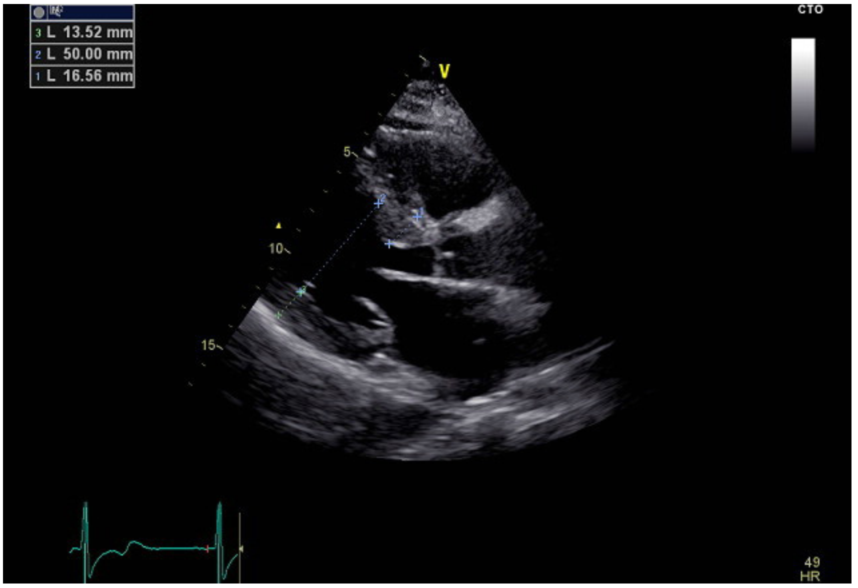

Figure S1 Ventricular septal hypertrophy.

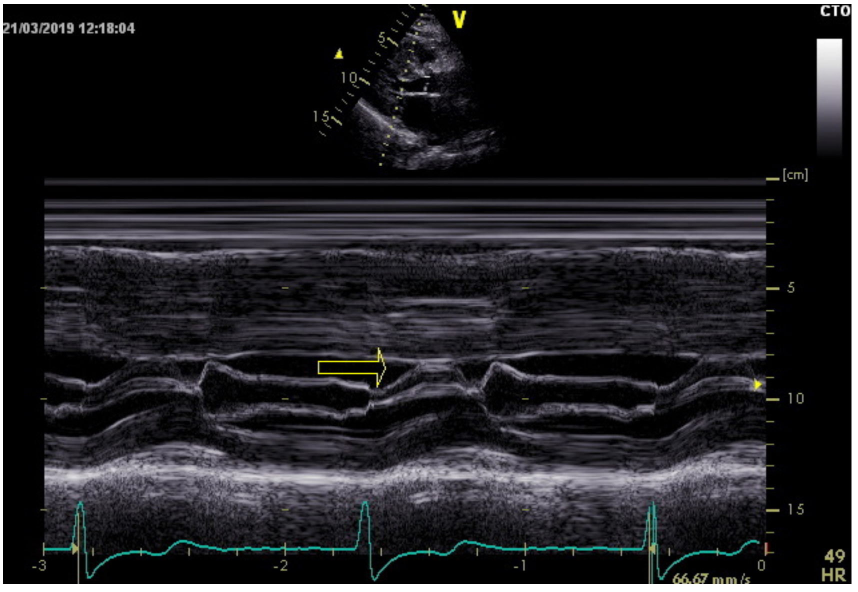

Figure S2 SAM of the mitral valve (arrow) before ablation. SAM, systolic anterior motion.

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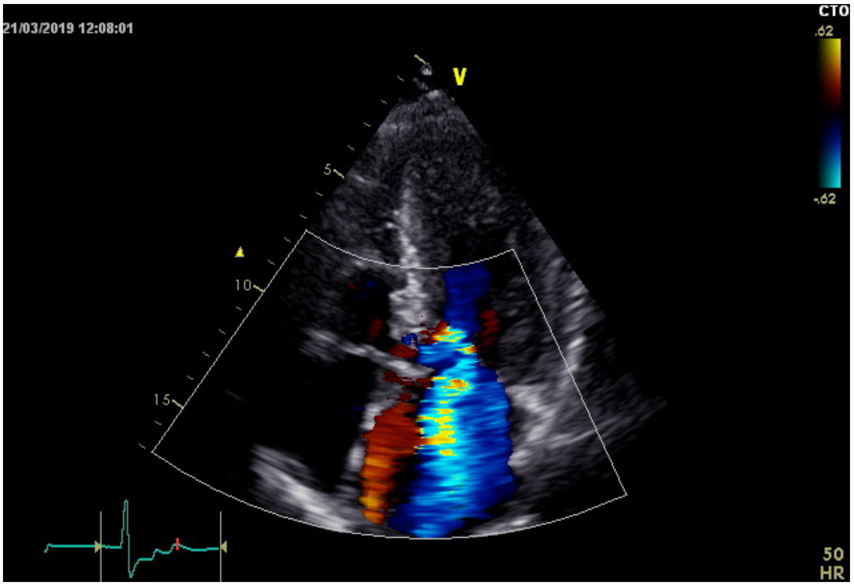

Figure S3 Severe mitral regurgitation before ablation.

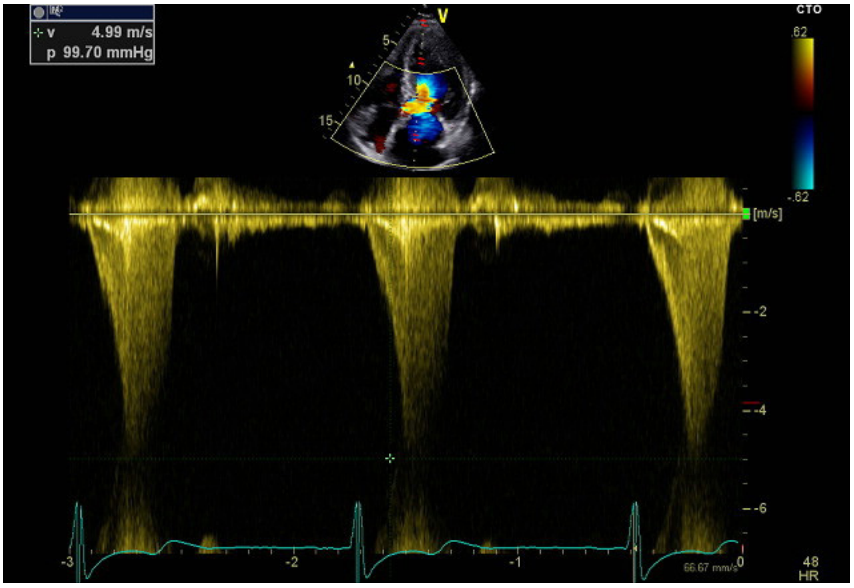

Figure S4 Left ventricular outflow tract obstructions before ablation.

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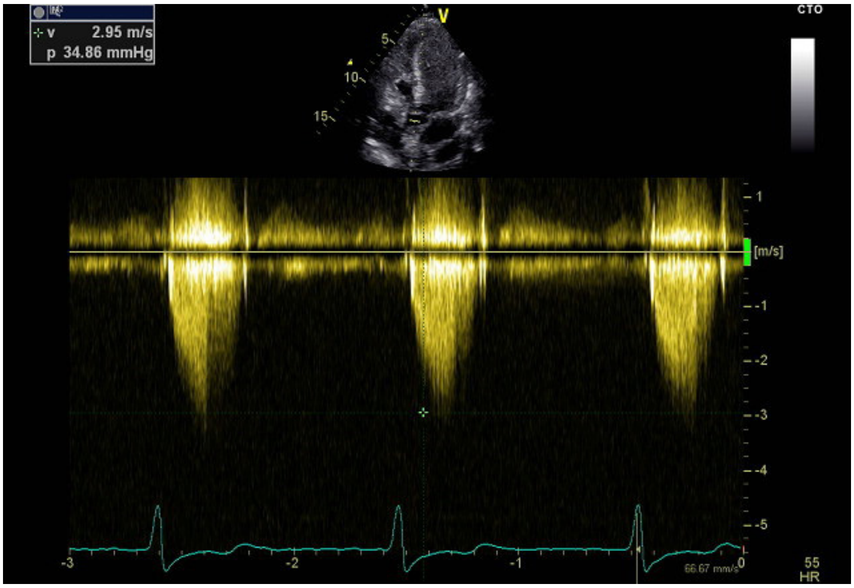

Figure S5 Left ventricular outflow tract obstructions relief after ablation.

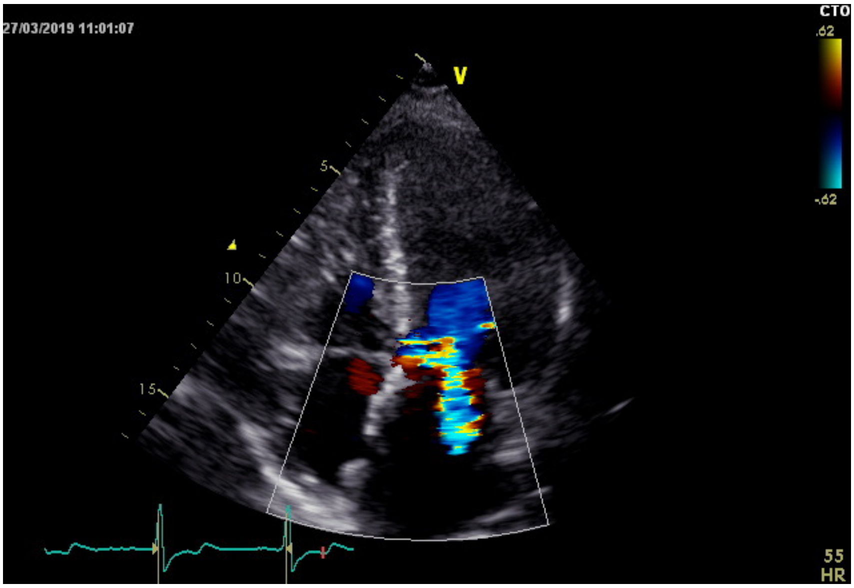

Figure S6 Mild mitral regurgitation before ablation.

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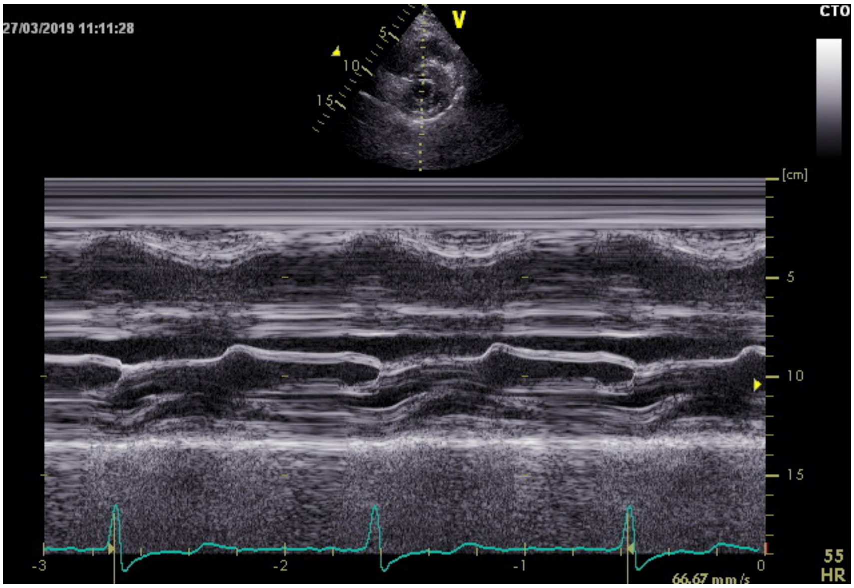

Figure S7 SAM sign relief after ablation. SAM, systolic anterior motion.

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