Acute and chronic effects of endocardial radiofrequency ablation of septal hypertrophy in HOCM

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Abstract

Introduction: Endocardial radiofrequency ablation of septal hypertrophy (ERASH) is an alternative to alcohol septal ablation (ASA) or surgical myectomy for hypertrophic obstructive cardiomyopathy (HOCM). Several studies have confirmed that septal radiofrequency ablation leads to a significant reduction in the left ventricular outflow tract gradient.

Objectives: We aimed to report the outcomes of 41 patients who underwent ERASH with a focus on severe complications.

Methods: Since 2004, 41 patients with HOCM (age: 58.2 ± 13 years) underwent ERASH at our institution. ERASH was performed, since ASA was ineffective (26 patients) or not possible (15 patients).

Results: The left ventricular outflow tract and the right ventricular septum were ablated in 26 and 15 patients, respectively. ERASH resulted in a significant reduction in acute gradient during the session and the results persisted during the 6-month follow-up (67% gradient reduction at rest and 73% after provocation, p = .0002). Pacemaker dependency after ERASH was 29% and pericardial tamponade occurred in two patients. In four patients, ERASH induced a paradoxical increase in obstruction (PIO), beginning suddenly at 30 min after the procedure and leading to lethal shock in one patient. PIO was not observed after ERASH from the right ventricular aspect.

Conclusion: Morbidity and mortality after ERASH were higher than those after ASA. PIO, a life-threatening complication, was observed in 9% of the patients. Our data indicate that ERASH might be considered in patients who are not candidates for surgical myectomy or ASA.

Keywords
alcohol septum ablation, endocardial radiofrequency ablation of septal hypertrophy, ERASH, HOCM, hypertrophic obstructive cardiomyopathy, TASH
1 INTRODUCTION

Surgical myectomy (SM) and alcohol septal ablation (ASA) are the standard invasive therapeutic options for reduction of the left ventricular outflow tract gradient (LVOTG) in drug-refractory hypertrophic obstructive cardiomyopathy (HOCM). Although the surgical approach is still considered the “gold standard” for treating HOCM,\(^1\) catheter-based treatment with ASA has been used increasingly due to its less invasive approach. Moreover, despite the lack of prospective randomized data on the comparison between SM and ASA, data from large hospital databases strongly suggest a lower in-hospital mortality after ASA when compared with SM.\(^2\) However, in up to 8% of the cases, ASA is not feasible due to unfavorable anatomy of the coronary septal branches.\(^3\) Therefore, we developed the concept of endocardial radiofrequency ablation of septal hypertrophy (ERASH) as an alternative treatment option for LVOTG reduction. It is independent of coronary anatomy and uses radiofrequency (RF) energy to ablate the septal target region directly from the left or the right ventricular cavity.\(^4,5\) Since our introduction in 2004, several other groups have confirmed that ERASH may lead to a significant and constant reduction in the LVOTG.\(^6–10\) However, most of the published studies included only a small number of patients.

2 OBJECTIVES

Little is known about the potential risks associated with ERASH. We report the outcomes of 41 patients treated with ERASH at our center, the largest cohort to date, with special consideration of the potential risks of the procedure.

3 PATIENTS AND METHODS

Since 2004, 41 patients with HOCM (Table 1) underwent ERASH at our institution due to ineffective ASA (26 patients) or unfavorable septal branch anatomy for ASA (15 patients). All patients refused to undergo SM and provided written consent to participate in the study. In all patients, LVOTG was measured using transthoracic echocardiography (TTE) at rest and after bicycle ergometry (5 min, 75 W). TTE, 6-min walking test, exercise, and 24-h Holter electrocardiogram were performed at baseline and after 6 months of follow-up. Cardiac enzyme release (creatine kinase, creatine kinase-MB, lactate dehydrogenase, and troponin I) was measured at baseline and on Days 1 and 2 after ERASH.

3.1 ERASH procedure

Ablation was performed using an irrigated tip catheter (Navistar\(^6,\) o-curve or F-curve; Biosense Webster, Inc.) and a steerable long 8F sheath (Agilis\(^6,\) small curve; St Jude) to improve catheter stability. We used a three-dimensional mapping system (CARTO\(^5\); Biosense Webster, Inc.) to visualize the septal bulge, ventricular cavity, and the bundle of His region. In addition, standard diagnostic electrophysiology catheters were placed in the right ventricle (RV), high right atrium, and the bundle of His positions for back-up pacing and provocation of post-pacing gradients (1 sensed ventricular extra at a cycle length of 380 ms) and to measure the atrioventricular nodal conduction times. Double pressure measurements of the LVOTG were performed using two 5F pigtail catheters in the left ventricular (LV) apex and in the ascending aorta. The catheter setup is shown in Figure 1. To localize the target region, we used the following technique. Initially, an LV angiogram and a CARTO map of the LV cavity were acquired. We then identified the zone of left ventricular outflow tract (LVOT) obstruction by pulling back the LV pigtail catheter. The ablation catheter was navigated to this area using a combination of CARTO guidance and fluoroscopy. In two cases, this was supported by intracardiac echocardiography (Figure 2). The power settings for RF ablation were empirically derived from experience with RF ablation of arrhythmias. The ablation protocol changed throughout the years, beginning with a lower maximum ablation power of 40 W in 2003 for the first three study patients and increasing it to 50 W for the following 10 patients (Table 2). To improve the effect of ablation, we changed the power protocol

| TABLE 1 Baseline characteristics of the study group |
|-----------------------------------------------|
| Mean ± standard deviation (range) |
| Age (years) | 58.70 ± 12.98 (31–84) |
| NYHA grade | 2.95 ± 0.21 (2,3) |
| Septal thickness (mm) | 21.58 ± 3.67 (15–30) |
| Resting gradient before ERASH (mmHg) | 65.05 ± 36.55 (7–143) |
| Provocable gradient (75 W bicycle ergometry) before ERASH (mmHg) | 152.31 ± 43.39 (50–230) |

Abbreviations: ERASH, endocardial radiofrequency ablation of septal hypertrophy; NYHA, New York Heart Association.
in 2006 to higher energy levels. In the last series of 28 patients, irrigated tip ablation was performed with a maximum power output of 75 W. If audible steam pops were noted, the ablation power was reduced by 10 W. A target zone of 2–3 cm² was treated by repeated ablation until a significant decrease (<2.5 mV) in the local electrogram at the tip electrodes of the mapping catheter was observed (Figure 3). Ablation of the bundle of His region was avoided. In cases of suspected difficulties in catheter stabilization (extremely narrowed LVOT, very high degree of obstruction), we performed septal ablation from the RV septum for safety reasons. In these cases, an RV CARTO map was acquired, and the opposite side of the septum was ablated adjacent to the area of LVOT obstruction. Procedural success was defined as a gradient reduction of at least 50% at rest and after provocation when compared with the baseline value.

### RESULTS

ERASH was feasible in all patients (cooled RF ablation, 22.8 pulses, 63.8 W). The procedural data are shown in Table 3. Significant myocardial enzyme release was detected on Days 2 and 3 after ERASH (Table 3). We ablated the LV aspect of the interventricular septum in 26 patients and the RV septum in 15 patients. ERASH resulted in a significant intraoperative LVOTG reduction (gradient at rest: 70.3 vs. 33.0 mmHg, after provocation with one extrasystole: 164.4 vs. 92.5 mmHg, p < .0001 for both). In all patients, the gradient at rest was significantly reduced (>50% reduction). However, in 20 patients, only a partial reduction in the LVOTG after provocation was achieved at the end of the session (35.3% reduction). After a 6-month follow-up, a further decrease in the LVOTG was observed (gradient at rest: 29.5 mmHg, after provocation: 67.3 mmHg, p < .0001 compared to baseline; Figures 4 and 5). There was no significant difference in the LVOTG after ablation from the LV aspect compared to that from the RV septal aspect (p > .05). LVOTG after ablation with high power (>60 W, exercise provoked gradient at 6 months follow-up: 65.3 ± 43 mmHg) did not differ significantly from that

| Table 2: Ablation protocol in patients with and without paradoxical increase of obstruction after endocardial radiofrequency ablation of septal hypertrophy (p > .05 for all) |
|-------------------------------------------------------------|
| **Number of patients** | **Maximum power (W)** | **Number of RF pulses (90 s)** | **Total RF time (min)** | **Irrigation flow (ml/min)** | **Audible steam pops (number of patients)** |
|------------------------|------------------------|-----------------------------|------------------------|-----------------------------|---------------------------------------------|
| Low-power Series 2003–2006 | 13 | 47.7 ± 4.4 | 29.4 ± 3.5 | 44.1 ± 14.3 | 0 |
| High-power Series 2006–2017 | 28 | 72.9 ± 5.4 | 19.4 ± 12.6 | 28.3 ± 19.4 | 11 |
| Patients with PIO | 4 | 69.2 ± 14.1 | 22.2 ± 13.5 | 33.4 ± 20.3 | 2 |
| Patients with severe PIO | 2 | 73.5 ± 7.7 | 11.0 ± 4.2 | 16.5 ± 6.4 | 1 |

Note: Data are presented as mean ± standard deviation, or frequency. Abbreviations: PIO, paradoxical increase of obstruction; RF, radiofrequency.
after ablation with low power (≤60 W, exercise-provoked gradient: 72.2 ± 51 mmHg, \( p > .05 \)).

The 6-min walking distance improved significantly during the follow-up (411.8 ± 26 vs. 466.2 ± 26 m, 13% improvement, \( p < .001 \)). Only four patients showed no improvement or deterioration during the 6-month follow-up compared to the baseline value. Three of these patients underwent successful SM. None of the patients died during the follow-up period.

## 5  COMPLICATIONS

A high-degree atrioventricular block with subsequent need for pacemaker (PM) implantation occurred in 12 patients (29%) after ERASH. In all cases, total heart block occurred during septal ablation despite careful monitoring of the His potential and the use of a three-dimensional mapping system (CARTO). All complete AV blocks were delayed during ablation without discernible His or left-bundle signals. No late total heart blocks were observed during the telemetric monitoring period of 7 days after ERASH. All patients who received permanent PMs were still PM-dependent after 6 months of follow-up. Two patients suffered from pericardial tamponade caused by perforation of the RV pacing catheter. One of these patients could be treated with pericardial drainage, while the other was treated surgically due to ongoing bleeding after pericardial drainage. In the latter patient, RV perforation caused by the PM lead was confirmed during the operation, while in the former patient, perforation was diagnosed using echocardiography. Both patients were in good condition at the 6-month follow-up. In four patients, ERASH induced a paradoxical increase in obstruction (PIO), beginning suddenly at approximately 30 min after the initial successful procedure (Figure 6). PIO led to an extreme narrowing of the LVOT in two patients, which could be visualized on transesophageal echocardiography. These
**FIGURE 5** Reduction in the left ventricular outflow tract gradients (mmHg) after provocation (5 min, 75 W bicycle)

**FIGURE 6** Course of obstruction after ERASH ergometry during the follow-up (patients with paradoxical gradient increase are indicated in red, †patient died) ERASH, endocardial radiofrequency ablation of septal hypertrophy
patients presented with a sudden, subtotal occlusion of the LVOT associated with an increased systolic anterior movement (SAM) of the anterior mitral valve leaflet, resulting in acute massive mitral regurgitation and a consequent reduction in the LV forward output (Figure 7). One patient died due to rapid cardiogenic shock despite the use of an Impella pump and emergency surgical mitral valve replacement. The decision of surgical mitral valve repair was made under the assumption of catheter-induced acute mitral valve injury. However, no damage to the mitral valve leaflets or papillary muscles could be observed during the surgery. Unfortunately, no autopsy was performed on this patient due to lack of consent. In the other patient, rescue use of the Impella pump and emergency SM (without reconstruction of the mitral valve) led to abrupt recovery and good results during the follow-up. In this patient, we started an anti-inflammatory medication (250 mg prednisolone intravenously, followed by 100 mg per day) until surgical treatment. Histopathological examination of the resected septum showed several small myocardial infarctions and discrete edema, but no hematoma. The differences between patients with and without PIO are shown in Tables 2 and 4, and Figure 8. The four patients with PIO

FIGURE 7 Rapid cardiogenic shock caused by complete occlusion of the left ventricular outflow tract by acute edema of the basal septum and severe systolic anterior motion of the mitral valve with severe mitral regurgitation. Rescue Impella implantation led to rapid normalization of systolic pressure.

| TABLE 4 | Differences between patients with and without paradoxical increase of obstruction after endocardial radiofrequency ablation of septal hypertrophy (p > .05 for all) |
|---------|-------------------------------------------------------------------------------------------------|
|         | No PIO (n = 37) | PIO (n = 4) |
| Age     | 55.75 ± 5.68   | 59.03 ± 13.55 |
| NYHA grade | 3.0 ± 0           | 2.95 ± 0.23 |
| Septal thickness | 21.00 ± 1.41      | 21.63 ± 3.84 |
| Left atrial diameter | 45.75 ± 4.35      | 44.62 ± 6.45 |
| Resting gradient on echocardiography before ERASH (mmHg) | 82.25 ± 50.12 | 65.21 ± 35.09 |
| Provoked gradient on echocardiography before ERASH (mmHg) | 65.21 ± 35.09 | 151.29 ± 44.77 |

Note: Data are presented as mean ± standard deviation. Abbreviations: ERASH, endocardial radiofrequency ablation of septal hypertrophy; NYHA, New York Heart Association; PIO, paradoxical increase of obstruction.
tended to be younger, with a higher degree of obstruction at baseline. In patients with PIO, the mean LVOTG was higher (82.2 ± 50 mmHg) compared to that in patients without PIO (65.2 ± 35 mmHg) \((p = .38)\). In all four patients, PIO occurred after ablation from the LV septal aspect and it was not observed in patients who underwent ERASH from the RV septal aspect. In both patients with severe PIO, ERASH was performed with a high power of 75 W. Out of the two patients with moderate PIO, one was treated with a maximum power of 50 W and the other was treated with a power of 70 W. An audible steam pop was recognized in one patient with severe PIO and in another patient with moderate PIO (Table 2).

6 | DISCUSSION

Patients with HOCM exhibiting symptoms refractory to negative inotropic drugs such as beta-blockers or verapamil are potential candidates for septal reduction therapy using SM or ASA. Studies directly comparing SM and ASA have usually been published from large centers with expertise in both the procedures.\(^{11,12}\) All of these studies were nonrandomized and retrospective in nature. Thus, they did not account for baseline differences in the treated population. The correlation between case volume and the morbidity and mortality associated with the procedure is much more pronounced with surgery.\(^{7}\) This is important since very few centers in the United States and Europe have such expertise in SM. Hence, ERASH has been developed as a nonsurgical alternative for LVOTG reduction in patients with failed ASA or with unfavorable coronary anatomy. To the best of our knowledge, 91 ERASH procedures have been reported in several single-center observational series.\(^{6-10,13}\) All of these studies demonstrated a significant reduction in the LVOTG, but were limited to small series of <19 patients. Our data support the efficacy of ERASH for the reduction of LVOTG and improvement in the clinical symptoms in a moderately sized patient population in which ASA failed or could not be performed. However, this series highlights the fact that ERASH may be an effective alternative for LVOTG reduction, but it is not a harmless procedure. The rate of PM implantation after ERASH in our series was approximately twice the rate expected after ASA.\(^{2}\) Importantly, the in-hospital mortality after ERASH (2.4%) was equal to that reported in a low-volume ASA center (2.3%) and more than three times the mortality at a high-volume center (0.6%).\(^{2}\) However, when compared with SM, the in-hospital mortality in our study group was still lower than that observed in high-volume surgical centers (3.8%).\(^{2}\) The occurrence of PIO associated with an acute increase in mitral regurgitation and subsequent rapid development of cardiogenic shock seems to be a specific complication of ERASH, which has not been described after ASA or SM. PIO occurred at approximately 30 min after a successful and uneventful ERASH procedure with a power of 75 W. Severe PIO, a life-threatening complication, was observed in two patients (4.8%, mild PIO in two patients). A similar case of lethal PIO-related cardiogenic shock was described by Seeram et al.\(^{7}\) in a 4-year-old girl who died despite extracorporeal membrane oxygenation after LVOT ablation with a power of 60 W. Cooper et al.\(^{8}\) reported a case of PIO after LVOT ablation with a power of 60 W, which was managed by RV pacing. Both of these authors assumed that ablation-related edema caused a significant swelling of the LVOT. The observation that severe PIO is noted only after high-power ablation (>60 W) might support this hypothesis. Septal edema has been described after ERASH in gadolinium-enhanced magnetic resonance studies.\(^{14}\) In one of our cases treated with acute SM, no damage to the mitral valve was observed. Thus, we also believe that PIO might be induced by myocardial edema at the site of ablation, leading to an acute increase in both LVOTG and traction of the mitral valve. This process in turn leads to an increase in regurgitation, further aggravating the hemodynamic situation. Transesophageal echocardiography during PIO

![FIGURE 8](image-url) Differences between patients with (yellow) and without (green) paradoxical increase of obstruction (PIO) after endocardial radiofrequency ablation of septal hypertrophy (\(p > .05\) for all)
revealed a dramatic increase in the SAM, leading to subtotal LVOT occlusion and acute mitral regurgitation without structural damage to the mitral valve apparatus by the ablation procedure (Figure 7). Rapid implantation of an Impella® pump in this setting appeared to improve the situation simply by pushing away the anterior mitral valve leaflet from the LV septum or bypassing the zone of obstruction. The SAM phenomenon and mitral regurgitation could be reduced instantaneously. However, Impella® explantation after a day led to severe PIO. In this patient, SM after Impella® replacement was performed on Day 3, leading to rapid recovery and good clinical results even after a 1-year follow-up.

7 | CONCLUSION

Our data indicate that ERASH can effectively reduce the LVOTG in HOCM. However, it might be associated with relevant complications. Therefore, ERASH should be reserved for patients who are not candidates for SM or ASA. Since a severe paradoxical increase in the LVOT gradients was observed only after high-power RF ablation, the maximal power used for ERASH should be limited to 60 W.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study was approved by the local ethics committee.

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