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Clinical Research

Effect of Institutional Experience on Outcomes of Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy

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ABSTRACT

Background: The current American College of Cardiology Foundation/American Heart Association guidelines on hypertrophic cardiomyopathy state that institutional experience is a key determinant of successful outcomes and lower complication rates of alcohol septal ablation (ASA). The aim of this study was to evaluate the safety and efficacy of ASA according to institutional experience with the procedure.

Methods: We retrospectively evaluated 1310 patients with symptomatic obstructive hypertrophic cardiomyopathy who underwent ASA and were divided into 2 groups. The first-50 group consisted of the first consecutive 50 patients treated at each centre, and the over-50 group consisted of patients treated thereafter (patients 51 and above).

RÉSUMÉ

Contexte : Les lignes directrices actuelles sur la cardiomyopathie hypertrophique de l'American College of Cardiology Foundation et de l'American Heart Association indiquent que l'expérience de l'établissement est un déterminant clé du succès de l'ablation septale à l'alcool (ASA) et du faible taux de complications de cette intervention. La présente étude visait à évaluer l'innocuité et l'efficacité de l'ASA en fonction de l'expérience de l'établissement relativement à cette intervention.

Méthodes : Nous avons effectué une évaluation rétrospective de 1310 patients atteints de cardiomyopathie hypertrophique obstructive symptomatique ayant subi une ASA, qui ont été divisés en 2 groupes. Le groupe des 50 premiers patients était constitué des 50 premiers patients consécutifs traités dans chaque centre, tandis que le groupe

Left ventricular (LV) outflow obstruction is present in approximately two-thirds of patients with hypertrophic cardiomyopathy (HCM).[1,2] Several studies have reported the excellent safety and efficacy of transcatheter relief of LV obstruction using alcohol septal ablation (ASA).[3-9] However, ASA is associated with intra- and postprocedural complications that might be related to institutional and personal experience.[10-12] The current American College of Cardiology Foundation/American Heart Association HCM guidelines state that expertise is a key determinant of successful outcomes and lower complication rates of this complex procedure, and recommend a minimal operator and institutional experience of 20 and 50 procedures, respectively (class I; level of evidence C).[1] To date, there are no robust data to support this recommendation. The aim of the present study was to assess

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Results: In the 30-day follow-up, there was a significant difference in the occurrence of major cardiovascular adverse events (21% in the first-50 group vs 12% in the over-50 group; $P < 0.01$), which was driven by the occurrence of cardiovascular deaths (2.1% vs 0.4%; $P = 0.01$) and implanted pacemakers (15% vs 9%; $P < 0.01$). In the long-term follow-up (5.5 ± 4.1 years), the first-50 group was associated with a significantly higher occurrence of major adverse events ($P < 0.01$) and higher cardiovascular mortality ($P < 0.01$). Also, patients in the first-50 group were more likely to self-report dyspnea of New York Heart Association class III/IV (16% vs 10%), to have a left ventricular outflow gradient > 30 mm Hg (16% vs 10%) at the last clinical check-up ($P < 0.01$ for both), and a probability of repeated septal reduction therapy ($P = 0.03$).

Conclusions: An institutional experience of > 50 ASA procedures was associated with a lower occurrence of ASA complications, better cardiovascular survival, better hemodynamic and clinical effect, and less need for repeated septal reduction therapy.

Résultats : Durant la période de suivi de 30 jours, une différence significative a été observée sur le plan de la survenue d'événements indésirables cardiovasculaires majeurs (21 % dans le groupe des 50 premiers patients comparativement à 12 % dans le groupe des patients suivant les 50 premiers; $p < 0{,}01$) attribuables principalement aux décès d'origine cardiovasculaire (2,1 % vs 0,4 %; $p = 0{,}01$) et à l'implantation de stimulateurs cardiaques (15 % vs 9 %; $p < 0{,}01$). Au cours du suivi à long terme (5,5 ± 4,1 ans), le groupe des 50 premiers patients était associé à un taux significativement plus élevé d'événements indésirables majeurs ($p < 0{,}01$) et de décès d'origine cardiovasculaire ($p < 0{,}01$). De plus, les patients du groupe des 50 premiers patients étaient plus nombreux à signaler spontanément une dyspnée de classe III/IV selon l'échelle de la New York Heart Association (16 % vs 10 %) et à afficher un gradient de pression au niveau du ventricule gauche supérieur à 30 mm Hg (16 % vs 10 %) lors du dernier bilan clinique ($p < 0{,}01$ pour ces deux paramètres), et présentaient également une probabilité plus élevée de répétition de l'intervention de réduction septale ($p = 0{,}03$).

Conclusions : Une expérience au sein de l'établissement supérieure à 50 ASA a été associée à un taux plus faible de complications de cette intervention, à une meilleure survie cardiovasculaire, à des effets hémodynamiques et cliniques supérieurs et à une diminution de la nécessité de répéter l'intervention de réduction septale.

the safety and efficacy of ASA according to institutional experience.

Methods

Patients and study design

A total of 1437 patients were enrolled in the Euro-ASA Registry. Because post-ASA complete heart block with subsequent pacemaker implantation was studied, we excluded 127 (9%) patients with permanent pacemakers or implantable cardioverter-defibrillators (ICDs) implanted before ASA. Thus, we identified 1310 patients with intractably symptomatic obstructive HCM who underwent ASA between 1997 and 2017 (Table 1).

Details of the Euro-ASA Registry have been published previously.[4] The diagnosis of HCM was made by cardiologists experienced in this disease, on the basis of typical clinical, electrocardiographic, and echocardiographic features, with ventricular myocardial hypertrophy occurring in the absence of any other cardiac or systemic disease that could have been responsible for the hypertrophy.[13] At each centre, the primary indications for invasive treatment were intractable symptoms despite maximal medical therapy. The decision regarding subsequent invasive therapies to relieve LV obstruction was made after detailed multidisciplinary evaluation with consensus among experts in management of HCM.

Clinical, demographic, and echocardiographic data and symptom status were recorded at baseline (Table 2) and during follow-up. The study was performed in compliance with the Declaration of Helsinki.

To compare outcomes related to institutional experience with the ASA procedure, we created 2 groups of patients. The first-50 group consisted of the first consecutive 50 patients treated in each centre, and the over-50 group consisted of patients treated thereafter at the respective centre; the number of patients in the first-50 group was chosen to reflect HCM guidelines.[1]

Interventional procedure and study follow-up

Details of the ASA technique have been published previously.[4,5] All included procedures were performed using myocardial echocardiography guidance and involved delivery of alcohol.

Most patients had a clinical examination 1-6 months after ASA and subsequently once every year. The follow-up program included recording of events, symptoms, physical examination, and electrocardiographic and echocardiographic examination. In patients with an implanted pacemaker or ICD, the device's memory and function were assessed, and ICD therapy was recorded. All clinical adverse events were confirmed by reviewing the medical records and respective national registries of deaths. For patients who died outside the participating hospitals, interviews and/or mail communications with the next of kin and/or the treating family doctor were performed to determine the cause of death.

Definitions and study end points

Clinical outcome after ASA was assessed and mortality was recorded. Cardiovascular death was defined as death related to any cardiovascular disease, including stroke and sudden death. Sudden death was defined as instantaneous and unexpected natural death within 1 hour after a witnessed collapse in a previously stable patient or death during sleep.

We wanted to determine the significance of institutional experience with ASA. Therefore, we focused on (1) 30-day major cardiovascular adverse events including cardiovascular

Table 1. Centres participating in the study

Hospital	Number of procedures without previous PM/ICD implantation	Average number of procedures per year	Number of operators performing ASA
Medical University Innsbruck, Innsbruck, Austria	30	4	1
University Hospital Motol, Prague, Czech Republic	161	10	1
St Anne's University Hospital, Brno, Czech Republic	55	4	1
Cardiocentre Podlesi, Třinec, Czech Republic	93	9	1
Rigshospitalet, Copenhagen, Denmark	106	7	2
Herlev-Gentofte Hospital, Hellerup, Denmark	24	4	1
Liverpool Heart and Chest Hospital, Liverpool, England	94	6	1
Heart and Diabetes Centre NRW, Bad Oyenhausen, Germany	472	26	2
St Antonius Hospital Nieuwegein, Nieuwegein, The Netherlands	197	16	2
Oslo University Hospital, Oslo, Norway	35	5	2
Institute of Cardiology, Warsaw, Poland	43	5	2

ASA, alcohol septal ablation; ICD, implantable cardioverter-defibrillator; PM, pacemaker.

death, electrical defibrillation for ventricular tachycardia/fibrillation (VT/VF), cardiac tamponade, and pacemaker implantation; (2) 30-day all-cause mortality rate; (3) periprocedural complications and long-term risk of pacemaker implantation; (4) long-term cardiovascular death; (5) treatment efficacy: LV outflow gradient reduction and improvement in functional status; and (6) rate of reintervention (re-ASA or myectomy).

Statistical analysis

All data were edited and analyzed by 2 independent statisticians (Marek Maly and Eva Hansvenclova). Student *t* tests, χ^2 tests, and Kaplan-Meier survival analysis were used, when appropriate. Cox proportional hazards regression was used to identify predictors of adverse cardiovascular events, cardiovascular mortality, residual LV outflow gradient > 30 mm Hg, New York Heart Association (NYHA) class III/IV at the last clinical check-up, and repeated septal reduction. The effects of the following parameters were evaluated, first in a predefined univariate model: age at time of ASA, sex, baseline LV outflow gradient, baseline septum thickness, volume of injected alcohol, ASA in the first-50 group, and year of the procedure. Second, variables with $P < 0.15$ in the univariate analysis were entered into a multivariable analysis, which was performed using a backward stepwise multiple Cox regression. Linear regression was used to describe the relationship between the percentage decrease of LV outflow gradient and potential predictors. Because the distribution of percentage of LV outflow gradient reduction was left skewed, logarithmic transformation was applied to 100 minus the percentage of LV outflow gradient decrease, to get closer to normality and to stabilize the variance before entering linear regression. The transformed variable satisfied linear regression model

Table 2. Clinical and echocardiographic characteristics at baseline and at the last check-up

Characteristic	First-50 group (n = 482)	Over-50 group (n = 828)	*P*
Age, years	58.3 ± 13.5	58.8 ± 13.3	0.721
Female sex, n (%)	246 (51)	400 (48)	0.359
Dyspnea, NYHA class			
Baseline	2.9 ± 0.5	2.9 ± 0.4	0.407
Last clinical check-up	1.8 ± 0.7	1.6 ± 0.7	0.002
NYHA class III/IV			
Baseline, n (%)	394 (82)	704 (85)	0.121
Last clinical check-up, n (%)	77 (16)	85 (10)	0.003
Angina, CCS class			
Baseline	1.3 ± 1.2	1.2 ± 1.2	0.057
Last clinical check-up	0.5 ± 0.7	0.7 ± 0.8	< 0.001
LV outflow gradient at rest, mmHg			
Baseline	73.9 ± 41.8	66.8 ± 34.5	0.027
Last clinical check-up	20.8 ± 27.5	14.0 ± 17.2	< 0.001
> 30 mm Hg, n (%)	75 (16)	85 (10)	0.007
LV diameter, mm			
Baseline	43.0 ± 6.3	43.1 ± 6.3	0.621
Last clinical check-up	46.4 ± 6.4	45.0 ± 5.9	0.008
LV ejection fraction, %			
Baseline	67 ± 10	71 ± 9	< 0.001
Last clinical check-up	63 ± 10	68 ± 9	< 0.001
Basal septum thickness, mm			
Baseline	20.8 ± 4.2	20.1 ± 3.9	< 0.002
Last clinical check-up	15.3 ± 4.4	15.2 ± 4.0	0.735
Left atrium diameter, mm			
Baseline	45.6 ± 6.7	48.0 ± 6.6	< 0.001
Last clinical check-up	45.7 ± 7.4	45.4 ± 7.0	0.662
Mean follow-up duration, years	7.15 ± 4.4	4.5 ± 3.6	

CCS, Canadian Cardiovascular Society; LV, left ventricular; NYHA, New York Heart Association.

Table 3. Causes of death during the first post-ASA month

Patient	Cause
First-50 group (n = 11)	
1	Complete heart block
2	Cardiac tamponade
3	Ventricular fibrillation
4	Ventricular fibrillation
5	Pulmonary embolism
6	Complete heart block
7	Ventricular fibrillation
8	Sepsis
9	Pulmonary embolism
10	Stroke
11	Sudden death
Over-50 group (n = 4)	
1	Cardiac tamponade
2	Heart failure
3	Pulmonary embolism
4	Carcinoma

ASA, alcohol septal ablation.

assumptions. The long-term occurrence of cardiovascular mortality, adverse events, and repeated septal reduction therapy were estimated using the Kaplan-Meier method; the curves of both groups were adjusted for age at ASA (60 years), baseline LV outflow gradient (60 mm Hg), baseline septum thickness (20 mm), and year of ASA (2006). A $P < 0.05$ was considered to indicate a statistically significant result. All reported P values were 2-sided. The statistical software GraphPad (release 6.05; GraphPad Software Inc, La Jolla, CA) and Stata (release 9.2; StataCorp LP, College Station, TX) were used.

Results

Short-term outcomes

A total of 1310 patients with obstructive HCM underwent ASA. At baseline, patients in the first-50 group had a significantly thicker interventricular septum, lower LV ejection fraction, higher LV outflow gradient at rest, and smaller left atrial diameter (Table 2). The volume of injected alcohol during ASA was 2.3 ± 1.1 mL and 2.0 ± 0.8 mL in the first-50 group and over-50 group, respectively ($P < 0.01$).

In the 30-day follow-up, there was a significant difference in the all-cause mortality rate (2.2% in the first-50 group vs 0.5% in the over-50 group; $P = 0.01$; Table 3), and in the occurrence of major cardiovascular adverse events (21% in the first-50 group vs 12% in the over-50 group; $P < 0.01$; Table 4). The significant difference in the early adverse events was driven by a higher rate of cardiovascular deaths ($P = 0.01$) and pacemaker implantation ($P < 0.01$) in the first-50 group.

Among 127 patients who were not included in the study because of permanent pacemaker or ICD implanted before ASA, the 30-day occurrence of major cardiovascular events was 1.6% (defibrillation for VT/VF in 2 cases) and none of them died during the same period.

Long-term outcomes

None of the patients were lost to follow-up. A total of 179 deaths (14%) occurred after the ASA procedure during a mean follow-up of 5.5 ± 4.1 years (7186 patient-years), yielding an all-cause mortality rate of 2.5% per year (3.4% per year in the first-50 group vs 1.7% per year in the over-50 group; $P < 0.01$).

A total of 65 (5%) patients underwent an ICD implantation (8.1% in the first-50 group vs 3.1% in the over-50 group; $P < 0.01$), and 18 (1.4%) patients experienced an appropriate discharge (1.7% in the first-50 group vs 1.2% in the over-50 group; $P = 0.62$).

Adverse events

Freedom from major adverse clinical events attributable to ASA (cardiovascular death at 30 days, electrical cardioversion for VT/VF at 30 days, cardiac tamponade at 30 days, or pacemaker implantation during the whole post-ASA period) in the first-50 group vs the over-50 group at 1, 5, and 10 years was 80% (95% CI, 76%-83%) vs 89% (95% CI, 87%-91%), 77% (95% CI, 73%-81%) vs 87% (95% CI, 85%-89%), 75% (95% CI, 71%-79%) vs 87% (95% CI, 84%-89%), respectively ($P < 0.01$). After adjustment the incidence of adverse events was still significantly different ($P < 0.01$; Fig. 1).

In adjusted multivariable analysis, the independent predictors of adverse cardiovascular events attributable to ASA were therapy in the first-50 group (HR, 1.99; 95% CI, 1.50-2.62; $P < 0.01$), and age at ASA (HR, 1.03; 95% CI, 1.01-1.04; $P < 0.01$).

Cardiovascular death

Survival free of cardiovascular death in the first-50 group vs the over-50 group at 1, 5, and 10 years were 96% (95% CI, 94%-98%) vs 99% (95% CI, 98%-99%), 92% (95% CI, 88%-94%) vs 96% (95% CI, 94%-98%) and 84% (95% CI, 80%-88%) vs 92% (95% CI, 88%-95%), respectively (all $P < 0.01$). Adjusted Kaplan-Meier curves of cardiovascular death are shown in Figure 2 ($P < 0.01$).

In adjusted multivariable analysis, the independent predictors of cardiovascular death were therapy in the first-50 group (HR, 2.04; 95% CI, 1.27-3.27; $P < 0.01$), age at ASA (HR, 1.04; 95% CI, 1.03-1.06; $P < 0.01$), thicker septum thickness (HR, 1.09; 95% CI, 1.04-1.15; $P < 0.01$),

Table 4. Thirty-day nonhierarchical occurrence of major cardiovascular adverse events

Event	First-50 group (n = 482)	Over-50 group (n = 828)	P
Cardiovascular death, n (%)	10 (2.1)	3 (0.4)	0.006
Electrical cardioversion for VT/VF or ICD discharge	11 (2.3)	10 (1.2)	0.171
Cardiac tamponade, n (%)	8 (1.7)	7 (0.9)	0.189
Permanent pacemaker, n (%)	73 (15.1)	76 (9.2)	0.002
Total, n (%)	102 (21.2)	96 (11.7)	< 0.001

ICD, implantable cardioverter-defibrillator; VF, ventricular fibrillation; VT, ventricular tachycardia.

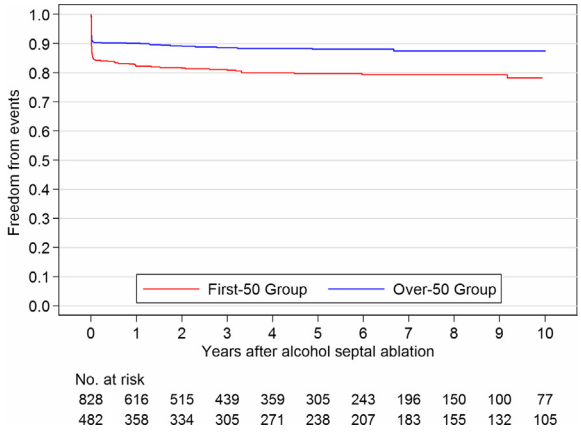

Figure 1. Kaplan-Meier curves describing survival free of cardiovascular adverse events attributable to ASA in the first-50 vs the over-50 group (adjustment for age, baseline pressure gradient, baseline septum thickness, and year of performed procedure) ($P < 0.01$).

and year of performed ASA (HR, 0.92; 95% CI, 0.87-0.97; $P < 0.01$).

LV outflow gradient

At the last clinical check-up, the resting LV outflow gradient was reduced from 74 ± 42 mm Hg to 21 ± 28 mm Hg and from 67 ± 35 to 14 ± 17 mm Hg in the first-50 group and the over-50 group, respectively ($P < 0.01$ for both). The independent predictors of a more pronounced percentage decrease in LV outflow gradient were baseline LV outflow gradient (regression coefficient 0.01; 95% CI, 0.01-0.01, $P < 0.01$), the volume of injected alcohol (regression coefficient 0.12; 95% CI, 0.07-0.17; $P < 0.01$), and therapy in the over-50 group (regression coefficient 0.39; 95% CI, 0.29-0.49; $P < 0.01$).

A total of 75 (16%) and 85 (10%) patients in the first-50 group and the over-50 group, respectively, had a LV outflow gradient > 30 mm Hg at the last clinical check-up ($P < 0.01$). According to multivariable analysis, a residual LV outflow gradient > 30 mm Hg was independently associated with

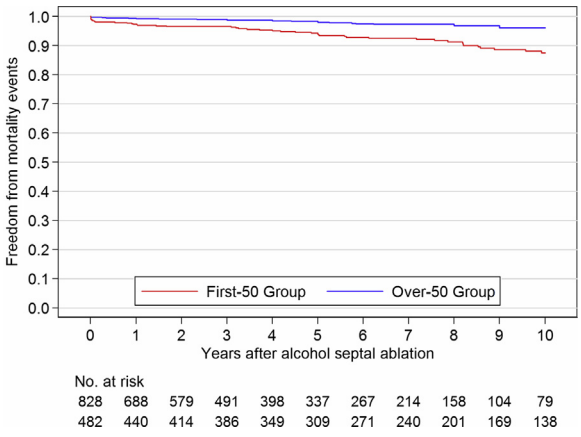

Figure 2. Kaplan-Meier curves describing survival free of cardiovascular death in the first-50 vs the over-50 group (adjustment for age, baseline pressure gradient, baseline septum thickness, and year of performed procedure) ($P < 0.01$).

Table 5. Repeated interventions

Intervention	First-50 group (n = 482)	Over-50 group (n = 828)	*P*
Repeated ASA, n (%)	52 (11)	56 (7)	0.012
Myectomy after ASA, n (%)	23 (5)	22 (3)	0.058
Any repeated intervention, n (%)	67 (14)	73 (9)	0.005

ASA, alcohol septal ablation.

treatment in the first-50 group (odds ratio [OR], 1.81; 95% CI, 1.26-2.60; $P < 0.01$), female sex (OR, 1.75; 95% CI, 1.21-2.53; $P < 0.01$), LV outflow gradient at baseline (OR, 1.01; 95% CI, 1.01-1.01; $P < 0.01$), and a lower volume of injected alcohol (OR, 0.79; 95% CI, 0.65-0.96; $P = 0.02$).

Dyspnea

A total of 75 patients (16%) and 85 patients (10%) in the first-50 group and the over-50 group reported NYHA class III/IV dyspnea at the last clinical check-up, respectively ($P = 0.01$). According to multivariable analysis, NYHA class III/IV at the last clinical check-up was independently associated with treatment in the first-50 group (OR, 1.61; 95% CI, 1.13-2.28; $P = 0.01$) and older age at ASA (OR, 1.04; 95% CI, 1.03-1.06; $P < 0.01$).

Repeated septal reduction

One hundred forty patients (11%) underwent repeated septal reduction therapy attributable to insufficient symptomatic relief (Table 5). After adjustment, the incidence of re-ASA or myectomy was significantly higher in the first-50 group ($P = 0.03$; Fig. 3).

In adjusted multivariable analysis, the independent predictors of repeated septal reduction were therapy in the first-50 group (HR, 1.47; 95% CI, 1.04-2.08; $P = 0.03$), year of performed ASA (HR, 1.10; 95% CI, 1.06-1.14; $P < 0.01$), LV outflow gradient at baseline (HR, 1.01; 95% CI, 1.01-1.01; $P = 0.01$), and age at ASA (HR, 0.98; 95% CI, 0.96-0.99; $P < 0.01$).

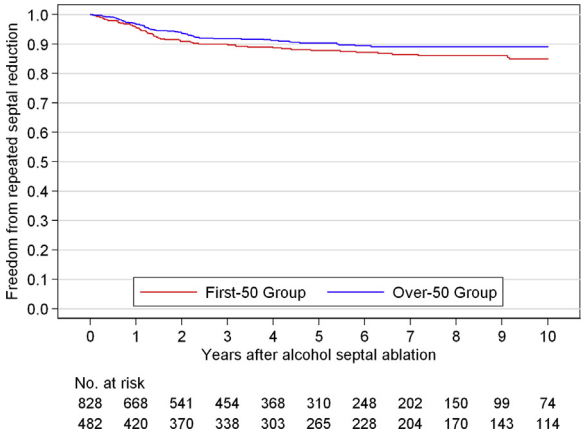

Figure 3. Kaplan-Meier curves showing survival free of repeated septal reduction therapy in the first-50 vs the over-50 group (adjustment for age, baseline pressure gradient, baseline septum thickness, and year of performed procedure; $P = 0.03$).

Discussion

This study from the multinational European registry had the following principal findings: an institutional experience of > 50 ASA procedures was associated with (1) a lower occurrence of periprocedural major cardiovascular adverse events; (2) a very low (0.4%) 30-day cardiovascular death rate; (3) fewer ASA-attributable complications during the whole post-ASA course; (4) a more pronounced LV outflow gradient reduction; (5) fewer patients in NYHA class III/IV at the last clinical check-up; and (6) less need for repeated septal reduction therapy.

Operator and institutional experience, especially the number of ASAs performed, is considered a key determinant of successful outcomes and lower complication rates for ASA.[1,2,14] Because HCM is relatively uncommon in general clinical practice and includes many different phenotypes, it is of a crucial importance to tailor the therapy specifically for each patient. Therefore, a careful clinical evaluation, echocardiographic, and magnetic resonance imaging assessment, risk stratification, and delivery of septal reduction should be performed in the context of a comprehensive program that addresses all aspects of HCM.[13-15] In this study, we confirmed the old saying, "practice makes perfect," and showed a significant association between institutional experience and an almost twofold lower incidence of periprocedural major adverse events, and significantly better efficacy and safety in long-term follow-up after an institutional experience of 50 ASA-procedures was achieved. Therefore, this is the first large study to confirm the expert opinion criteria for competence to perform ASA included in the 2011 American College of Cardiology Foundation/American Heart Association HCM guidelines.[1]

The fact that current guidelines recommend centralization of HCM patients in centres of excellence is not always followed by clinical practice. Recently, data from the Nationwide Inpatient Sample database showed that the real-world mortality rate associated with myectomy (or surgery that involves myectomy) to be 5.9%,[16] which stands in contrast to mortality rates < 1% reported by the best HCM centres of excellence.[17] Also, Kim et al. showed that 60% of US centres performed < 10 myectomies and 67% of centres performed < 10 ASA procedures during a 9-year period, suggesting that most American patients are offered septal reduction therapy in inexperienced centres.[18] Therefore, The Task Force on Clinical Competence and Training in Interventional Procedures proposed that each operator should perform the first 5 ASAs in a proctored situation with a skilled assistant.[19] However, on the basis of our results, this number of interventions might be still insufficient to achieve optimal results. Notably, clinical practice in the centres participating in this study showed that in all centres ASA was wisely kept in the hands of just 1 or 2 operators.

This study has some limitations. First, some inherent limitations of this sort of observational studies on the basis of institutional registries exist. Moreover, several centres established their ASA program at different times, and year of performed ASA was shown to be an independent predictor of long-term cardiovascular death. Therefore, institutions currently establishing an ASA program should incorporate contemporary knowledge about lower doses of alcohol, slower alcohol injections, improved septal branch selection on the basis of myocardial contrast echocardiography, and more judicious ASA case selection, which could help to achieve better results[20-22] (eg, during the start-up phase with the procedure), than suggested in this study. Additionally, a low rate of periprocedural complications in group of initially excluded patients (with implanted permanent pacemaker or ICD before ASA) suggests that complications related to manipulation with pacemaker lead and an appropriate therapy of a complete heart block or VT/VF might play a significant role in the short-term results of ASA. Second, the long-term prognosis of ASA can be influenced by the baseline risk profile of included patients. Because we do not know all of the risk factors of the patients included in this study and because the study was not randomized, it is not certain that treatment in experienced centres can improve the long-term cardiovascular mortality.

Accepting the limitations discussed previously, an institutional experience of > 50 ASA procedures was associated with a lower occurrence of ASA-attributable complications, better cardiovascular survival, better hemodynamic and clinical effect, and less of a need for repeated septal reduction therapy.

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Disclosures

The authors have no conflicts of interest to disclose.

References

1. Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy. Circulation 2011;124:e783-831.

2. Elliott PM, Anastasakis A, Borger MA, et al. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy. Eur Heart J 2014;35:2733-79.

3. Liebregts M, Vriesendorp PA, Mahmoodi PK, et al. A systematic review and meta-analysis of long-term outcomes after septal reduction therapy in patients with hypertrophic cardiomyopathy. JACC Heart Fail 2015;11:896-905.

4. Veselka J, Jensen MK, Liebregts M, et al. Long-term clinical outcome after alcohol septal ablation for obstructive hypertrophic cardiomyopathy: results from the Euro-ASA Registry. Eur Heart J 2016;37:1517-23.

5. Veselka J, Krejčí J, Tomašov P, Zemánek D. Long-term survival after alcohol septal ablation for hypertrophic obstructive cardiomyopathy: a comparison with general population. Eur Heart J 2014;35:2040-5.

6. Veselka J, Tomašov P, Krejčí J, Januška J, Adlová R. Obstruction after alcohol septal ablation is associated with cardiovascular mortality events. Heart 2016;102:1793-6.

7. Veselka J, Tomasov P, Zemanek D. Long-term effects of varying alcohol dosing in percutaneous septal ablation for obstructive hypertrophic

cardiomyopathy: a randomized study with a follow-up up to 11 years. Can J Cardiol 2011;27:763-7.

8. Jensen MK, Prinz C, Horstkotte D, et al. Alcohol septal ablation in patients with hypertrophic obstructive cardiomyopathy: low incidence of sudden cardiac death and reduced risk profile. Heart 2013;99:1012-7.

9. Nagueh SF, Groves BM, Schwartz L, et al. Alcohol septal ablation for the treatment of hypertrophic obstructive cardiomyopathy: a multicenter North American registry. J Am Coll Cardiol 2011;58:2322-8.

10. Veselka J, Lawrenz T, Stellbrink C, et al. Low incidence of procedure-related major adverse cardiac events after alcohol septal ablation for symptomatic hypertrophic obstructive cardiomyopathy. Can J Cardiol 2013;29:1415-21.

11. Veselka J, Krejčí J, Tomašov P, et al. Outcome of patients after alcohol septal ablation with permanent pacemaker implanted for periprocedural complete heart block. Int J Cardiol 2014;171:e37-8.

12. Steggerda RC, Damman K, Balt JC, et al. Periprocedural complications and long-term outcome after alcohol septal ablation versus surgical myectomy in hypertrophic obstructive cardiomyopathy: a single-center experience. JACC Cardiovasc Interv 2014;7:1227-34.

13. Veselka J, Anavekar NS, Charron P. Hypertrophic obstructive cardiomyopathy. Lancet 2017;389:1253-67.

14. Van der Lee C, Scholzel B, ten Berg JM, et al. Usefulness of clinical, echocardiographic, and procedural characteristics to predict outcome after percutaneous transluminal septal myocardial ablation. Am J Cardiol 2008;101:1315-20.

15. Sorajja P. Alcohol septal ablation for obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol 2017;70:489-94.

16. Panaich SS, Badheka AO, Chothani A, et al. Results of ventricular septal myectomy and hypertrophic cardiomyopathy (from Nationwide Inpatient sample [1998-2010]). Am J Cardiol 2014;114:1390-5.

17. Maron BJ, Yacoub M, Dearani JA. Controversies in cardiovascular medicine. Benefits of surgery in obstructive hypertrophic cardiomyopathy: bring septal myectomy back to European patients. Eur Heart J 2011;32:1055-8.

18. Kim LK, Swaminathan RW, Looser P, et al. Hospital volume outcomes after septal myectomy and alcohol septal ablation for treatment of obstructive hypertrophic cardiomyopathy. US Nationwide Inpatient Database, 2003-2011. JAMA Cardiol 2016;1:324-32.

19. Harold JG, Bass TA, Bashore TM, et al. ACCF/AHA/SCAI 2013 update of the clinical competence statement on coronary artery interventional procedures: a report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training (Writing Committee to Revise the 2007 Clinical Competence Statement on Cardiac Interventional Procedures). Circulation 2013;128:436-72.

20. Fifer MA, Sigwart U. Hypertrophic obstructive cardiomyopathy: alcohol septal ablation. Eur Heart J 2012;32:1059-64.

21. Veselka J, Procházková S, Duchonová R, et al. Alcohol septal ablation for hypertrophic obstructive cardiomyopathy: Lower alcohol dose reduces size of infarction and has comparable hemodynamic and clinical outcome. Catheter Cardiovasc Interv 2004;63:231-5.

22. Cooper RM, Raphael CE, Liebregts M, Anavekar N, Veselka J. New developments in hypertrophic cardiomyopathy. Can J Cardiol 2017;33:1254-65.