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Myectomy versus alcohol septal ablation in patients with hypertrophic obstructive cardiomyopathy

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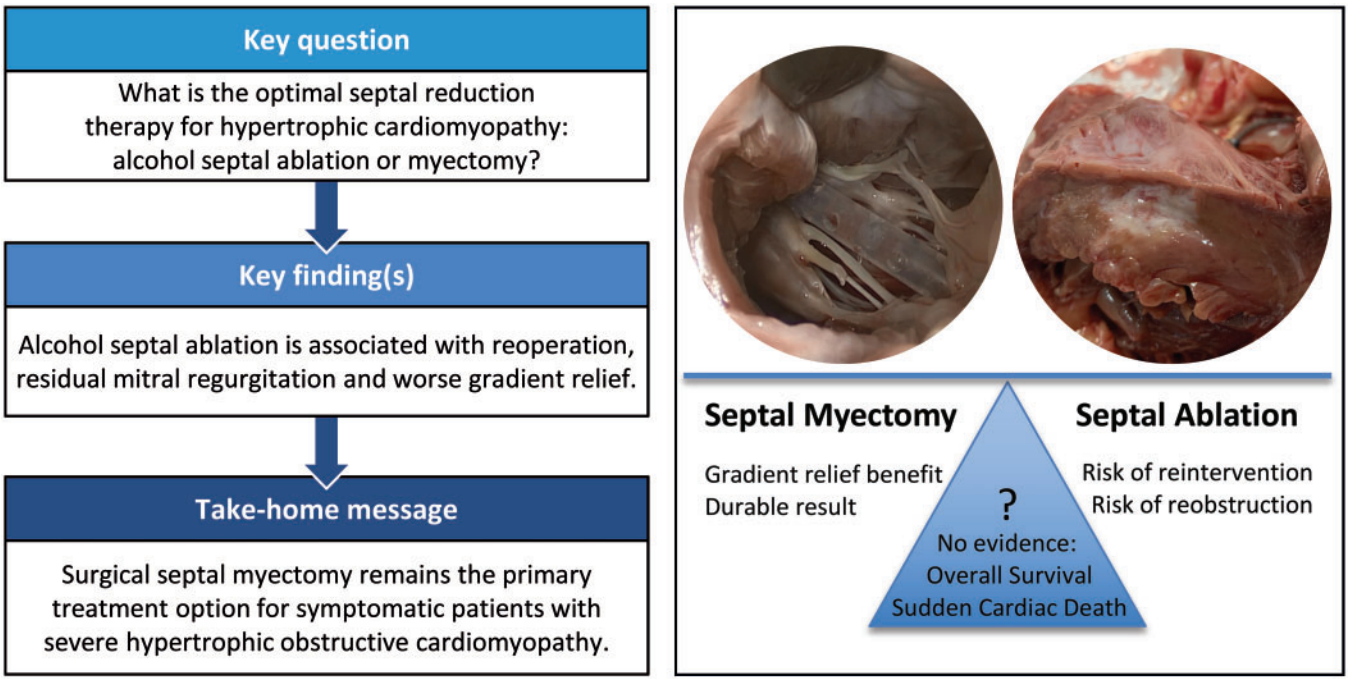

Abstract

OBJECTIVES: There is very little evidence comparing the safety and efficacy of alcohol septal ablation versus septal myectomy for a septal reduction in patients with hypertrophic obstructive cardiomyopathy. This study aimed to compare the immediate and long-term outcomes of these procedures.

METHODS: Following propensity score matching, we retrospectively analysed outcomes in 105 patients who underwent myectomy and 105 who underwent septal ablation between 2011 and 2017 at 2 reference centres.

Presented at the 33rd Annual Meeting of the European Association for Cardio-Thoracic Surgery, Lisbon, Portugal, 3–5 October 2019.

RESULTS: The mean age was 51.9 ± 14.3 and 52.2 ± 14.3 years in the myectomy and ablation groups, respectively ($P = 0.855$), and postoperative left ventricular outflow tract gradients were 13 (10–19) mmHg vs 16 (12–26) mmHg; $P = 0.025$. The 1-year prevalence of the New York Heart Association class III–IV was higher in the ablation group (none vs 6.4%; $P = 0.041$). The 5-year overall survival rate [96.8% (86.3–99.3) after myectomy and 93.5% (85.9–97.1) after ablation; $P = 0.103$] and cumulative incidence of sudden cardiac death [0% and 1.9% (0.5–7.5), respectively $P = 0.797$] did not differ between the groups. The cumulative reoperation rate within 5 years was lower after myectomy than after ablation [2.0% (0.5–7.6) vs 14.6% (8.6–24.1); $P = 0.003$]. Ablation was associated with a higher reoperation risk (subdistributional hazard ratio = 5.9; 95% confidence interval 1.3–26.3, $P = 0.020$). At follow-up, left ventricular outflow tract gradient [16 (11–20) vs 23 (15–59) mmHg; $P < 0.001$] and prevalence of 2+ mitral regurgitation (1.1% vs 10.6%; $P = 0.016$) were lower after myectomy than after ablation.

CONCLUSIONS: Both procedures improved functional capacity; however, myectomy better-resolved classes III–IV of heart failure. Septal ablation was associated with higher reoperation rates. Myectomy demonstrated benefits in gradient relief and mitral regurgitation elimination. The results suggest that decreasing rates of myectomy procedures need to be investigated and reconsidered.

Keywords: Hypertrophic cardiomyopathy • Alcohol septal ablation • Surgical myectomy

ABBREVIATIONS

ASA	Alcohol septal ablation
CI	Confidence interval
HCM	Hypertrophic cardiomyopathy
HR	Hazard ratio
IQR	Interquartile range
IVS	Interventricular septum
LVOT	Left ventricular outflow tract
MR	Mitral regurgitation
NYHA	New York Heart Association
SAM	Systolic anterior motion
SHR	Subdistributional hazard ratio
SM	Septal myectomy

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a common genetic cardiovascular disease with a 1 in 500 prevalence in the general population [1] with a global burden in at least 122 countries with populations exceeding 500 000 [2]. HCM involves symptoms of chronic heart failure, with some patients complaining of palpitations and/or chest pain at rest or during exertion; however, most people are asymptomatic [3]. In the absence of randomized trials [4], initial drug therapy with non-vasodilating β-blockers, disopyramide, or verapamil is usually administered to reduce the left ventricular outflow tract (LVOT) obstruction and improve functional capacity. If patients are in the New York Heart Association (NYHA) functional class III–IV with an LVOT gradient >50 mmHg despite maximum tolerable medical therapy, invasive septal reduction therapy is indicated [1, 3]. Previously, the standard surgical procedure for HCM was septal myectomy (SM) (Morrow procedure). According to a recent review, SM offers better LVOT gradient resolution [5] than alcohol septal ablation (ASA). Nevertheless, the SM procedure is disappearing in Western countries, giving way to less invasive procedures. In North America, the annual rate of SM decreased by 24.5% between 2003 and 2011, and the rate of ASA increased by 56.2% [6]. Although ASA was introduced more than 20 years ago as a feasible alternative to SM, there are still no randomized trials comparing SM and ASA. When researchers compare SM and ASA in a non-randomized study, selection bias is always present. Thus, we aimed to compare the long-term outcomes of SM and ASA in 2 reference centres and used propensity score matching to identify groups with similar background covariates that need to be controlled.

PATIENTS AND METHODS

In this retrospective database study involving propensity score analysis, we investigated 345 consecutive patients who underwent SM for obstructive HCM at Meshalkin National Research Center and 150 consecutive patients who underwent ASA at Sverdlovsk Regional Hospital #1 between 2011 and 2017. The present study was conducted in compliance with the Declaration of Helsinki. All patients received optimal preoperative medical therapy comprising non-vasodilating β-blockers and/or calcium-channel blockers. The inclusion criteria were as follows: age ≥18 years, interventricular septum (IVS) thickness ≥15 mm (on echocardiography) and instantaneous peak Doppler LVOT pressure gradient ≥50 mmHg. This retrospective study was approved by the Institutional Review Board on 6 November 2018 (88.3-PP-19); the need for obtaining individual patient consent was waived because of the retrospective nature of the study.

After 1:1 propensity score matching, the study cohort included 105 patients in each group (Fig. 1). The primary endpoint was overall survival. The secondary endpoints were cumulative reoperation or reintervention rate, residual and recurrent LVOT gradient, residual mitral regurgitation (MR), rate of permanent pacemaker implantation, functional capacity 1 year after the procedure, and cumulative incidence of sudden cardiac death. Patient follow-up examinations were scheduled at 6 and 12 months postoperatively, and annually thereafter. The last follow-up was performed by phone in March 2019.

SURGICAL PROCEDURES

Surgical septal myectomy

The aorta was cross-clamped, and a cold crystalloid cardioplegic solution (Custodiol® HTK Solution; Dr. Franz Köhler Chemie GmbH, Alsbach-Hähnlein, Germany) provided myocardial protection with an antegrade root flow. A transverse aortotomy exposed the septum. Transaortic extended myectomy was performed in all cases using the operative technique previously described by Morrow and modified by Messmer [7, 8]. When necessary, myectomy was combined with coronary artery bypass

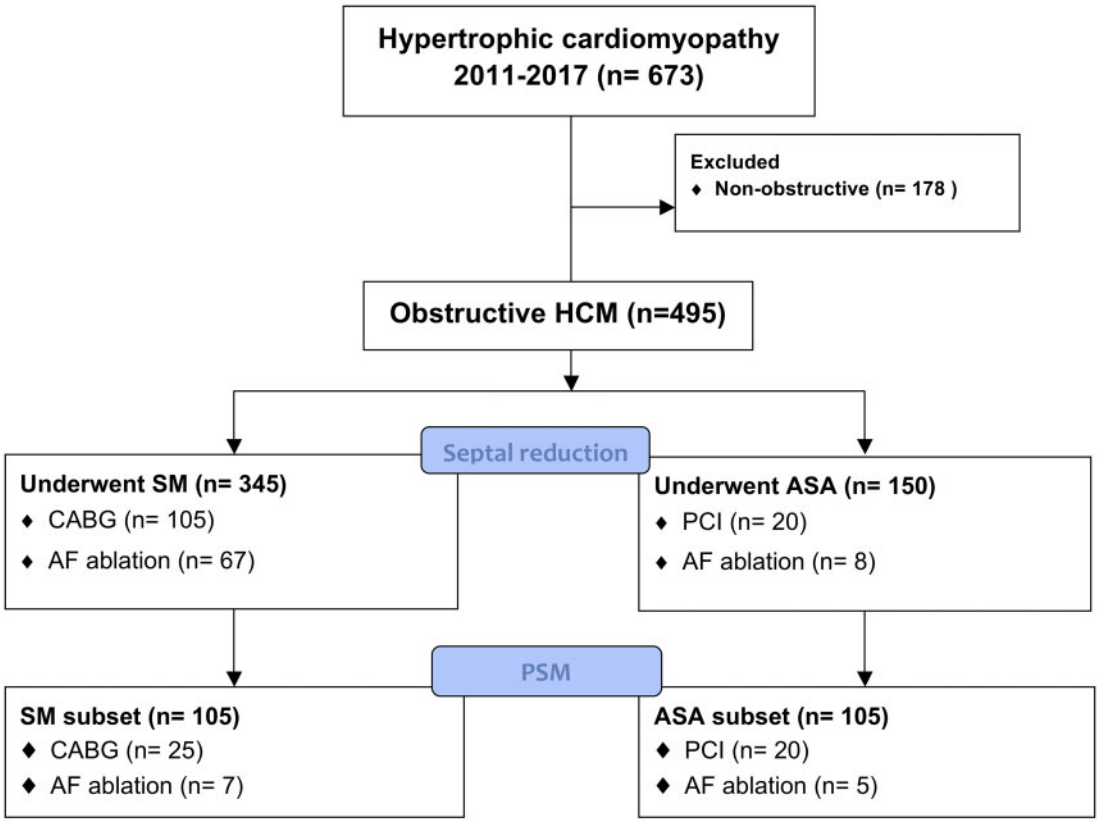

Figure 1: Patient enrolment flowchart. AF: atrial fibrillation; ASA: alcohol septal ablation; CABG: coronary artery bypass grafting; HCM: hypertrophic cardiomyopathy; PCI: percutaneous coronary intervention; PSM: propensity score matching; SM: septal myectomy.

grafting or surgical ablation for atrial fibrillation. To assess residual MR, systolic anterior motion (SAM) syndrome and LVOT obstruction after surgery, intraoperative transoesophageal echocardiography was used.

Alcohol septal ablation

The ASA technique is described in the Supplementary Material. Briefly, the tightness of the balloon occlusion was assessed by injecting dye into the septal branch. Intraoperative transoesophageal echocardiography was performed to evaluate the perfusion zone of the target septal perforator. The gradient had to be reduced by at least 50% during the 'occlusive test' for ablation. When this was achieved, 3 ml of ethanol was infused slowly for 3–5 min. Then, the balloon was flushed with contrast dye. Ethanol was applied for 5 min. On achieving the target haemodynamic effect, the procedure was terminated. When necessary, ASA was combined with percutaneous coronary intervention or catheter ablation for atrial fibrillation before/after ASA.

Statistical analysis

Statistical analysis was performed using STATA version 13.0 (StataCorp LP, College Station, TX, USA). The Shapiro–Wilk test was used to test the normality of continuous variables. Continuous data were presented as mean ± standard deviation for variables with normal distribution and median (25–75th percentile) for variables with non-normal distribution. Categorical data were described as absolute numbers and relative frequencies. Before propensity score matching, the 2 groups were compared using the independent samples *t*-test (normal distribution) or the Kolmogorov–Smirnov 2-sample test (non-normal distribution) for continuous variables, and Pearson's χ^2 test with an $(N\text{-}1)/N$ correction factor for categorical variables. After propensity score matching, between-group differences were compared using the paired *t*-test or the Wilcoxon signed-rank test for continuous variables, and McNemar's test for categorical variables. Using multiple logistic regression analysis, a propensity score was calculated for each patient, defined as the probability that the patient received SM. The baseline variables included in the propensity score analysis are listed in *Table 1*. The nearest neighbour approach, without replacement, and 5-to-1 digit-matching was used to identify 1:1 matched patients (Caliper 0.1). The balance between variables before and after matching was assessed in terms of percentage standardized bias (reported as a percentage). The Kaplan–Meier method was used to evaluate overall survival, and results were presented with 95% confidence intervals (95% CIs). Survival curves were compared using a stratified log-rank test for matched pairs. Baseline variables, including age, sex, NYHA class III–IV, moderate or severe MR, left ventricular ejection fraction, IVS thickness and LVOT gradient were evaluated to identify the predictors of a high LVOT gradient (>50 mmHg) after ASA, and multivariable analysis was performed using logistic regression models. Risks of sudden cardiac death and reintervention were analysed using a competing risk proportional hazard model (Fine and Gray method). The inclusion criterion for the full regression model was $P \leq 0.200$ or clinical significance, and the limit for stepwise backwards elimination was $P < 0.100$. The results of the competing risk regression analysis were

Table 1: Baseline characteristics of septal myectomy and alcohol septal ablation groups before propensity score matching

Covariates before matching	SM ($n = 345$)	ASA ($n = 150$)	Bias (%)	P-value
Age (years)	55.0 ± 13.4	50.7 ± 14.6	30.7	0.001
Male, *n* (%)	155 (44.9)	72 (48.0)	-6.1	0.529
PM/ICD, *n* (%)	9 (2.6)	3 (2.0)	4.0	0.686
NYHA class III–IV, *n* (%)	222 (64.3)	71 (47.3)	36.6	<0.001
AF, *n* (%)	67 (19.4)	8 (5.3)	43.7	<0.001
AH, *n* (%)	206 (59.7)	81 (54.0)	12.7	0.193
CAD, *n* (%)	105 (30.4)	20 (13.3)	41.5	<0.001
DM, *n* (%)	33 (9.6)	7 (4.7)	19.1	0.066
MR 2+, *n* (%)	255 (73.9)	36 (24.0)	115.0	<0.001
LVEF (%)	71.1 ± 8.2	70.9 ± 8.0	2.9	0.769
PG (mmHg)	83 (70–96)	57 (38–84)	48.8	<0.001
IVS (mm)	24 (22–27)	22 (19–26)	39.4	<0.001

AF: atrial fibrillation; AH: arterial hypertension; ASA: alcohol septal ablation; CAD: coronary artery disease; DM: diabetes mellitus; ICD: implantable cardioverter-defibrillator; IVS: interventricular septum; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; NYHA: New York Heart Association; PG: instantaneous peak Doppler left ventricular outflow tract pressure gradient; PM: pacemaker; SM: septal myectomy.

expressed as subdistribution hazard ratios (SHRs), with respective 95% CIs. A P-value of <0.05 was considered statistically significant.

RESULTS

Before propensity score matching

Baseline demographic and echocardiographic data are presented in *Table 1*. Before propensity score matching, SM was related to older age (55.0 ± 13.4 vs 50.7 ± 14.6 years), NYHA class III–IV (64.3% vs 47.3%), moderate or severe MR (73.9% vs 24.0%), higher instantaneous peak Doppler LVOT pressure gradient [83 (interquartile range, IQR 70–96) mmHg vs 57 (IQR 38–84) mmHg] and thicker IVS [24 (IQR 22–27) mm vs 22 (IQR 19–26) mm]. The ASA group had a significantly lower proportion of patients with atrial fibrillation (5.3% vs 19.4%) and coronary artery disease (13.3% vs 30.4%).

The non-matched groups (ASA vs SM) did not differ in terms of hospital mortality rate (0% vs 1.7%; $P = 0.104$) and incidence of permanent pacemaker implantation during the early postoperative period (12.0% vs 10.1%; $P = 0.540$). There were 5 (1.4%) and 4 (2.7%) early complications ($P = 0.352$) that required intervention/surgery in SM and ASA groups, respectively. Iatrogenic ventricle septal defects ($n = 3$, 0.9%) and left ventricular free wall ruptures ($n = 2$, 0.6%) were successfully treated intraoperatively in the SM cohort. In ASA cohort, right coronary artery thrombosis, requiring percutaneous intervention ($n = 1$, 0.7%), the left main dissection, requiring bypass grafting ($n = 1$, 0.7%) and femoral pseudoaneurysm, requiring early surgical intervention ($n = 2$, 1.3%), were observed. The non-matched groups (ASA vs SM) did not differ in terms of 5-year overall survival [93.6% (95% CI 87.6–96.8%) vs 96.5% (95% CI 93.6–98.2%); log-rank test $P = 0.712$; Supplementary Material, Fig. S1], or cumulative incidence of sudden cardiac death within 5 years (0% vs 1.4%; 95% CI 0.3–5.3%; log-rank test $P = 0.337$; Supplementary Material, Fig. S2). SM was neither associated with all-cause mortality [hazard ratio, HR = 1.15 (95% CI 0.2–2.5); $P = 0.713$] nor sudden cardiac death [SHR = 1.9 (95% CI 0.2–17.8); $P = 0.570$].

Residual LVOT pressure gradient measured by transthoracic echocardiography before discharge was significantly higher in the ASA group than in the SM group [16 (IQR 12–26) mmHg vs 14 (IQR 11–19) mmHg; $P = 0.004$]. Nevertheless, there were 21 (14.0%) and 4 (1.2%) patients in the ASA and SM groups ($P < 0.001$), respectively, who underwent reoperation. Cumulative reoperation rates within 5 years were 1.2% (95% CI 0.4–3.1%) and 15.3% (95% CI 10.1–22.9%) in the SM and ASA groups, respectively ($P < 0.001$, Supplementary Material, Fig. S3). Therefore, ASA was associated with significantly higher reoperation rates, with an SHR of 9.3 (95% CI 2.5–35.0, $P = 0.001$, Supplementary Material, Table S1).

After propensity score matching

Baseline characteristics with minimal standardized bias in the 2 propensity score-matched groups are presented in *Table 2*. The mean age (51.9 ± 14.3 vs 52.2 ± 14.3 years, $P = 0.855$), the proportion of NYHA class III–IV (53.3% vs 54.3%, $P = 0.891$), rate of moderate or severe SAM-mediated MR (33.3% vs 34.3%, $P = 0.855$), LVOT gradient [78 (IQR 63–90) vs 72 (IQR 48–90) mmHg, $P = 0.642$] and IVS thickness [23 (IQR 21–26) vs 23 (IQR 20–27) mm, $P = 0.630$] did not differ between the SM and ASA groups.

Early outcomes. There were no in-hospital deaths after ASA, while 1 patient (1.0%) died after SM due to myocardial infarction ($P = 1.000$). Nine (8.6%) patients in the SM group required permanent pacemaker implantation postoperatively, including 8 (7.6%) with complete atrioventricular block and 1 (1.0%) with sinus node dysfunction after surgical ablation for atrial fibrillation. There were 10 (9.5%) patients with complete atrioventricular blocks after ASA, and there were no differences in the need for permanent pacemaker implantation between matched groups ($P = 1.000$).

In general, both SM and ASA resulted in significant decreases in LVOT pressure gradient and MR severity between presurgery and discharge. Nevertheless, SM demonstrated benefits in SAM-mediated MR elimination: only 1 (1.0%) patient had residual moderate MR, and there were no patients with residual severe MR after surgery. However, 12 (11.4%) patients in the ASA group were discharged with residual MR ($P = 0.006$), including 1 patient (1.0%)

Table 2: Baseline characteristics of septal myectomy and alcohol septal ablation groups after propensity score matching

Covariates	SM (n = 105)	ASA (n = 105)	Bias (%)	P-value
Age (years)	51.9 ± 14.3	52.2 ± 14.3	-2.7	0.855
Male, n (%)	57 (54.3)	55 (52.4)	3.8	0.783
PM/ICD, n (%)	1 (1.0)	2 (1.9)	-8.0	0.563
NYHA class III–IV, n (%)	56 (53.3)	57 (54.3)	-2.0	0.891
AF, n (%)	7 (6.7)	5 (4.8)	8.2	0.554
AH, n (%)	56 (53.3)	58 (55.2)	-3.9	0.783
CAD, n (%)	25 (23.8)	20 (19.1)	10.4	0.403
DM, n (%)	8 (7.6)	5 (4.8)	9.7	0.393
MR 2+, n (%)	35 (33.3)	36 (34.3)	-2.2	0.885
LVEF (%)	70.6 ± 7.4	70.8 ± 8.3	-3.6	0.787
PG (mmHg)	78 (63–90)	72 (48–90)	4.8	0.642
IVS (mm)	23 (21–26)	23 (20–27)	7.7	0.630

AF: atrial fibrillation; AH: arterial hypertension; ASA: alcohol septal ablation; CAD: coronary artery disease; DM: diabetes mellitus; ICD: implantable cardioverter-defibrillator; IVS: interventricular septum; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; NYHA: New York Heart Association; PG: instantaneous peak Doppler left ventricular outflow tract pressure gradient; PM: pacemaker; SM: septal myectomy.

with severe MR (P = 1.000). Furthermore, the LVOT gradient after SM was lower than that after ASA [13 (IQR 10–19) mmHg vs 16 (IQR 12–26) mmHg; P = 0.025]. Only 1 (1.0%) and 7 (6.7%) patients in the SM and ASA groups, respectively, had residual LVOT obstruction with a pressure gradient >50 mmHg (P = 0.077) at discharge. The ASA group multivariable logistic regression analyses identified the preoperative LVOT gradient as the only factor associated with residual LVOT gradient >50 mmHg after ASA with odds ratio 1.03 (95% CI 1.01–1.05, P = 0.018, Supplementary Material, Table S2). In these cases, non-vasodilating β-blockers, titrated to a maximum tolerated dose, were administrated to reduce heart failure symptoms and improve functional capacity, and dynamic evaluation was selected over reoperation.

Follow-up data. The follow-up was complete (clinical follow-up or death) in 97.1% of patients. The mean follow-up duration was 61.8 ± 36.2 months. Four and 12 deaths occurred in SM and ASA groups, respectively. In the SM group, 2 deaths occurred after thromboembolism complications, and sudden cardiac death occurred in 2 cases (6 and 7 years after SM). Causes of late death in the ASA cohort were sudden cardiac arrest (n = 3), myocardial infarction (n = 2), thromboembolic complications (n = 2), non-cardiac complications (n = 2) and unknown (n = 3). The 5-year overall survival rates were 96.8% (95% CI 86.3–99.3%) and 93.5 (95% CI 85.9–97.1%; P = 0.103, Fig. 2) and cumulative incidence of sudden cardiac death within 5 years was 0% and 1.9% (95% CI 0.5–7.5%; P = 0.797, Fig. 3) in the SM and ASA groups, respectively. The HR for risk of death was 1.8 (95% CI 0.5–5.7; P = 0.353) and SHR for the competing risk of sudden cardiac death after ASA was 0.8 (95% CI 0.1–8.5; P = 0.868).

Both procedures improved functional capacity; however, the prevalence of NYHA class III–IV among survived matched patients was significantly higher in the ASA group 1 year postoperatively [6 (6.4%) vs 0 (0%); P = 0.041]. The overall incidence of new-onset atrial fibrillation among survived matched patients was 6 (6.4%) and 9 (9.6%) in the SM and ASA groups, respectively (P = 0.606).

Significantly more ASA patients required reoperation (Supplementary Material, Table S3; 14.3% vs 1.9%; P = 0.004).

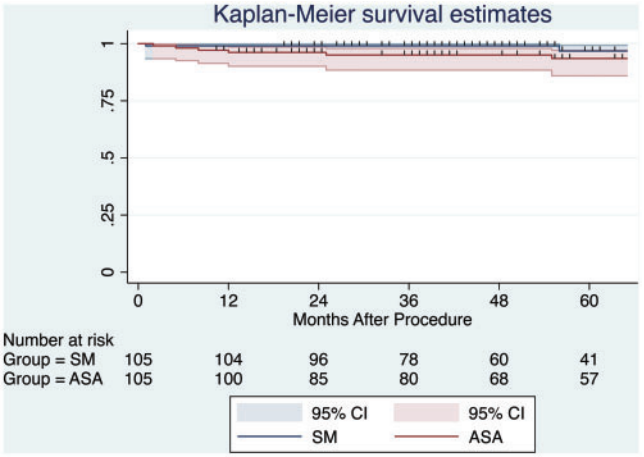

Figure 2: Overall survival in propensity score-matched groups (SM vs ASA). ASA: alcohol septal ablation; CI: confidence interval; SM: septal myectomy.

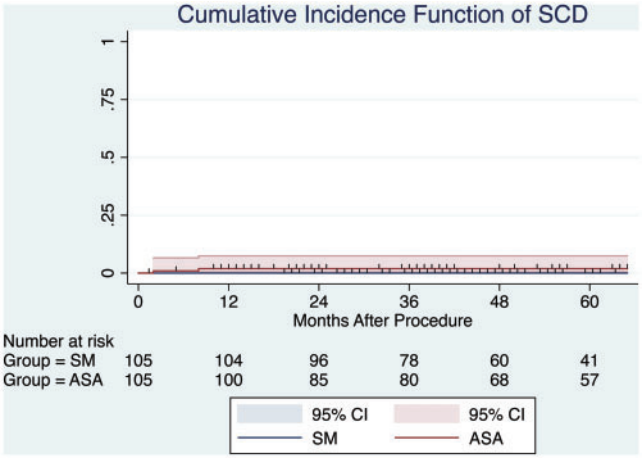

Figure 3: Cumulative incidence of sudden cardiac death within 5 years in propensity score-matched groups (SM vs ASA). ASA: alcohol septal ablation; CI: confidence interval; SCD: sudden cardiac death; SM: septal myectomy.

Cumulative reoperation rates within 5 years were 2.0% (95% CI 0.5–7.6%) and 14.6% (95% CI 8.6–24.1%) in SM and ASA groups, respectively (P = 0.003, Fig. 4). Competing-risks regression analysis (Supplementary Material, Table S4) confirmed that ASA was associated with reintervention (SHR = 5.9; 95% CI 1.3–26.3, P = 0.020).

Echocardiographic follow-up results were available in 86% of patients (87 SM, 94 ASA). Therefore, 81 matched pairs were analysed. Residual LVOT gradients after SM and ASA were 16 (IQR 11–20) and 23 (IQR 15–59) mmHg, respectively (P < 0.001). At the last follow-up, there was a significantly higher rate of residual LVOT gradient >30 mmHg in the ASA group (5.7% vs 40.4%; P < 0.001). The rate of LVOT obstruction (>50 mmHg) was higher in the ASA group (27.7% vs 1.1%, P < 0.001). There were higher rates of residual SAM-mediated MR grade 2 or greater in the ASA group (10.6% vs 1.1%; P = 0.016).

DISCUSSION

The main finding of our study was that freedom from reoperation and LVOT gradient relief was superior after SM; although,

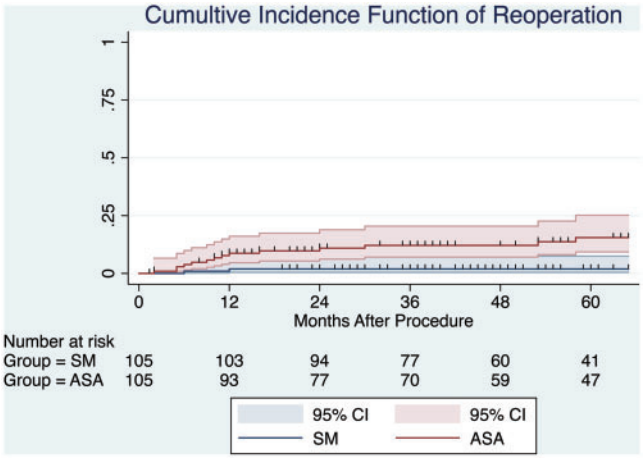

Figure 4: Cumulative incidence of reoperation within 5 years in propensity score-matched groups of patients stratified according to the choice of septal reduction therapy (SM vs ASA). ASA: alcohol septal ablation; CI: confidence interval; SM: septal myectomy.

overall survival and freedom from sudden cardiac death did not differ between groups. Functional capacity, in terms of NYHA class improvement, favoured SM 1 year after treatment.

Survival

Whether ASA or SM is more beneficial for long-term survival remains unclear. Previously, Noseworthy *et al.* [9] detected an increased risk of life-tethering ventricular arrhythmias in patients with a high residual gradient after ASA. Additionally, in a large international multicentre cohort study, Vriesendorp *et al.* [10] concluded that sudden cardiac death risk was significantly higher after ASA (HR = 2.1) than after SM. According to ten Cate *et al.* [11], ASA was also an independent predictor of cardiac death and aborted sudden cardiac death for ventricular tachycardia/fibrillation (unadjusted HR = 5.2, propensity-score adjusted HR = 6.1). Nevertheless, a recently published systematic review and meta-analysis [5, 12], conducted on retrospective cohort studies, found similarly low rates of long-term mortality. A single-centre study from Mayo Clinic reported that SM was associated with a significant survival benefit compared with ASA among unadjusted patients [13]. The difference was explained by the fact that unadjusted ASA patients were older and more likely to have comorbidities. After propensity matching, there was no significant difference in overall survival. However, patients in the SM group in our study were older with comorbidities. Additionally, our cohort was relatively young compared to the Mayo group (52 vs 65 years). We did not find benefits in survival rate or sudden cardiac death rate in either the unadjusted or matched groups. Steggerda *et al.* [14] found that overall survival after ASA and SM was comparable, and age was the only independent predictor of all-cause mortality. Considering the low event rates after both SM and ASA, an adequately powered randomized trial comparing the long-term benefits of SM and ASA is never feasible [15]. Thus, future prospective non-randomized studies accessing long-term outcomes would be a good alternative.

Permanent pacemaker implantation

The main non-fatal complication after septal reduction therapy was a complete atrioventricular blockage. According to a US nationwide inpatient database [6], the need for permanent pacemaker insertion after SM was 9.8%, and it varied based on hospital volume (8.9–13.8%; $P < 0.001$). However, undergoing ASA in a lower-volume centre was not associated with worse outcomes (pacemaker implantation) compared with that of high-volume centres (11.5%). In our study, events occurred in 8.6–9.5% of patients, which is consistent with the in-hospital rate of pacemaker implantation after SM and ASA in high-volume (tertiary) hospitals. Findings from the Poon *et al.* [5] systematic review showed that ASA was associated with an increased likelihood of permanent pacemaker implantation (odds ratio 3.1, $P < 0.001$) and varied between 2.4% and 12.5% in SM and 1.7–22.0% in ASA. A Dutch meta-analysis [12] also emphasized that patients had more than twice the risk of pacemaker implantation after ASA (10.0%; 95% CI 7.8–12.1%) compared to that after SM (4.4; 95% CI 2.6–6.2%; $P < 0.001$). Authors from the Mayo Clinic [13] recently reported a four-fold higher rate of permanent pacemaker implantation after ASA (17.4%) compared with that after SM (3.9%). The authors suggested that lower risk of pacemaker insertion after SM reflects the surgical experience and is possible in other dedicated HCM centres. In our study, ASA was not associated with higher atrioventricular-block risk requiring pacemaker implantation. We suspect that this due to the learning curve for SM. The pacemaker implantation rate after SM in our practice has decreased significantly over the years to 3.1% [16]. The risk of pacemaker implantation should be taken into consideration at the time of the selection of optimal septal reduction therapies.

Gradient relief

In this study, both SM and ASA were considered effective and resulted in significant LVOT gradient reduction post-procedure. This was consistent with the results of Liebregts *et al.* [12]. We observed significantly higher postoperative LVOT pressure gradients after ASA compared to that after SM. Steggerda *et al.* [14] reported post-procedure LVOT gradients of 12 (8–20) mmHg after SM and 10 (0–20) mmHg after ASA ($P < 0.001$); however, they emphasized that gradients were evaluated using different modalities, the invasive measurement for ASA and transoesophageal echocardiography for SM, and therefore, such comparisons were not applicable. Nevertheless, during follow-up, resting and provoked echocardiographic gradients were higher after ASA than SM. Our findings are consistent with the propensity score-matched study by Nguyen *et al.* [13], where more complete LVOT gradient relief was observed after SM. Moreover, authors found that the early follow-up gradient in ASA patients was strongly related to preoperative gradients and suggested that ASA may not adequately relieve LVOT obstruction in patients with high (>40 mmHg) preoperative resting LVOT gradient [13]. We also demonstrated the relationship between baseline LVOT gradient and residual LVOT gradient (>50 mmHg) after ASA. Nevertheless, there were no significant differences in residual LVOT obstruction with >50 mmHg gradient between groups at discharge. The high residual gradient is regarded as a failure of the initial procedure and is a clear indication for reintervention in patients with residual symptoms. Both a recent systematic

review [5] of the Mayo Clinic data [13] and our study have reported a more complete LVOT gradient resolution following SM. We found that during follow-up, residual LVOT gradient increased from 21.4 (18.4–24.3) mmHg to 42.2 (35.5–48.0) mmHg after ASA, and the number of patients with LVOT obstruction >50 mmHg increased from 6.7% to 27.7%. However, there were no negative trends in haemodynamic results after SM. Despite the immediate LVOT gradient and symptom relief obtained after ASA, high LVOT gradients may recur long-term. This should be considered when initial therapy is selected. Moreover, Quintana *et al.* [17] revealed that patients who undergo SM following a previously unsuccessful ASA are at an increased risk of preoperative diastolic dysfunction and arrhythmias and postoperative complete heart block.

Reoperation

In their meta-analysis comparing 16 SM cohorts and 11 ASA cohorts, Liebregts *et al.* [12] reported a higher need for reintervention after ASA (7.7%) compared to that after SM (1.6%) ($P = 0.001$). One limitation of this analysis was that SM patients were treated earlier than 1990 (13 out of 16 studies), and ASA patients were treated after 1990 (9 out of 11 studies). A systematic search conducted by Poon *et al.* [5] based on the best evidence articles published in the last 2 decades also found that the rate of reintervention was significantly higher following ASA. An updated meta-analysis by Osman *et al.* [18] (including 40 observational studies comparing long-term outcomes of ASA and SM) reported that the need for reoperation was significantly higher after ASA (11.6% vs 1.5%; $P < 0.001$).

Although at least 3 previously published systematic reviews and meta-analyses confirmed evidence that SM provides more durable results in terms of a lower need for repeat septal reduction, all studies had limitations, such as inherently different baseline characteristics in SM and ASA cohorts, analyses conducted on cohort data instead of individual patient data, and differing enrolment periods. Therefore, the interpretation of these results must be undertaken with caution.

Since the last systematic reviews and meta-analyses were published [18], only one study has reported long-term outcomes after SM and ASA [13]. This study was unique for several reasons. It was the first analysis based on a relatively large prospectively maintained database with propensity score matching to identify ASA and SM groups with similar preoperative characteristics. They observed overall reinterventions rates of 1.0% after SM and 35.0% after ASA (HR = 33.3). This finding is consistent with our report, with a 1.9% reoperation rate after SM and 14.3% after ASA (HR = 7.0). Most patients in the Nguyen *et al.* [13] study underwent SM after failed ASA, while in our series, most patients underwent ASA again after unsuccessful ASA. This discrepancy may be explained by referral bias. In the Nguyen *et al.* [13] single-centre study, patients were referred to the same clinic for SM after failed ASA, and that may have already provided more durable outcomes. However, in our 2 centre study, most patients, after unsuccessful ASA, were not referred for SM given that a dedicated SM centre was 1500 km far. In fact, in our study, all consecutive patients referred to Meshalkin Center during the study period were scheduled for SM, whereas all consecutive patients referred to Sverdlovsk Hospital underwent ASA. Therefore, in contrast to the results reported by Nguyen *et al.* [13], our results are more likely to be limited by referral, rather than by selection bias.

Finally, it is important to note that patients with failed ASA, referred for SM, may have an increased risk of cardiac death, advanced heart failure, and implantable cardioverter-defibrillator discharges. This supports SM as the preferred treatment option for septal reduction [17].

Limitations

The present study had several limitations. Although data were collected prospectively, our findings were limited by confounding factors and bias associated with retrospective studies. In addition, our study was limited by a relatively small sample size after matching; therefore, the study may be underpowered to detect differences in primary and secondary clinical outcomes. Using the propensity score analysis, we sought to minimize the effects of these factors. Propensity score matching restricts the SM cohort to ASA patients with similar baseline data; therefore, the cohort may not represent typical SM/ASA patients. Finally, our cohort may not be representative one because of national, selection and referral biases.

CONCLUSION

The findings of our analysis suggest that SM eliminates LVOT obstruction and SAM-mediated MR more effectively, as well as providing longer freedom from reoperation in HCM patients. Additionally, ASA is associated with higher reoperation rates. Our findings suggest that the disappearance of SM needs to be investigated due to its benefits over ablation.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

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Author contributions

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