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Periprocedural, Short-Term, and Long-Term Outcomes of Alcohol Septal Ablation in Patients with Hypertrophic Obstructive Cardiomyopathy: A 20-Year Single-Center Experience

ORIGINAL INVESTIGATION

ABSTRACT

Background: Alcohol septal ablation is recommended for hypertrophic obstructive cardiomyopathy patients who had refractory symptoms despite optimal medical treatment. We compared the periprocedural, short-, and long-term clinical outcomes and mortality predictors in hypertrophic obstructive cardiomyopathy patients who underwent alcohol septal ablation.

Methods: Hypertrophic obstructive cardiomyopathy patients aged ≥18 years (63 females and 71 males) who underwent alcohol septal ablation were included. The primary endpoint was all-cause mortality.

Results: The mean patient age was 60.0 (standard deviation 13.7) years. The median follow-up time was 13 (7.6-18.5) years. During the procedure, 9, 2, and 1 patients developed ventricular fibrillation, remote site myocardial infarction, and pericardial tamponade, respectively, but none died. One patient died during hospitalization. During the long-term follow-up, 17, 5, 20, and 8 patients developed heart failure, myocardial infarction, chronic atrial fibrillation, and non-fatal stroke, respectively, and 24 died. There was no significant difference between the sexes (all $P > .05$). Age (hazard ratio = 0.69, 95% CI = 0.61–0.78, $P < .001$), body mass index (hazard ratio = 1.20, 95% CI = 1.04-1.40, $P = .01$), age at diagnosis (hazard ratio = 1.57, 95% CI = 1.34-1.78, $P < .001$), and time from diagnosis to ablation (hazard ratio = 1.57, 95% CI = 1.35-1.84, $P < .001$) predicted all-cause mortality. In Kaplan–Meier curves, long-term all-cause mortality was similar in men and women (P[log-rank] = .43).

Conclusion: Alcohol septal ablation has similar short- and long-term outcomes for both sexes in hypertrophic obstructive cardiomyopathy patients. Risk factors for long-term mortality were age, body mass index, diagnosis age, and time delay to operation. Therefore, alcohol septal ablation timing is essential for better clinical outcomes. Our findings may contribute to the increased performance of alcohol septal ablation in hypertrophic obstructive cardiomyopathy patients in our country.

Keywords: Alcohol septal ablation, hypertrophic obstructive cardiomyopathy, outcomes, sex

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease.[1] In the absence of predisposing conditions, a left ventricular wall thickness of ≥15 mm indicates HCM.[2] Approximately one-third of patients do not have left ventricular outflow tract (LVOT) obstruction. In the rest, LVOT obstruction causes symptoms, systolic anterior movement of the mitral valve, and changes in ventricular geometry. Additionally, systolic and diastolic dysfunction, myocardial ischemia, and atrial arrhythmias also contribute to patients' symptoms.[3,4]

Septal reduction therapy (alcohol septal ablation and surgical myectomy) is recommended in hypertrophic obstructive cardiomyopathy (HOCM) patients with refractory symptoms despite optimal medical treatment.[5,6] Septal reduction decreases LVOT obstruction, mitral regurgitation, left atrial diameter, left ventricular filling pressure, pulmonary pressure.[4,6] Although surgical myectomy was the first-choice treatment, the recommendations for alcohol septal ablation have changed. It was previously recommended only in patients with advanced

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age, high risk, or comorbidities. However, its indications have been expanded with reports of complication rates and long-term survival times were comparable with myectomy. It is indicated as an alternative to surgery in the current guidelines.[5] However, there is no consensus regarding the choice between surgical myectomy and alcohol septal ablation.[7]

Single-center and multicenter studies have shown the periprocedural, short-term, and long-term results of alcohol septal ablation in HOCM patients.[8-11] However, no such study has been conducted in Turkey. Moreover, few studies have examined the differences in clinical outcomes of alcohol septal ablation in HOCM patients between the sexes.[12-14]

Therefore, this study aimed to determine and compare the periprocedural, short-term, and long-term clinical outcomes and mortality predictors in male and female HOCM patients who underwent alcohol septal ablation.

METHODS

Three hundred twenty-four HOCM patients were retrospectively evaluated based on medical records. Ethical approval was obtained from the Hospital Regional Ethics Committee (No. 2021-07-28, Date: April 5, 2021). All participants' rights were protected, and written informed consent was obtained before the procedures, according to the Helsinki Declaration of 2013.

The criteria for alcohol septal ablation were as follows: interventricular septal (IVS) thickness ≥ 15 mm on echocardiography, maximal LVOT gradient ≥ 30 mmHg or ≥ 50 mmHg with provocative maneuvers, New York Heart Association (NYHA) class 3-4 dyspnea, or Canadian Cardiovascular Society class 3-4 angina, despite optimal medical treatment, and recurrent syncope episodes. Overall, 138 patients met the criteria for alcohol septal ablation. Four patients were excluded due to procedural failure. Thus, 134 HOCM patients aged ≥ 18 years who underwent alcohol septal ablation between 2000 and 2020 at our institution were included in this retrospective cohort study. The patients were divided into female (n = 63, 47%) and male (n = 71, 53%) groups.

Procedural Technique

A transvenous temporary pacemaker was applied at the start of the procedure because of the total A-V block risk. Coronary artery disease was ruled out by diagnostic coronary angiography in suspected patients. Pressure gradients were recorded using catheters placed in the aorta and LVOT. Undiluted contrast agents were used for the septal artery injection.

The estimated target septal artery was wired using a double-curved soft floppy guidewire. An "over-the-wire" balloon was then advanced and inflated to avoid backflow of alcohol into the left anterior descending artery, thereby preventing infarction of remote myocardial areas. A single marker balloon was chosen for easier insertion of the balloon catheter into the septal artery. After the guidewire was withdrawn, a contrast agent was injected through the balloon catheter with simultaneous transthoracic echocardiography.

Selective angiography of the target septal branch through the inflated balloon catheter documented the adequate sealing of the septal branch. It excluded filling of any other coronary artery through the septal collaterals.

Up to 2-4.5 cm^3 (1 cm^3/1 cm septal thickness) of absolute alcohol was injected slowly and continuously through the lumen of the balloon catheter under fluoroscopic, hemodynamic, and electrocardiographic monitoring. Ten minutes after the last alcohol injection, the balloon catheter was withdrawn. A final angiogram showed complete occlusion of the septal branch and normal flow in the left anterior descending artery. Measurements of the outflow tract pressure gradient at rest and with provocation were repeated. If LVOT gradients remained at >25 mm Hg, the same procedure was repeated for the other target septal artery.

Demographic data, cardiovascular history, echocardiographic findings, ECG and Holter findings, symptoms, and medications of all patients were obtained from the institutional database. Procedural results and complications were also recorded. Postprocedural LVOT gradients were evaluated at catheter laboratory discharge. The patients' septal thickness and NYHA class were assessed at the first-month follow-up visit.

The ICD selection criteria were as follows:

- History of sudden cardiac death and documented sustained ventricular tachycardia.
- History of sudden cardiac death in first-degree relatives under 50 years of age.
- Recurrent syncope episodes, suspected to be from arrhythmia.
- Patients with an apical aneurysm.
- Patients with scare rate>5% in cardiac MRI. The decision to implant a device was based on the relevant guidelines and the attending physician's discretions.

Outcomes

The primary endpoint of the study was all-cause mortality. Patients' follow-up visits were planned for 1 and 6 months, and then yearly, after the procedure. Long-term adverse event data were obtained at patient visits or telephonically. Patients with implanted cardioverter defibrillator devices (ICD-D) were evaluated for arrhythmic events. Cardiovascular mortality was defined as sudden cardiac

HIGHLIGHTS

- Current guideline recommendations have been changed in favor of alcohol septal ablation in patients with symptomatic hypertrophic obstructive cardiomyopathy.
- Results were similar in both sexes and were consistent with the findings of other series.
- Age, body mass index, diagnosis age, and time from diagnosis to ablation were predictors of mortality.

death, fatal myocardial infarction (MI), fatal stroke, and heart failure/cardiogenic shock-related death as unexpected death within 1 hour or sudden night death without any symptoms. Major procedural complications were defined as cardiac tamponade requiring pericardiocentesis, sustained ventricular tachycardia, ventricular fibrillation, permanent total A-V block, large anterior MI, left main coronary artery dissection, and cardiac death.

Patients were discharged from the hospital after at least 5 days after ASA.

Statistical Analysis

The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Normally distributed variables were presented as mean ± standard deviation (SD) and compared using independent samples *t* test. Non-normally distributed variables were expressed in median [interquartile range (IQR)], and Mann–Whitney *U* test was used to determine the significant differences among the groups. The categorical variables are expressed in frequencies and percentages. chi-square test or Fisher exact tests were used to compare categorical variables. Time-to-event analysis was conducted for all-cause mortality, and a log-rank test was used to compare curves. Cox proportional hazard regression analysis was performed with all-cause mortality as the dependent variable. Covariates with a P-value < .15 or those considered clinically significant were entered into the multivariate model. For all analyses, a 2-sided P-value < .05 was considered statistically significant. Statistical Package for the Social Sciences (SPSS) V20 (IBM SPSS Inc., Armonk, NY, USA) was used for all statistical analyses.

RESULTS

Patient Characteristics

The baseline demographic characteristics of the patients are summarized in Table 1. Male patients were significantly younger than female patients ($P = .006$). The mean age (SD) at HOCM diagnosis and the mean age at alcohol ablation was significantly lower in male than in female patients ($P = .03$ and $P = .009$, respectively) (Table 1). The time from diagnosis to alcohol ablation was similar between the 2 groups ($P = .17$). Body mass index (BMI) was not significantly different between male and female patients ($P = .45$). Almost 1 in 3 and 1 in 5 patients had a family history of HOCM and sudden cardiac death, respectively.

The most common symptom was dyspnea, followed by near-syncope/syncope. The frequencies of all symptoms were similar between the groups (all $P > .05$). The most common baseline rhythm was sinus rhythm, followed by atrial fibrillation. Left bundle-branch block was significantly more frequent in male than in female patients ($P = .03$), while other ECG/Holter rhythms were similar in both groups (all $P > .05$).

The mean maximal baseline LVOT gradient and IVS thickness were similar in both groups ($P = .67$ and $P = .67$). Overall, 71.6% of patients had a systolic anterior motion on echocardiography. Systolic anterior movement (SAM) occurred after the provocation in 20% of the patients. Only the Valsalva maneuver was used as a provocation test. Only 20.1% had severe mitral regurgitation. The mean ejection fraction left ventricular end-diastolic diameter, left ventricular end-systolic diameter, posterior wall thickness, and left atrial diameter were similar between the 2 groups (all $P > .05$).

The most common medication administered to HOCM patients was beta-blockers (76.9%). Patients on disopyramide and calcium channel blockers were 15.7% and 15.7%, respectively. The administration rates of calcium channel blocker, disopyramide, diuretic, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, acetylsalicylic acid, and novel oral anticoagulant were similar in both the sexes (all $P > .05$).

Procedural Characteristics

Alcohol ablation was performed in 138 patients. The procedure was unsuccessful in 4 patients. The procedural characteristics and complications are summarized in Table 2. The mean alcohol consumption during the operation was not significantly different between the groups ($P = .56$). In 70.9% of the patients, a single septal branch contrast injection was performed under echocardiography guidance, and in 88% of the patients, a single septal branch alcohol injection was performed. The number of contrast- and alcohol-injected septal branches and maximal CK-MB levels after the procedure were similar between the 2 groups (all $P > .05$).

The major procedural complication rates were similar between the sexes ($P = .06$). During the procedure, 9 patients (6.7%) developed ventricular fibrillation (achieved sinus rhythm with defibrillation), 1 patient developed anterior MI, and 1 developed pericardial tamponade requiring pericardiocentesis. Only 2 patients (1.4%) had a permanent pacemaker. No mortality occurred during alcohol septal ablation (Table 2).

Thirty-one patients (23.1%) developed temporary total A-V block, and 7 patients (5.2%) developed pericardial effusion, which was minor complications.

During the hospital stay, 2 patients (1.4%) developed ventricular fibrillation (and achieved sinus rhythm with defibrillation), 2 patients (1.4%) developed acute heart failure and cardiogenic shock, 2 patients (1.4%) developed acute kidney disease, and 2 (1.4%) patients developed remote site acute MI; 1 patient (0.7%) died due to MI. All in-hospital complication rates were similar between the 2 groups ($P = .05$) (Table 2).

The mean LVOT maximal gradient on echocardiography at catheter laboratory discharge was not significantly different between the groups ($P = .84$). The mean IVS thickness decreased to 18 mm (range, 15-20 mm), and the NYHA 3-4 symptom rate dropped to 2.2% in the first-month post-procedure, without significant difference between the groups ($P > .05$; Table 2).

Implanted cardioverter defibrillator was successfully implanted in 22% of patients during hospitalization. There were no procedural complications.

Table 1. Baseline Demographic Characteristics of the Alcohol Septal Ablation Patients

	Total (n = 134)	Female, n = 63 (47%)	Male, n = 71 (53%)	*P*
Age, mean ± SD	60.0 (13.7)	63.4 (13.3)	56.9 (13.4)	**.006**
BMI, mean ± SD	26.1 (3.7)	26.4 (4.4)	25.9 (2.9)	.450
Diagnosis age, mean ± SD	44.3 (12.7)	46.7 (12.9)	42.2(12.2)	**.030**
Ablation age, mean ± SD	47.4 (13.8)	50.7 (14.2)	44.5 (12.8)	**.009**
Diagnosis to ablation (years), median (IQR)	1.0 (0.16-4.2)	1.0 (0.16-5.0)	1.0 (0.16 (4.0)	.170
Prior ICD, n (%)	5 (3.7%)	1 (1.6%)	4 (5.6%)	.370
Prior pacemaker, n (%)	2 (1.5%)	0	2 (2.8%)	.490
ICD after ablation, n (%)	30 (22.6%)	14 (22.6%)	16 (22.5%)	.990
Family HOCM, n (%)	39 (29.3%)	17 (27.4%)	22 (31.0%)	.660
Family SCD, n (%)	24 (17.9%)	11 (17.5%)	13 (18.3%)	.890
Dyspnea, n (%)	111 (82.8%)	54 (85.7%)	57 (80.3%)	.400
NYHA 3-4 (before ablation), n (%)	78 (58.2%)	42 (66.7%)	36 (50.7%)	.060
1	20 (14.9%)	8 (12.7%)	12 (16.9%)	
2	36 (26.9%)	13 (20.6%)	23 (32.45)	
3	74 (55.2%)	38 (60.3%)	36 (50.7%)	
4	4 (3.0%)	4 (6.3%)	0	
Near syncope/syncope, n (%)	53 (39.6%)	25 (39.7%)	28 (39.4%)	.970
Angina, n (%)	52 (39.1%)	24 (38.7%)	28 (39.4%)	.930
Palpitation, n (%)	36 (26.9%)	16 (25.4%)	20 (28.2%)	.710
Prior AF, n (%)	26 (19.4%)	12 (19.0%)	14 (19.7%)	.920
CAD, n (%)	12 (9.0%)	5 (7.9%)	7 (9.9%)	.690
HT, n (%)	64 (47.8%)	32 (50.8%)	32 (45.1%)	.500
ECG/Holter synus rythm, n (%)	103 (76.9%)	48 (76.2%)	55 (77.5%)	.860
ECG/Holter AF, n (%)	31 (22.9%)	16 (25.0%)	15 (21.1%)	.420
ECG/ Holter RBBB, n (%)	47 (35.1%)	26 (41.3%)	21 (29.6%)	.150
ECG/Holter LBBB, n (%)	42 (31.3%)	14 (22.2%)	28 (39.4%)	**.030**
Holter VT, n (%)	27 (20.1%)	12 (19.0%)	15 (21.1%)	0.760
LVOT resting (mm Hg), median (IQR)	80 (63-95)	80 (58-95)	80 (65-96)	.670
LA (mm), mean ± SD	42.6 (4.6)	42.4 (4.7)	42.8 (4.5)	.550
IVS before ablation (mm), median (IQR)	24 (21-26)	24 (21-26)	24 (21-27)	.670
PW (mm), median (IQR)	13 (13-15)	13 (13-15)	14 (13-15)	.070
SAM, n (%)	96 (71.6%)	48 (76.25)	48 (67.6%)	.270
Severe MR (3-4), n (%)	27 (20.1%)	11 (17.5%)	16 (22.5%)	.460
0	18 (13.4%)	7 (11.1%)	11 (15.5%)	
1	41 (30.6%)	16 (25.4%)	25 (35.2%)	
2	48 (35.8%)	29 (46.0%)	19 (26.8%)	
3	20 (14.9%)	9 (14.3%)	11 (15.5%)	
4	7 (5.2%)	2 (3.2%)	5 (7.0%)	
LVEDD (mm), median (IQR)	42 (39-45)	41 (39-44)	42 (40-47)	.130
LVESD (mm), median (IQR)	26 (23-29)	24 (22-29)	26 (23-30)	.500
EF, n (%)	64 (58-66)	64 (60-66)	64 (57-67)	.790
Beta-blocker, n (%)	103 (76.9%)	51 (81.0%)	52 (73.2%)	.290
Calchium channel blocker, n (%)	21 (15.7%)	12 (19.0%)	9 (12.7%)	.310
Diuretic, n (%)	15 (11.2%)	6 (9.5%)	9 (12.7%)	.560
Dysopiramid, n (%)	21 (15.7%)	12 (19.0%)	9 (12.7%)	.310
Amiodarone, n (%)	23 (17.2%)	11 (17.5%)	12 (16.9%)	.930
ACEI/ARB, n (%)	29 (21.6%)	14 (22.2%)	15 (21.1%)	.870
ASA, n (%)	24 (18.2%)	11 (17.5%)	13 (18.8%)	.830
NOAC, n (%)	27 (20.1%)	17 (27.0%)	10 (14.1%)	.060

BMI, body mass ındex; ICD, implantable cardioverter-defibrillator; HOCM, hypertrophic obstructive cardiomyopathy; SCD, sudden cardiac death; NYHA, Newyork Heart Association; AF, atrial fibrillation; CAD, coronary artery disease; HT, hypertension; RBBB, right bundle branch block; LBBB, left bundle branch block; VT, ventricular tachycardia; LA, left atriıum; LVOT, left ventricle outflow tract; IVS, interventricular septum; PW, posterior wall; LVEDD, left ventricle end-diastolic dimension; LVESD, left ventricle end-systolic dimension; EF, ejection fraction; SAM, systolic anterior movement; MR, mitral regurgitation; ACEI/ARB, angiotensin receptor inhibitor/angiotensin receptor blocker; ASA, acetylsalicylic acute; NOAC, novel oral anticoagulant; SD, standard deviation.

Long-Term Clinical Outcomes

The median follow-up duration was 13 (7.6-18.5) years. Seventeen (12.7%) patients developed CHF, 5 patients (3.7%) developed MI, 20 patients (14.9%) developed chronic AF, and 8 patients (6%) developed non-fatal stroke during follow-up. There was no significant difference in these complications between the groups (all $P > .05$). Only 2 patients (1.55%) underwent re-ablation. Fifteen patients (11.3%) received an ICD-D, 3 patients (2.2%) received a pacemaker, and 8 patients underwent coronary revascularization. The need for ICD-D implantation was found to be significantly higher in female patients ($P = .006$), while other intervention rates were similar in both sexes ($P > .05$). Two patients (1.5%) underwent myectomy, and 1 (0.7%) patient underwent mitral valve replacement.

During a mean follow-up of 13 years, 24 patients died. Twelve of these patients (9.0%) had cardiovascular mortality. Seven patients (5.2%) suffered SCD, and 2 patients (1.5%) died of stroke, 2 (1.5%) of heart failure, and 1 patient (0.7%) of MI. Twelve patients (9%) had non-cardiac-related mortality. Four patients died of cancer, 2 of kidney failure, 2 of respiratory failure, 2 of pneumonia, and 2 of sepsis. Cardiovascular and all-cause mortality rates were similar in both groups ($P = .84$ and $P = .43$, respectively).

Mortality Predictors

The predictors of all-cause mortality were assessed using Cox regression analysis. Only BMI, age at diagnosis, and time from diagnosis to ablation time were significant according to the univariate analysis ($P = .005$, $P = .001$, and

Table 2. Periprocedural, In-Hospital, and Long-Term Outcomes of the Patients

	Total (n = 134)	Female, n = 63 (47%)	Male, n = 71 (53%)	*P*
Alcohol (cm^3), median (IQR)	3.0 (2.5-3.5)	3.0 (2.5-3.5)	3.0 (2.5-3.5)	.560
Contrast injected branch, n (%)				
1	95 (70.9%)	45 (71.4%)	50 (70.4%)	.740
2	36 (26.9%)	16 (25.4%)	20 (28.2%)	
3	1 (0.7%)	1 (1.6%)	0	
4	2 (1.5%)	1 (1.6%)	1 (1.4%)	
Alcohol injected branch, n (%)				
1	118 (88.1%)	57 (90.55%)	61 (85.9%)	.530
2	15 (11.2%)	6 (9.5%)	9 (12.7%)	
3	1 (0.7%)	0	1 (1.4%)	
Peak CK-MB (mg/dL), median (IQR)	212 (171-279)	206 (150-255)	225 (180-298)	.200
Major procedural complications, n (%)	16 (11.9%)	11 (17.5%)	5 (7.0%)	.060
All inhospital complications, n (%)	21 (15.7%)	14 (22.4%)	7 (9.9%)	.050
LVOT-max-after ablation (mm Hg), median (IQR)	21 (10-32)	21 (10-33)	21 (11-32)	.840
IVS (1 month), median (IQR)	18 (15-20)	18 (16-209	17 (15-21)	.660
NYHA 3-4 (after 1 month), n (%)	3 (2.2%)	2 (3.2%)	1 (1.4%)	
1	75 (56.0%)	29 (46.0%)	46 (64.8%)	
2	56 (41.8%)	32 (50.8%)	24 (33.8%)	
3	3 (2.2%)	2 (3.2%)	1 (1.4%)	
Long-term follow-up				
Follow-up (years), median (IQR)	13.0 (7.6-18.5)	14.0 (8.0-18.0)	12.0 (7.0-19.0)	.920
CHF, n (%)	17 (12.7%)	10 (15.9%)	7 (9.9%)	.290
MI, n (%)	5 (3.7%)	1 (1.6%)	4 (5.6%)	.370
Coronary revascularization, n (%)	8 (6.0%)	3 (4.8%)	5 (7.0%)	.720
Chronic AF, n (%)	20 (14.9%)	11 (17.5%)	9 (12.7%)	.430
ICD, n (%)	15 (11.3%)	12 (19.4%)	3 (4.2%)	**.006**
Pace-maker n (%)	3 (2.2%)	1 (1.6%)	2 (2.8%)	1.000
Myectomy, n (%)	2 (1.5%)	0	2 (2.8%)	.490
Re-ablation, n (%)	2 (1.55%)	2 (3.2%)	0	.210
MVR, n (%)	1 (0.7%)	1 (1.6%)	0	.470
Nonfatal stroke, n (%)	8 (6.0%)	4 (6.3%)	4 (5.6%)	1.000
Cardiovascular mortality, n (%)	12 (9.0%)	6 (9.5%)	6 (8.6%)	.840
All-cause mortality, n (%)	24 (17.9%)	13 (20.6%)	11 (15.5%)	.430

CK-MB, creatine kinase muscle brain; LVOT, left ventricle outflow tract; IVS, interventricular septum; NYHA, Newyork Heart Association; CHF, congestive heart failure; MI, myocardial infarction; AF, atrial fibrillation; ICD, implantable cardioverter-defibrillator; MVR, mitral valve replacement.

P = .001, respectively). These factors were included in the multivariate analysis.

Age [hazard ratio (HR) 0.69, 95% CI 0.61-0.78, P < .001], BMI (HR 1.20, 95% CI 1.04-1.40, P = .01), age at diagnosis (HR 1.57, 95% CI 1.34-1.78, P < .001), and time from diagnosis to ablation (HR 1.57, 95% CI 1.35-1.84, P < .001) were found to be predictors of long-term all-cause mortality in HOCM patients who underwent alcohol septal ablation (Table 3). Sex, IVS thickness, and the NYHA class before the procedure were not predictors of long-term cardiac mortality (P = .30, P = .72, and P = .72, respectively). The Kaplan–Meier curves revealed that long-term all-cause mortality was similar in both men and women (P[log-rank] = .43) (Figure 1).

The mean survival time was 17.9 ± 0.8 (95% CI: 16.3-19.4) years for females and 18.6 ± 0.6 (95% CI: 17.6-20.08) years for male patients. The overall estimated survival time was 18.3 ± 0.5 (95% CI 17.3-19.3) years.

Survival analyses showed an estimated 5-year survival rate of 91% (95% CI: 80-96%), the 10-year survival rate of 85% (95% CI: 73-92%), and a 20-year survival rate of 72% (95% CI: 56-83%) in female patients and an estimated 5-year survival rate of 93% (95% CI: 81-98%), the 10-year survival rate of 89% (95% CI: 78-95%), and 20-year survival rate of 72% (95% CI: 50-85%) in male patients (Figure 2).

DISCUSSION

This study showed that periprocedural, short-, and long-term outcomes in Turkish HOCM patients were similar in both sexes. Age, BMI, age at diagnosis, and time from diagnosis to ablation were predictors of long-term all-cause mortality. To the best of our knowledge, no previous study had such a long follow-up period or as many HOCM patients who underwent alcohol septal ablation in Turkey. Previous studies involved fewer patients and had shorter follow-up periods.[15,16]

Because the patient's chronological age at the time of study inclusion, the age at which the diagnosis was established, and the age at which the procedure was performed differed significantly (in years), we defined these separately. The higher the age and the time delay between the diagnosis and procedure, the greater was the mortality.

Female patients were older, and the age at diagnosis and ablation was higher in females than in males in our study. These findings are compatible with other studies.[13,14] The most common symptom of patients was dyspnea, similar to other studies.[4,17]

Calcium blocker and disopyramide usage rates seem low; however, they are similar to large septal ablation series.[4,6] Disopyramide was used only in patients with refractory symptoms despite beta-blocker therapy. Furthermore, it is not available in our country. Lower rates of calcium channel

Table 3. Cox Proportional Hazard Regression Analysis for All-Cause Mortality

	Univariable			Multivariable		
	HR	**95% CI**	***P***	**HR**	**95% CI**	***P***
Age	1.02	0.99-1.05	.110	0.69	0.61-0.78	**<.001**
Sex	0.72	0.32-1.63	.440	1.74	0.62-4.9	.290
BMI	1.14	1.04-1.26	**.005**	1.20	1.04-1.40	**.010**
Diagnosis age	1.06	1.02-1.11	**.001**	1.57	1.34-1.78	**<.001**
Diagnosis to ablation	1.10	1.03-1.17	**.001**	1.57	1.35-1.84	**<.001**
Septum thickness (before)	1.006	0.91-1.11	.900	0.97	0.85-1.11	.720
NYHA class (before)	1.65	0.68-4.00		1.19	0.46-3.06	.720
Family SCD	0.52	1.23-2.22	.380			
ICD	0.48	0.11-2.07	.320			
Syncope	0.58	0.24-1.42	.230			
Holter VT	0.87	0.29-2.55	.800			
Holter AF	1.10	0.43-2.78	.830			
LVOT max discharge	1.01	0.99-1.03	.100			
SAM	2.12	0.78-5.74	.130			
EF %	0.97	0.91-1.03	.350			
ICD	0.35	0.04-2.66	.310			
Coroner revascularization	0.04	0.00-94.76	.420			
Beta-blocker	0.80	0.33-1.93	.620			
Amiodarone	1.71	0.67-4.31	.250			

HR, hazard ratio; BMI, body mass ındex; ICD, implantable cardioverter-defibrillator; SCD, sudden cardiac death; NYHA, Newyork Heart Association; AF, atrial fibrillation; VT, ventricular tachycardia; LVOT, left ventricle outflow tract; EF, ejection fraction; SAM, systolic anterior movement.

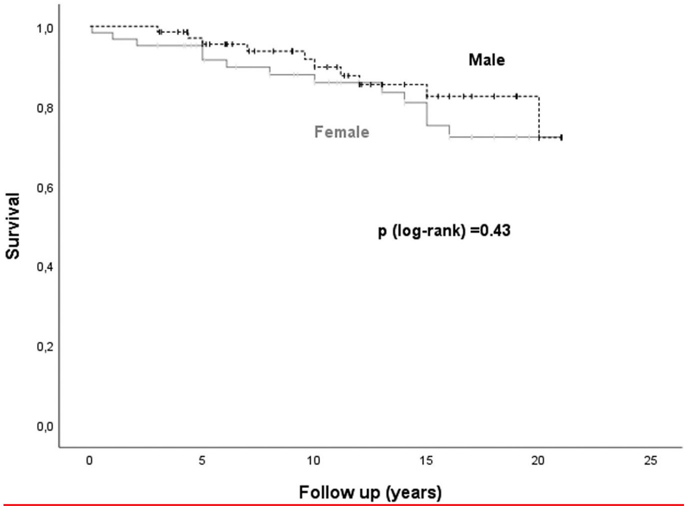

Figure 1. Kaplan–Meier curves revealed that long-term cardiac all-cause mortality was similar in both males and females.

blockers may be due to patients' intolerability because of bradycardia.

As expected, there was a significant improvement in the NYHA functional capacity of the patients from the first month after the procedure. The IVS thickness and LVOT gradient decreased, and symptomatic improvement continued during the long-term follow-up. Our cohort's baseline ECG, Holter, and echocardiographic characteristics were similar to those in other studies.[9-11,18]

In most patients, echocardiography-guided contrast injection and alcohol injection into the first septal artery were sufficient to ensure procedural success, with results consistent with those of similar previous studies.[4,9,11,18] However, the mean amount of alcohol injected in our study patients was slightly higher than that in other single-center cohorts.[19,20] The Euro-ASA registry concluded that a higher amount of alcohol was more effective in reducing LVOT

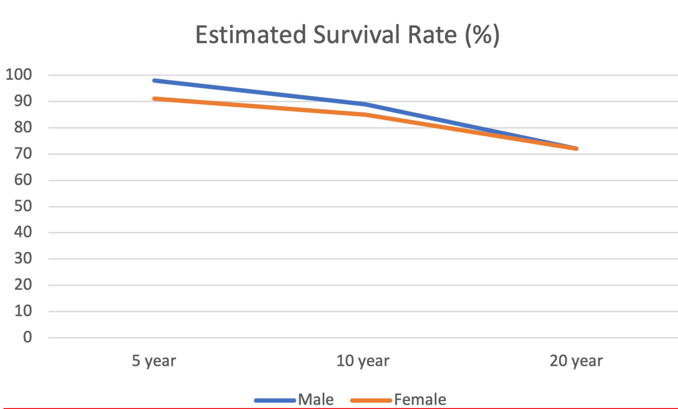

Figure 2. An estimated 5-year survival rate of 91% (95% CI: 80%-96%), 10-year survival rate of 85% (95% CI: 73%-92%), and 20-year survival rate of 72% (95% CI: 56%-83%) in female patients and 5-year survival rate of 93% (95% CI: 81%-98%), 10-year survival rate of 89% (95% CI: 78%-95%), and 20-year survival rate of 72% (95% CI: 50%-85%) in male patients.

gradient, with a concomitantly higher risk of total A-V block.[21] Veselka et al[22] showed that long-term mortality rates were similar to smaller (1-1.98 mL) and larger (2-3.8 mL) amounts of alcohol in a recent study. Moreover, a smaller amount of alcohol was associated with a higher rate of repeated ablations.[22] It is plausible that serious arrhythmic complications would be rarer due to the prophylactic pacemaker implantation in all patients and the relatively lower mean age at ablation in our patients; thus, more significant amounts of alcohol were used in this study. Nevertheless, our center has decreased mean alcohol dose during septal ablation in recent years.

Although acute procedural complications occurred in approximately one-third of patients, only 12% of them were major complications. Moreover, there was no mortality during the procedure, and only 1 patient died during hospitalization. These low mortality rates are likely due to the operator's experience, catheter laboratory, intensive care team, and a coordinated multidisciplinary approach. In addition, these low mortality rates were consistent with those in other studies.[4,13,18,23]

Although the rate of permanent pacemakers appears to be low (2.2%) in our study cohort, the rate of ICD implantation must be added to the pacemaker ratio (11.3%) as it includes the pacemaker function.

The frequency of ICD application was significantly higher in female patients, which may be due to several reasons. Some studies have shown that the long-term prognosis of female patients is worse in the course of HOCM.[12,13] It is known that the frequency of ICD implantation is higher. Women were older at diagnosis, which increases the risk of ventricular arrhythmia and sudden death in these patients.

The predictors of long-term mortality in HOCM patients differed between the studies. Consistent with several studies, age, ablation age, and BMI were predictors of long-term mortality in our study.[13,18,21] In addition, we also examined the effect of the time between HOCM diagnosis and ablation on long-term mortality and found a significant impact. While age at ablation, septal thickness, and LVOT gradient were predictors of mortality in the Euro-ASA registry, baseline EF, baseline NYHA class, number of alcohol-injected septal branches, beta-blocker usage, and number of ablations were predictors of all-cause mortality in the North American registry.[8,21] Sorajja et al[24] found that patients aged ≥65 years with a septal thickness of <18 mm and a left anterior descending artery diameter of <4 mm had better 4-year symptoms and survival rates. Veselka et al[25] found that excessive septal thickness (≥30 mm) was associated with cardiac mortality. Contrary to these studies, female, NYHA class, septal thickness, and LVOT gradient at catheter discharge did not predict all-cause mortality in our study. These differences may be due to cohort characteristics, operator and clinical experience, alcohol dose, and follow-up duration. Suppose the number of patients in our study was more extensive. In that case, septal thickness, SAM, NYHA class, etc., which were not significant in the univariate analysis but had significant HR, could be predictors of mortality. In addition, the endpoint of our study was all-cause mortality, not cardiac mortality, which may affect the regression analysis's mortality predictors.

In a recently published meta-analysis involving 4547 patients from 20 studies, the efficacy of alcohol septal ablation and myectomy in HOCM patients were compared. No significant difference was found between the groups in terms of all-cause death, cardiac death, and SCD.[26] Additionally, Nguyen et al[27] showed no difference between the survival of HOCM patients after myectomy or alcohol septal ablation. With the recently updated guidelines, alcohol septal ablation has become the first choice in treating HOCM patients with severe symptoms resistant to medical treatment.[5]

Limitations of Study

This study has several limitations, including its single-center and retrospective design and relatively small sample size. Moreover, cardiac MRI and late echocardiographic findings were not included in the analysis because these data were incomplete. Some of the patients who underwent septal ablation were diagnosed in our center, and a few were referred from another institution. This may cause a gap in the data regarding age at diagnosis and time to ablation. However, these shortcomings were, to some extent, offset by the long follow-up duration of the study.

CONCLUSION

Alcohol septal ablation has similar short- and long-term outcomes for both sexes in HOCM patients. The risk factors for long-term all-cause mortality were age, BMI, diagnosis age, and time delay to operation. Therefore, alcohol septal ablation timing is essential for ensuring better outcomes. Our findings may contribute to the increased performance of alcohol septal ablation in HOCM patients in our country. More extensive, multicenter studies are required to confirm our findings.

Ethics Committee Approval: Ethical approval was obtained from the İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital Regional Ethics Committee (No. 2021-07-28, Date: April 5, 2021).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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