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, χ² 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.

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.

Acknowledgments

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Conflict of interest

The authors declare no conflict of interest.

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