



## Přehledový článek | Review article

# Efficacy and safety of endocardial radiofrequency catheter ablation of interventricular septal hypertrophy in the treatment of hypertrophic obstructive cardiomyopathy

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### SOUHRN

Hypertrofická obstrukční kardiomyopatie je charakterizována ztluštěním stěn a zvětšením masy myokardu nedilatované levé komory srdeční bez vysvětlujících hemodynamických příčin a přítomnosti obstrukce ve výtokovém traktu levé komory. V minulosti byla invazivní nefarmakologickou metodou volby k redukcii septální hypertrofie chirurgická myektomie, kterou v devadesátých letech vystřídala alkoholová septální ablaci, nyní všeobecně užívaná, bezpečná a účinná metoda v redukci septální hypertrofie. Toto review se zabývá novou metodou používanou v redukci septální hypertrofie, kterou je endokardiální radiofrekvenční ablaci septální hypertrofie (ERASH). Naše práce shrnuje dosud publikované studie a srovnává jejich výsledky s jinými metodami redukce septální hypertrofie. ERASH se jeví jako srovnatelně účinná a bezpečná metoda jako alkoholová septální ablaci se srovnatelným poklesem gradientu ve výtokovém traktu levé komory a subjektivním zlepšením stavu pacienta charakterizovaným poklesem v třídě NYHA.

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### ABSTRACT

Hypertrophic obstructive cardiomyopathy is characterized by abnormal thickening or enlargement of the left ventricular myocardium mass of non-dilated left ventricle not explained solely by loading conditions and presence of obstruction in outflow tract of left ventricle. Surgical septal myectomy was the first choice method of invasive treatment of septal hypertrophy in the past which was replaced by alcohol septal ablation in the nineties of the 20th century and nowadays it is still worldwide used, safe, and effective method in reduction of septal hypertrophy.

This review introduces and describes new method in invasive reduction of septal hypertrophy which is endocardial radiofrequency ablation of septal hypertrophy. Our review summarizes all so far published studies and compares this new method with other methods of invasive reduction of septal hypertrophy.

Endocardial radiofrequency ablation of septal hypertrophy seems to be comparably safe and effective in comparison to alcohol septal ablation with comparable decrease of left ventricle outflow tract gradient and also subjective improvement of a patient characterized by NYHA class.

## Introduction

Hypertrophic obstructive cardiomyopathy (HOCMP) is characterized by abnormal thickening or enlargement of the left ventricular myocardium mass, and no hemody-

namic causes are present.<sup>1</sup> HOCMP is the most frequent genetically transmitted disease with an autosomal dominant pattern caused by >1500 known mutations in as many as 15 different cardiac sarcomere protein genes<sup>2</sup> in the adult population with a prevalence of 1 : 500.<sup>3</sup>

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In an adult, hypertrophic cardiomyopathy (HCM) is defined by a wall thickness of  $\geq 15$  mm in one or more left ventricle (LV) myocardial segments, as measured by any imaging technique and is not explained solely by loading conditions.<sup>1</sup> The obstructive form is characterized by obstruction of the LV outflow tract with a maximal gradient of  $\geq 30$  mmHg at rest and/or after provocative maneuvers.<sup>4</sup> Hemodynamically significant left ventricular outflow obstruction occurs in up to 25% of patients diagnosed with hypertrophic cardiomyopathy.<sup>5</sup> The obstructive form is often associated with the presence of systolic anterior motion (SAM) of the anterior leaflet of the mitral valve. Clinical diagnosis is determined by the detection of typical phenotypes (hypertrophic walls of the LV – most likely interventricular septum [IVS] – and nondilated cavity of LV). Interventricular obstruction caused by hypertrophy of the interventricular septum, elongated leaflets of the mitral valve, and abnormal papillary muscles are the main causes of clinical symptoms and subjective problems in patients, which commonly include dyspnea, stenocardia, palpitations, exertion syncope, or sudden cardiac death.

### Pharmacological treatment

Symptomatic pharmacological treatment is the basis of the HOCMP therapy. The symptomatology and the presence of left ventricle outflow tract gradient (LVOTG) are the main indicators of pharmacotherapy.<sup>1</sup> Generally, medicaments with negative inotropic effects help decrease myocardial oxygen consumption and prolong end-diastolic filling. The first choice of medication are beta-blockers, which help to decrease the exerted LVOTG. The second choice is likely verapamil, a non-dihydropyridine antagonist of calcium channels, with a positive effect on rest LVOTG. However, verapamil should be used carefully because of the possibility of the opposite effect of increasing gradient. Disopyramide and cibenzolin can also be used to decrease the gradient.<sup>1</sup> At present, the most perspective medication appears to be mavacamten, which has been proven by several studies that are currently afoot. Mavacamten is an experimental orally administered drug. It is a first-in-class, selective allosteric inhibitor of cardiac myosin, which reduces the number of myosin-actin cross bridges, thus, decreases the excessive contractility that is characteristic of hypertrophic cardiomyopathy. The clinical trial PIONEER-HCM with 21 symptomatic patients treated for 12 weeks with mavacamten resulted in a rapid and marked reduction in postexercise left ventricular outflow tract (LVOT) gradient,<sup>6</sup> which showed promise for future treatment.

### Non-pharmacological treatment

Interventional methods to reduce LVOTG are indicated in cases of persisting symptoms despite the maximum tolerated dose. The main indicators are an LVOT gradient  $\geq 50$  mmHg, moderate-to-severe symptoms (New York Heart Association [NYHA] functional class III–IV), and/or recurrent exertional syncope despite maximally tolerated

drug therapy. In some centers, invasive therapy is also considered in patients with mild symptoms (NYHA class II) who have a resting or maximum provoked gradient of  $\geq 50$  mm Hg (exercise or Valsalva) and moderate-to-severe SAM-related mitral regurgitation, atrial fibrillation (AF), or moderate-to-severe left atrial dilation.<sup>7</sup> Decrease in LVOTG is the main factor that determines mortality in total or eventual cardiovascular mortality. A decrease in LV outflow gradient after interventional procedure results in almost comparable mortality with the healthy population, independent of the interventional method used.<sup>1,8</sup>

The oldest method is surgical septal myectomy (Morrow procedure), which has been used since 1960s and is still considered a method of choice in the United States. The principle is resection of the hypertrophic part of the IVS to the papillary muscles bases with partial resection and mobilization.<sup>9</sup> Concomitant mitral valve surgery is required in 11–20% of patients undergoing myectomy.<sup>10</sup> Open heart surgery in extracorporeal circulation has a total mortality of <1–2% in the best cardiosurgical centers. The proportion of permanent pacemaker dependency after myectomy was 4.0%.<sup>11</sup>

Less invasive therapeutic methods, such as implantation of a dual-chamber pacemaker or defibrillator (PM/ICD DDD), were developed in 1970s.<sup>12</sup> The principle is the apical preexcitation effect, which is the shortening of the atrioventricular conduction interval. First, contraction of the apex and apical part of the IVS is present, while the basal parts of the IVS participate in LVOT narrowing and contract at the end of systole, which leads to improved ejection fraction of the left ventricle. Presently, this treatment is not used because it has no effect on LVOTG reduction.

In the case of a suitable coronary artery anatomy, it is possible to use alcohol septal ablation (ASA), which was first performed by Ulrich Sigwart in 1994.<sup>13</sup> It is the most recent method of interventional treatment for HOCMP. This catheter-based intervention relies on the injection of 96% alcohol into the septal branch of the left coronary artery to induce a small, controlled infarction of the hypertrophic septum and consequently abolishes the dynamic outflow obstruction. LVOTG decrease was correlated with a significant clinical improvement in the patient's symptomatology and left ventricular remodeling. The total mortality is less than 1% in tertiary centers. The survival of patients who undergo this procedure is comparable to that of a healthy population.<sup>1,8,14</sup> However, there is an increasing risk of temporary or permanent atrioventricular conduction block (20–50%).<sup>15</sup> Therefore, the number of implanted PMs (7–20%) is much higher than that of surgical myectomy, mainly in the presence of left bundle branch block. The risk of complete atrioventricular block increases with higher amounts of alcohol.<sup>16</sup> A total volume of 2 ml is generally safe. Higher doses of alcohol are slightly more effective in reducing LV obstruction and result in a higher incidence of peri-procedural complete heart block,<sup>17</sup> and other severe risks are potential developing defects of the interventricular septum. Therefore, ASA should be indicated in cases of IVS thickness  $>15$  mm as recommended by American guidelines in 2011<sup>18</sup> and  $>16$  mm as recommended by European guidelines in 2014.<sup>1</sup> After the procedure, reduction of LVOTG significantly de-

creased total mortality, which is likely comparable to the healthy population.<sup>14,19</sup> However, in 10–15% of patients, ASA could not be performed because of unsuitable coronary artery anatomy.<sup>20</sup>

The percutaneous septal cryothermal catheter ablation procedure was also tested as an alternative to treating septal hypertrophy in 2005 in three patients with a mean age of 38.15 years. Acute procedural success, defined as a significant reduction (>50%) in the LVOT gradient at the end of septal cryoablation, was achieved in two of the three cases with no subjective improvement of symptoms at six-month follow-up. All three procedures were well tolerated with no major adverse cardiovascular/cerebrovascular events.<sup>21</sup> Although authors believe that there may be a considerable potential for cryoablation as an alternative percutaneous treatment strategy for septal hypertrophy, there have been no other larger studies to prove it.

MitraClip is rarely used as a treatment for HOCMP due to the restriction of the anterior leaflet motion in the vicinity of the LVOT, thereby reducing SAM-septal contact and mitral regurgitation. The first use of MitraClip for HOCMP was reported in a patient who had previously undergone surgical myectomy with residual SAM and mitral regurgitation<sup>22</sup> with a significant reduction of LVOTG. Several procedures have been performed, and one case was complicated by tamponade requiring pericardiocentesis. Recently, this method has been used for a highly selected group of patients and is not mentioned in the guidelines.

In addition, the thermal effects of high-intensity ultrasound (HIFU) have been investigated to develop HIFU as an ablative treatment of cardiac arrhythmias, mainly atrial fibrillation ablation.<sup>23</sup> The closed-chest transthoracic approach with successful ablations performed up to 9 mm in size in the intraventricular septum of live canines has been tested recently.<sup>24</sup> Recently, this method has been investigated and not yet used in the clinics.

A study using a new method, percutaneous intramyocardial septal radiofrequency (PIMSRA), was also published in 2018 by Liu et al.<sup>25,26</sup> The aim of this study was to prove that PIMSRA is less invasive, comparably safe, and effective method as endocardial radiofrequency ablation of septal hypertrophy (ERASH). Fifteen consecutive patients with HOCMP were enrolled in this study. The procedure was performed under general anesthesia in the left lateral decubitus position with temporary pacing used in all cases. A radiofrequency electrode needle was inserted via a percutaneous intramyocardial approach to hypertrophied IVS under transthoracal echocardiography control, and radiofrequency ablation was applied until LVOTG decreased to <30 mmHg or when the area of necrosis reached 30–40 mm wide around the short axis of the IVS. One pericardial tamponade occurred due to coronary vein injury. Follow-up was done after 6 months with a significant decrease of baseline resting gradient of  $83.3 \pm 32.4$  mmHg and provoked of  $147.8 \pm 58$  mmHg to resting post-ablation gradient of  $11.8 \pm 5.7$  mmHg and provoked of  $25.5 \pm 11.4$  mmHg. PIMSRA has been shown to be a safe and effective method with a significant hemodynamic and symptomatic involvement. The enrollment of patients will continue due to the authors.

## Endocardial radiofrequency ablation of septal hypertrophy

Radiofrequency ablation has been discovered as an alternative approach in recent years. The first series of patients treated with ERASH were published by Lawrenz et al. in 2004.<sup>27</sup> ERASH has been shown to be a highly effective and safe invasive method for the treatment of septal hypertrophy. The principle of the procedure is percutaneous catheter radiofrequency ablation of the hypertrophic part of the interventricular septum from the left and/or right ventricle via the retrograde (via the femoral artery and aorta) or transseptal (via inferior vena cava, right atrium, and left atrium) approach. First, patients were ablated in a standard manner, and recently, with different 3D electroanatomical mapping systems and intracardiac ultrasound (ICE) or transesophageal echocardiography (TEE). The method is safe, with minimum risk of coronary artery damage and a lower risk of conduction disorders. The procedure can be repeated in case of failure.

The first experience (published in 2004) using the endocardial radiofrequency ablation method was provided by Lawrenz et al. on three symptomatic patients with HOCMP.<sup>27</sup> The procedure in the first two patients was performed via a transseptal approach with no success in reducing the LVOT gradient, probably due to instability of the catheters. The third patient, who is a 45-year-old man, suffered from severe symptoms of NYHA class III due to HOCMP. During the procedure, the retrograde approach was applied using only fluoroscopy and a cooled-tip ablation catheter was used. The procedure successfully led to a decrease in LVOTG from the baseline resting gradient of 107 to 53 mmHg and provoked gradient of 210 to 144 mmHg, and decreased left ventricle septal thickness. These results likely led to the belief that ERASH could be a promising alternative to the ASA procedure.

Six years later, Lawrenz et al. published probably the largest retrospective study including 19 patients aged  $60 \pm 12$  years with HOCMP meeting the inclusion criteria of LVOT resting or provoked gradients of >50 mmHg and severe symptoms despite maximal adequate medication.<sup>28</sup> The first five patients had been treated via the right ventricle approach, and with more experience, switched to the LV approach. In total, the left ventricular septum was ablated in nine patients and the right ventricular septum was ablated in 10 patients. A retrograde transaortic approach was used for LV ablation and an inferior vena cava approach for RV ablation. Transseptal puncture was performed in one patient. All procedures were performed using the CARTO electroanatomic mapping system and an irrigated-tip ablation catheter. Significant reduction of resting LVOTG from  $77.7 \pm 30$  mmHg to  $26.5 \pm 22$  mmHg and provoked LVOTG reduction from  $157.5 \pm 37$  mmHg to  $64.2 \pm 44$  mmHg was achieved. After six months, there was a significant improvement of NYHA functional class from 3.0 to  $1.6 \pm 0.7$ . The six-minute walking distance significantly improved by 58 m. During RF ablation, complete heart block occurred in four patients (21%). All patients received a dual-chamber pacemaker. One patient had an acute tamponade during RV ablation, which required surgical revision. This study has shown promising gradient reduction after the procedure and subjective improve-

ment of symptoms. However, all enrolled patients were severely affected, including many with previously failed ASA. The question of whether an LV or RV approach is more appropriate remains questionable.

Case reports on septal hypertrophy in patients with HOCMP were performed by Emmel et al.<sup>29</sup> on two child patients. The first patient is a 5-year-old boy with progressive hypertrophic obstructive cardiomyopathy and increasing symptoms despite appropriate pharmacologic therapy and the second patient is an 11-year-old girl with symptoms of tiredness and peak instantaneous LVOT gradient of 80 and 90 mmHg. Ablation was performed via a retrograde approach using an irrigated-tip ablation catheter, LocaLisa 3D electroanatomical navigation system, fluoroscopy, and continual monitoring of TEE. The procedure performed in the first patient was complicated by two episodes of ventricular fibrillation which required cardioversion. No further complications were observed. Follow-up echocardiography performed 5 days later revealed a residual left ventricular outflow gradient of 25 mmHg, which had diminished further to less than 20 mmHg after six weeks. In small children in whom selective cannulation of the target septal artery and controlled myocardial necrosis without permanent sequelae of AV block have not previously been reported, ERASH seems to be a very promising alternative. Therefore, there was no risk of ventricular fibrillation in this case.

A larger retrospective ERASH study was performed later in 2011 by Sreeram et al.<sup>30</sup> in 32 children using an irrigated-tip ablation catheter performed via the retrograde approach. Fluoroscopy and CARTO mapping systems were used as basic imaging methods during LocalLisa and TEE. The LVOT gradient improved directly after the procedure and at follow-up (3–144 months). The median pre-procedure pullback gradient was 80 mmHg (range: 10–130 mmHg, mean: 78.5±26.2) and decreased to 34 mmHg (range: 10–90 mmHg, mean: 36.1±16.5,  $p <0.01$ ), and one patient died because of paradoxical increase in LVOT obstruction requiring ECMO; in two cases, a permanent pacemaker was needed due to an AV block.

In 2015, there were more studies on ERASH published. Shelke et al.<sup>31</sup> published a retrospective study on seven patients with unappropriate coronary artery anatomy for ASA. The procedure was performed with an irrigated-tip ablation catheter by a retrograde approach using CARTO or EnSite NavX, and ICE was used. The mean baseline LVOT gradient was 81±14.5 mmHg, which was reduced to 48.5±22.6 mmHg in 1 month, 49.8±19.3 mmHg in 6 months, and 42.8±26.1 mmHg in 12 months. Symptoms improved in at least one NYHA functional class in one patient. Only transient pulmonary edema occurred immediately after the procedure.

Next, radiofrequency ablation of septal hypertrophy HOCMP study using the CARTOsound navigation system was published by Cooper et al. in 2015.<sup>32</sup> In this retrospective study, five patients were included in 6-month follow-up. Five successive patients underwent CARTOsound-guided RFA using ICE and contact force equipped irrigated-tip ablation catheter, which was performed via a retrograde approach. In one patient, the transseptal approach was used. Eighty percent were female, with a mean age of 59 (44–79) years. All patients had a resting or exercise provoked LVOT gradient >50 mmHg associated with sig-

nificant SAM. All patients had NYHA class III dyspnea. As the 6-month follow-up, three patients had improved from NYHA class III to II and one patient had improved from NYHA class III to I. Average peak resting gradients improved from 64.25±50.60 to 12.25±2.50 mmHg. Valsalva- or exercise-induced gradient improved from 93.50 (+30.88) to 23.25 (+8.30) mmHg. There were also other echocardiography and MRI parameters measured, with a significant improvement. Severe complications were observed in one patient, which is retroperitoneal hemorrhage during sheath removal. Urgent surgical repair of the right femoral artery was initially successful, but a secondary bleed within 24 h led to mesenteric ischemia and patient death. One patient developed an increasing LVOT gradient, which led to pulmonary edema during the procedure, but the patient recovered well. No AV block was observed. It seems obvious that the use of integrated technologies such as the CARTO mapping system and ICE allows accurate delivery of RF energy to the basal septum, and a small area of myocardial injury delivered by RFA at a specific location may lead to successful treatment of LVOT gradients of HOCMP.

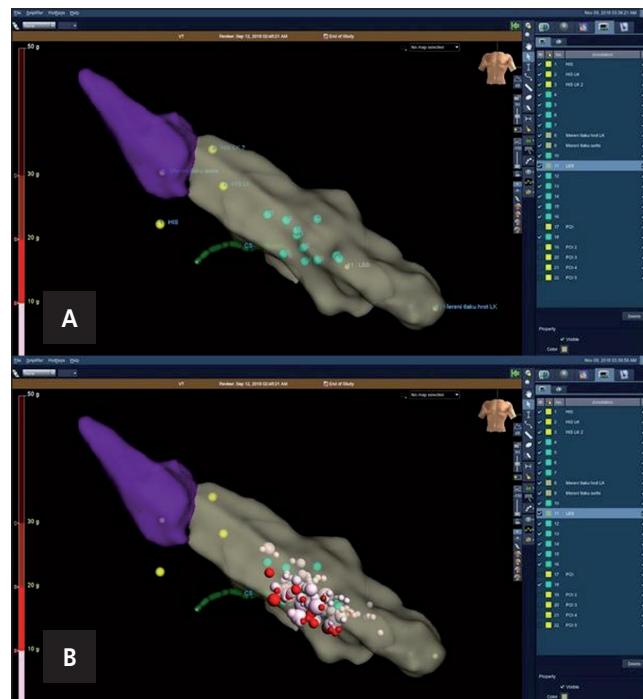
The next study was published in 2016 by Crossen et al.<sup>33</sup> Eleven consecutive symptomatic patients aged 50–81 years with HCOMP and LVOT gradient >50 mmHg were reported. One patient had undergone prior septal myectomy, and three patients had undergone prior ASA procedure. Patients were ablated under general anesthesia via the transseptal approach using the EnSite NavX mapping system and standard fluoroscopy, which was performed by an irrigated-tip ablation catheter. Follow-up was performed at 12 months, and mean resting gradient was reduced from 66.7 mmHg to 10 mmHg. The mean provable gradient was reduced from 136.2 to 20.0, and NYHA functional class has improved from class 3.0 to 1.8±0.8. Two patients required permanent pacemaker placement because of a complete AV block. In this protocol, a dual-chamber pacemaker was implanted in each patient immediately after the procedure.

In 2018, Beaser et al.<sup>34</sup> published another study with five pilot patients with the aim of comparing ERASH with the disopyramide effect. During the procedure, the LV septum was ablated via transseptal access using ICE. The mean baseline resting gradient was 65.6±37.8 mmHg and was reduced to 10.4±10.6 mmHg at one- and three-month follow-up, respectively. These promising results provided a basis for larger prospective randomized trials comparing ERASH to disopyramide.

The most recent clinical case report of a patient with septal hypertrophy managed by ERASH was published in 2020 by Peigh et al.<sup>35</sup> The aim of this case report was to prove the efficacy and safety of the ERASH procedure. ICE and electroanatomical mapping systems were used, and ablation was performed using the retrograde approach. In 4-month follow-up, the peak LVOT gradient was 4 mmHg. The patient's basal septal wall thickness decreased from 2.07 cm on his pre-procedure TTE to 1.80 cm on 4-month postprocedure with improvement of subjective symptoms.

## Discussion

Endocardial radiofrequency ablation is a well-known and accepted method of treating cardiac arrhythmias. It

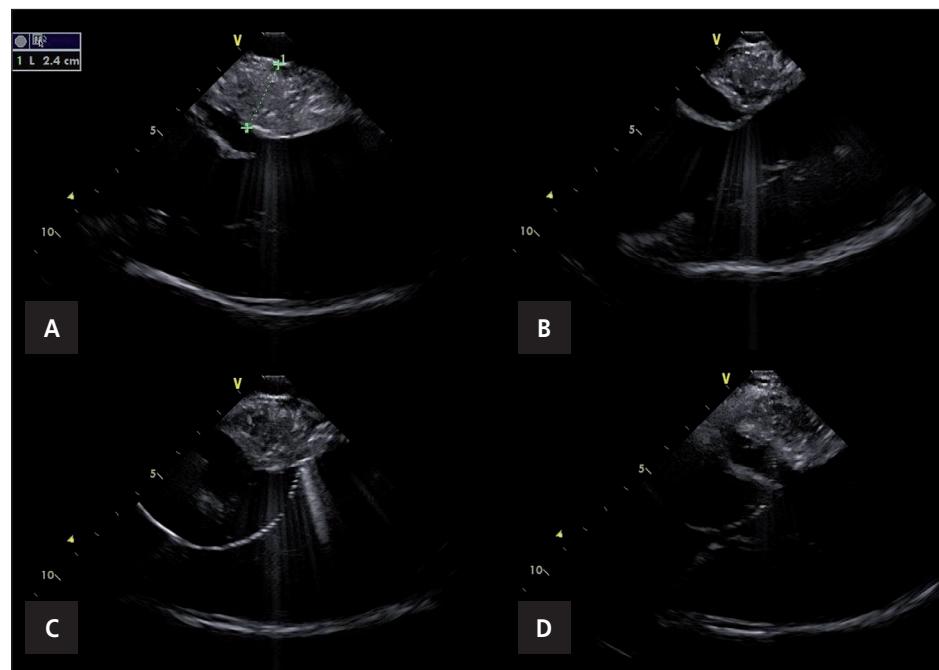


**Fig. 1 – 3D electroanatomical map of the left ventricle and aorta; EnSite Precision system, anteroposterior view. (A) Localization of the atrio-ventricular conduction system (yellow points, HIS); septum hypertrophy – blue points. (B) Display of ablation points on the hypertrophic septum; contact force ablation catheter Tacticath – pink and red points.**

seems to be a promising method for the treatment of patients with HOCMP by radiofrequency ablation of septal hypertrophy, which leads to a decrease in LVOTG.

Since 2004, nine studies using the radiofrequency ablation method to reduce LVOTG due to septal hypertrophy have been published. A total of 100 patients, including 35 children, underwent ERASH. Two patients underwent previous septal myectomy, and 16 patients had previous ASA. During the procedure, only irrigated-tip ablation catheter was used.

Ablation of septal hypertrophy was performed from the left to the right ventricle using an alternating trans-septal and retrograde approach. In 2004, only fluoroscopy has been used; from 2005, additional navigation systems such as 3D electroanatomical mapping systems (Fig. 1), transesophageal echocardiography (TEE), and intracardiac echocardiography (ICE) (Fig. 2) were utilized. From periprocedural complications, two deaths (2%) were reported due to heart failure secondary to pulmonary edema from paradoxical increase of LVOTG. The other mortality was caused by retroperitoneal hemorrhage leading to acute surgery which was caused by sheaths removal which is seen rarely during radiofrequency catheter ablation procedures. Eight permanent pacemakers (8%) were implanted because of permanent AV block. In a study by Crossen, five patients had bundle branch block patterns before ablation, and five developed intraventricular conduction delays postprocedure. Therefore, two patients required pacing support for complete AV block.



**Fig. 2 – Intracardial echocardiography (ICE) images during hypertrophic obstructive cardiomyopathy (HOCMP) catheter ablation. ICE probe is situated in the right ventricle, you can see interventricular septum (IVS), left ventricle (LV), left ventricle output tract (LVOT), septal leaflet of the mitral valve and left atrium. (A) Measurement of the septal hypertrophy, (B) septal anterior movement (SAM), septal leaflet of the mitral valve is pressed against hypertrophy septum during early systole and obturates LVOT, (C) ablation catheter on the hypertrophic septum, catheter is introduced transseptally and tip of the catheter is resting on the apical part of the septal hypertrophy region, (D) position of the tip of the ablation catheter on the septum hypertrophy more basally near the aortic valve. The situation after several ablations in this region. Under the surface of the septum in the vicinity of the catheter tip you can see several finished radiofrequency ablation lesions (white regions).**

A significant decrease in resting or provoked LVOTG of usually >50% was seen in all follow-up cases compared to baseline values. The potential mechanisms for gradient reduction are not clear and may be related to several factors including reduction of septal thickness, a focal reduction of motility-localized myocardial scar at the contact point with the mitral valve anterior leaflet and interventricular septum, reduced myocardial motion of the hypertrophied septum,<sup>35</sup> and not significantly reduced septal thickness after ERASH (1.3 mm). Therefore, a significant decrease in the LVOT gradient could be only due to a localized reduction of endo-myocardial tissue in contact point. However, this contact point presented was the main mechanism of the dynamic obstruction of LVOT. RF septal ablation does not reduce the LVOT gradient primarily through significant thinning of the septum, but rather through hypokinesis or akinesis of the ablated region.

Yang et al. described 82 patients who underwent ERASH and found that the average decrease in resting LVOTG was 58.8 mmHg. The average decrease in LVOTG in the Euro-ASA registry was 51 mmHg and 64 mmHg in the Mayo myectomy study. There seems to be no significant difference. Subjective symptom relief for ERASH was described by NYHA class decrease from class III to class II. According to a meta-analysis comparing ASA versus septal myectomy, the difference between the efficacy of both in LVOT gradient reduction seems comparable. There is a small, yet significantly higher residual LVOTG among the ASA group patients as compared with the septal myectomy group patients. In addition, functional status was comparable between the two methods.<sup>36</sup>

There was a decreasing tendency of AV block and pacemaker dependency after using electroanatomical mapping systems and ICE. The primary location of the His conduction tissue helps to avoid damage to the atrioventricular conduction, which is a potential advantage of ERASH. The incidence of permanent pacemaker implantation was 6.9%. On the other hand, ASA requires implanted permanent pacemaker after procedure in 12% according to the Euro-ASA registry<sup>17</sup> and 3.9–4% for myectomy.<sup>37</sup> There is a question about the influence of previous ASA on AVB during ERASH, which is not mentioned in separate studies. The highest incidence of AVB III was observed in the study with the highest number of previous ASA (Lawrenz 2011, Crossen 2016), but definitive evidence for this idea requires a larger, randomized study. Septal myectomy entails removal of sub-endocardial tissue in the anterior septum containing the left bundle branch fibers, which increase the risk of LBBB compared with SA. Given these considerations, patients with pre-existing RBBB are more likely to require a permanent pacemaker after SA. On the other hand, those with LBBB are more likely to need pacing after ASA according to our experiences with previous ASA with subsequent RBBB. RBBB and LAH also lead to a higher risk for AVB.<sup>38</sup>

ERASH also has similar mortality from reported studies (2%) compared to ASA, which ranges between 1–4%<sup>36</sup> and 1–2% after myectomy.<sup>38</sup> Therefore, ERASH promises to have comparable safety with septal myectomy and ASA.

## Limitations

All studies published so far are observational studies with small sample size and including children. These studies were conducted usually after failure of other invasive therapeutic methods or due to unsuitable coronary artery anatomy. In particular, the presence of a previous ASA could lead to a higher complication rate, mainly AV conduction disturbances.

## Conclusion

The results of several previous studies show that ERASH seems to be an efficient and safe interventional therapeutic method for HOCMP comparable to ASA. The potential advantage of this method is the lower risk of subsequent atrioventricular conduction injury and the repeatability of the ERASH procedure. However, comparably to ASA there is only a small number of patients so far. Euro-ASA registry with amount of 1275 patients shows rate of 2.42 deaths per 100 patients, in case of ERASH was 2 deaths per 100 patients so far. One death was caused by perioperative retroperitoneal bleeding caused by removal of sheaths which is a rare complication of catheter ablation procedure in general, and the second death caused by LV dysfunction with paradoxical increase of LVOTG is not quite explained, but may be associated for example with hypovolemia or different conditions during procedure and perioperative oedema of tissue of hypertrophic septum after ablation. Incidence of perioperative atrioventricular conduction damage and pacemaker implantation do not seem to be higher than during ASA so far.

But still it is necessary to conduct a more extensive study focused on safety of this new method. Efficacy seems to be proved, but safety is a key factor for clinical use of this method. We need to be careful and prove ERASH safety with bigger studies with a higher number of participants, including randomized controlled studies comparing well-accepted methods such as ASA. It is possible there will be also a learning curve to be passed even for experienced operators. Recently there are no data about learning curve and comparing of the learning curve for ERASH and ASA.

## Conflicts of interest

All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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