Long-term outcome of repeated septal reduction therapy after alcohol septal ablation for hypertrophic obstructive cardiomyopathy: insight from the Euro-ASA registry

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Two-thirds of patients with hypertrophic cardiomyopathy (HCM) have a significant left ventricular outflow tract (LVOT) obstruction that may be treated with alcohol septal ablation (ASA) dependent on symptoms [1]. However, some degree of obstruction may remain after ASA and if the patient remains symptomatic repeated septal reduction therapy (RSRT) may be indicated [1–5]. The outcome of RSRT remains unknown. In this study, we sought to determine the long-term outcomes of patients treated with ASA or myectomy after previous ASA.

A total of 1385 consecutive patients (48% women, mean age: 58 ±14 years) from nine European centres (Euro-ASA registry) who had been treated once with ASA as first time septal reduction therapy were enrolled in the study. We identified 145 (10%) patients who subsequently underwent RSRT, including 99 (68%) who underwent re-ASA, 31 (21%) who underwent myectomy, 12 (8%) who underwent re-ASA and myectomy, and 3 (2%) who underwent two further ASA procedures.

Patients were divided into those who had undergone only the initial ASA (group A, 1240 patients) and those who had undergone RSRT (group B, 145 patients). The primary end-point was major adverse cardiovascular events (MACE), defined as death related to any cardiovascular dis-

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

Parameter	Group A (n = 1240)	Group B (n = 145)	P-value
Age at baseline [years]	58.7 ±13.4	55.1 ±14.0	0.005
Females, *n* (%)	597 (48)	70 (48)	1.000
Dyspnoea, NYHA class:			
Baseline	2.9 ±0.5	2.9 ±0.4	0.760
Last clinical follow-up	1.7 ±0.7	2.0 ±0.8	< 0.001
NYHA class III/IV, *n* (%):			
Baseline	1041 (84)	124 (86)	0.628
Last clinical follow-up	142 (11)	38 (26)	< 0.001
Angina, CCS class:			
Baseline	1.2 ±1.2	1.1 ±1.1	0.339
Last clinical follow-up	0.7 ±0.8	0.5 ±0.8	< 0.001
LV outflow gradient at rest [mm Hg]:			
Baseline	69 ±38.9	78.3 ±37.1	< 0.001
Last clinical follow-up	15.4 ±20.8	21.5 ±26.6	< 0.001
> 30 mm Hg, *n* (%)	170 (14)	30 (21)	0.033
Delta gradient, % reduction	74.6 ±30.3	71.2 ±28.8	0.143
LV systolic diameter [mm]:			
Baseline	43.0 ±6.3	42.3 ±6.0	0.271
Last clinical check-up	45.4 ±6.2	45.7 ±6.2	0.639
LV ejection fraction (%):			
Baseline	70 ±9	69 ±9	0.061
Last clinical follow-up	66 ±10	65 ±8	0.054
Basal interventricular septum thickness [mm]:			
Baseline	20.5 ±4.2	21.4 ±4.2	0.004
Last clinical check-up	15.3 ±4.5	16 ±4.1	0.022
Left atrium diameter [mm]:			
Baseline	47.4 ±6.8	47.6 ±5.7	0.702
Last clinical check-up	45.8 ±7.2	46.1 ±6.5	0.499
Alcohol [ml]	2.1 ±0.9	3 ±1.5	< 0.001
Pacemaker, *n* (%):			
Baseline	51 (4.1)	6 (4.1)	1.000
Last clinical check-up	198 (16.0)	37 (25.5)	0.007
Implantable cardioverter-defibrillator, *n* (%):			
Baseline	63 (5.1)	6 (4.1)	0.840
Last clinical check-up	110 (8.9)	19 (13.1)	0.098
Mean follow-up duration [years]	5.4 ±4.2	6.5 ±4.1	

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

ease, sudden death, an appropriate implantable cardioverter-defibrillator discharge, resuscitation for ventricular fibrillation or death due to an unknown cause. Secondary endpoints were clinical symptoms and echocardiographic variables and number of implanted pacemakers at the last clinical check-up.

The septal reduction procedure was performed as described previously [1–6]. The indication for RSRT was at the discretion of each participating centre. Most patients underwent a routine clinical examination 3–6 months after ASA and then once per year including echocardiography [7–9]. All adverse events were confirmed by reviewing the medical records and/or national death registries.

Student's *t*-test, χ^2 test and Kaplan-Meier analysis were used as appropriate. The long-term occurrence of MACE was estimated using the Kaplan-Meier method, with the curves of groups A and B adjusted for age at ASA (60 years), baseline LVOT gradient (70 mm Hg), baseline septum thickness (20 mm) and baseline NYHA class (2.5). A *p*-value of < 0.05 was considered statistically significant.

A total of 1385 consecutive patients underwent ASA. A total of 12 (0.9%) patients died within 30 days after the first ASA and none died early after RSRT. In group B, the first RSRT was performed 1.9 ±1.9 years (range: 0.04–10.77 years) after the first ASA. The mean follow-up period was 6.5 ±4.1 years and none of the patients were lost to follow-up. The baseline (before first ASA) and long-term results are summarised in Table I. At the most recent clinical follow-up, group B patients were more symptomatic, had a higher residual LVOT gradient, and a larger proportion of the patients had a pacemaker implanted compared to group A patients (Table I). A total of 24 (24%) patients treated with ASA and re-ASA and 6 (19%) patients treated with ASA and myectomy underwent pacemaker implantation ($p = 0.81$). The percentage reduction of LVOT gradient was similar in patients who underwent ASA and re-ASA versus ASA and myectomy (71 ±29% vs. 70 ±29%; $p = 0.84$).

Survival free from MACE is presented in Figure 1.

The major findings in this study were as follows: 1) the incidence of MACE was similar among both groups of patients; 2) patients who required RSRT were younger, had a higher LVOT gradient and had a thicker interventricular septum at baseline; 3) RSRT is safe; 4) despite RSRT the patients had a higher residual LVOT gradient and worse dyspnoea and chest pain at the most recent follow-up; 5) repeated procedures were associated with an increased cumulative need for pacemaker implantation.

Currently, patients with only mild basal hypertrophy and redundant mitral apparatus, marked papillary muscle abnormalities, and mid-cavity obstruction are considered good candidates for myectomy. On the other hand, patients with less complex pathology might be treated with ASA. A growing body of evidence suggests that patients with HCM and a high LVOT gradient should be treated aggressively in order to eliminate or reduce the gradient to < 30 mm Hg [2, 3, 7]. However, it has not yet been established whether these patients should be submitted to the risk of undergoing RSRT or whether a conservative treatment approach would be more beneficial. Although this was an observational study only, our results suggest that the risk of MACE after repeated procedures is not increased compared to patients with a clinically satisfactory result after the first ASA.

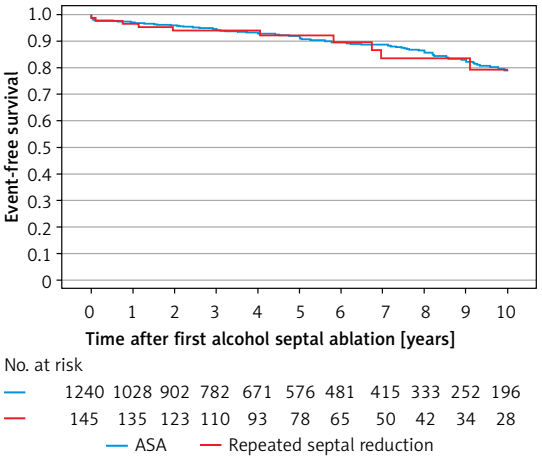

Figure 1. Kaplan-Meier curves showing MACE in patients after the first ASA (group A) and RSRT (group B) ($p = 0.165$)

In conclusion, repeated septal reduction therapy after ASA is not associated with a higher risk of major cardiovascular events over a long-term follow-up period but patients more often require pacemaker implantation.

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Conflict of interest

The authors declare no conflict of interest.

References

1. 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.
2. 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.

3. Maron MS, Olivotto I, Betocchi S, et al. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. N Engl J Med 2005; 384: 295-303.
4. 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.
5. Veselka J, Duchonova R, Palenickova J, et al. Age-related hemodynamic and morphologic differences in patients undergoing alcohol septal ablation for hypertrophic obstructive cardiomyopathy. Circ J 2006; 70: 880-4.
6. Veselka J, Zemánek D, Fiedler J, Šváb P. Real-time myocardial contrast echocardiography for echo-guided alcohol septal ablation. Arch Med Sci 2009; 5: 271-2.
7. Ziolkowska L, Petryka J, Boruc A, Kawalec W. Comparison of echocardiography with tissue Doppler imaging and magnetic resonance imaging with delayed enhancement in the assessment of children with hypertrophic cardiomyopathy. Arch Med Sci 2017; 13: 328-36.
8. Veselka J. Alcohol septal ablation for hypertrophic obstructive cardiomyopathy: a review of literature. Med Sci Monitor 2007; 13: RA62-8.
9. Scisło P, Kochanowski J, Kołtowski Ł, Opolski G. Utility and safety of tree-dimensional contrast low-dose dobutamine echocardiography in the evaluation of myocardial viability early after an acute myocardial infarction. Arch Med Sci 2018; 14: 488-93.