

## ORIGINAL ARTICLE

# Reduction of left ventricular mass, left atrial size, and N-terminal pro-B-type natriuretic peptide level following alcohol septal ablation in patients with hypertrophic obstructive cardiomyopathy

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## Abstract

**Background:** Alcohol septal ablation (ASA) is an alternative to surgical treatment in patients with hypertrophic obstructive cardiomyopathy (HOCM). Through alcohol-induced necrosis, ASA leads to an increase in left ventricular outflow tract (LVOT) diameter and a decrease in LVOT pressure gradient.

**Aim:** We sought to assess the effect of ASA on left ventricular (LV) wall thickness and mass, left atrial (LA) size, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) level.

**Methods:** The study cohort consisted of 50 patients with HOCM (30 in the ASA group, 20 in the optimal pharmacotherapy group [OPG]). Transthoracic echocardiography (TTE), cardiac magnetic resonance (CMR), and NT-proBNP level analysis were performed at baseline and at six months.

**Results:** All parameters are presented as means. In the ASA group, the maximal LVOT pressure gradient decreased from 122.7 to 54.8 mmHg directly after ASA and to 37.2 mmHg after a further six months ( $p < 0.0001$ ). The NT-proBNP level decreased from 2174.4 to 1103.4 pg/mL ( $p < 0.001$ ). On TTE, the interventricular septum (IVS) thickness decreased to from 23.6 to 19.4 mm ( $p < 0.0001$ ) and the lateral wall (LW) thickness decreased from 15.9 to 14.2 mm ( $p < 0.007$ ). On CMR, basal IVS thickness decreased from 23.7 to 18.0 mm ( $p < 0.0001$ ) and the LW thickness decreased from 13.2 to 12.2 mm ( $p = 0.02$ ). IVS mass reduced from 108.9 to 91.5 g (−16%;  $p < 0.001$ ). All of the above parameters remained unchanged in the OPG.

**Conclusions:** Successful ASA reduces LV hypertrophy and improves parameters of the LV overload, resulting in LV wall hypertrophy regression, and LA size and NT-proBNP level reduction. The above parameters may be as useful in assessing the efficacy of ASA as the LVOT gradient itself.

**Key words:** alcohol septal ablation, hypertrophic obstructive cardiomyopathy, hypertrophy regression

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## INTRODUCTION

Alcohol septal ablation (ASA) was introduced two decades ago as a method of treatment for patients with hypertrophic obstructive cardiomyopathy (HOCM). Published data from high-volume centres confirmed its favourable short- and long-term clinical

outcomes. ASA results in regression of the basal segment of the interventricular septum (IVS) as well as reduction of mitral leaflet systolic anterior movement (SAM) and mitral regurgitation (MR). In effect, it reduces left ventricular outflow tract (LVOT) gradient, leading to clinical improvement of HOCM symptoms [1–4].

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Typically, successful ASA leads to a gradual reduction of LVOT gradient. The reduction may continue for as long as six to 12 months after the procedure, as a consequence of post-infarct left ventricular (LV) remodelling [5–8].

Some data point out the fact that the N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentration in HOCM patients is elevated [9, 10]. The highest NT-proBNP levels are usually observed in patients with LVOT obstruction, LV diastolic dysfunction, and massive LV hypertrophy (LVH) [9, 11]. Type B natriuretic peptide is released mostly by cardiomyocytes of the left ventricle in response to stretch stimuli. The serum concentration of NT-proBNP is directly proportional to the LV filling pressure and is considered a sensitive biochemical marker of LV dysfunction [12].

Until now few studies have evaluated the influence of ASA on the LV filling parameters [13, 14]. We attempted to reduce this gap by assessing the changes in left atrial (LA) size and NT-proBNP concentration, indirectly reflecting LV filling pressure, as well as LV mass changes.

## METHODS

This was a single-centre, prospective, observational study including 50 patients recruited between December 2006 and August 2010. The study was performed at the Institute of Cardiology, Warsaw, Poland.

The study group consisted of 30 consecutive HOCM patients (15 men) with a mean LVOT peak gradient of  $122.7 \pm 32.8$  mmHg, fulfilling the criteria for non-surgical ASA IVS gradient reduction. The final decision to perform ASA by injecting alcohol into the septal branch was made during an invasive diagnostic procedure directly preceding the injection, which involved several assessment modalities, including contrast echocardiography. The procedure was performed according to established standards [15]. Written, informed consent was obtained from all patients.

The optimal pharmacotherapy group (OPG) consisted of 20 patients (eight men) with a mean LVOT peak gradient of  $72.5 \pm 29$  mmHg, in whom ASA was not performed for the following reasons: lack of patient consent (six patients), thickness of the basal septal segment  $< 18$  mm (five patients), and unfavourable anatomy (lack of the septal branch or its location supplying the wrong area of the septum on echocardiographic contrast assessment, or a fistula from the septal branch to the right or left ventricle; nine patients). Because patients in the OPG were not candidates for surgical evaluation (myectomy), optimal pharmacotherapy was maintained.

All patients underwent transthoracic echocardiography (TTE) and had NT-proBNP serum levels assessed before and six months after the ASA procedure. In all eligible patients, cardiac magnetic resonance (CMR) was also performed. In OPG patients, blood samples were drawn at inclusion and at six months. In all cases, the samples were obtained after at least 30 min of bed rest.

The aims of the study were to confirm whether successful gradient reduction in patients with HOCM improves

selected parameters indirectly related to LV overload and to compare selected parameters between ASA-treated patients and the OPG.

## Ablation procedure

The technique of the ASA procedure has been described in our earlier papers [16, 17].

## CMR methodology and data analysis

Cardiac magnetic resonance imaging was performed in the supine position, using a 1.5 T Siemens Avanto scanner (Siemens, Erlangen, Germany). All examinations were done at the Institute of Cardiology, Warsaw, Poland.

Based on the preliminary views acquired using the black-blood spin echo sequences (half-Fourier acquisition single-shot turbo spin echo) in three planes — frontal, sagittal, and transverse — the long axis and the short axis of the heart were determined in each case.

Next, moving cinematic views were obtained using the steady-state free precession (SSFP) technique for the assessment of heart chamber dimensions and function. All acquisitions were electrocardiogram-gated. The two-chamber, three-chamber, and four-chamber long-axis views were recorded, as well as the serial short-axis views starting at the base of the heart and extending to the apex. The basic acquisition parameters of the balanced SSFP sequence were as follows: repetition time of 33–54 ms, echo time of 1.2 ms, flip angle of 64–79°, time resolution of 25 phases for each R-R interval, slice thickness of 8 mm, interslice interval of 1.6 mm, and field of view and matrix adjusted accordingly to suit the examination parameters.

All cinematographic acquisitions were analysed using the MASS software system (Medis, Leiden, Netherlands). This software allows for automatic delineation of endocardial borders with papillary muscle exclusion and manual fine tuning as necessary in all acquired layers, in end-systole and end-diastole. Based on this, ejection fraction as well as end-diastolic and end-systolic volumes are calculated. Muscle mass may be calculated as well. Late gadolinium enhancement was defined as heart muscle area with signal intensity after contrast enhancement equal to half of the maximum muscle signal intensity registered (full length at half maximum).

All flow sequences were analysed using dedicated software (Argus, Siemens, Erlangen, Germany). The extent of MR was presented as the regurgitation fraction calculated using the following formula:  $(LVSV [mL] - \text{aortic flow [mL]}) / LVSV [mL] \times 100\%$ , where LVSV represents LV stroke volume.

Cardiac magnetic resonance imaging was performed before ASA and six months after the procedure.

## Methodology of echocardiographic evaluation

Transthoracic echocardiography examinations were done at the Echocardiography Lab of the Institute of Cardiology

in Warsaw. M-mode, two-dimensional, and Doppler images were registered using Philips HD 15, GE Vivid 7, or GE Vivid I equipment (Philips, Amsterdam, Netherlands and GE, Boston, Massachusetts, USA). Standard views, including parasternal long-axis view, short-axis view at the levels of the mitral valve, chords, and papillary muscles, as well as apical four-chamber and two-chamber views were acquired. LV end-systolic and end-diastolic diameters were assessed, and the LA and diastolic muscle thickness (IVS, lateral wall [LW], and anterior wall) were measured. Other parameters assessed included the level of outflow obstruction, LVOT gradient, the extent of MR, SAM, the extent of LVH (and whether the middle LV segment was significantly affected), and the presence of an intraventricular obstruction.

Transthoracic echocardiography examination was performed at rest before, during, and two days after the ASA procedure. The examination was repeated before discharge, as well as at three- and six-month follow-up.

### Statistical analysis

Continuous variables were presented as means  $\pm$  standard deviation and categorical data as percentages. The sample size ( $n = 30$ ) for the study group was calculated based on  $\alpha = 0.05$  and  $\beta = 0.8$  and expected LVOT gradient reduction by 50% in TTE measurement. The study cohort consisted of 50 patients: 20 in the OPG and 30 in the study group.

All statistical analyses were done using the SAS 9.2 software (SAS Institute, Cary, NC, USA). The significance of normally distributed data was assessed with the paired Student *t* test, while for non-normally distributed data, non-parametric rank and log-rank tests were used. The normality of distribution was evaluated using Shapiro-Wilk test. The relation of variables was assessed by Pearson's correlation and linear regression in the case of normally distributed data. Non-parametric Spearman correlation was used for other variables. The significance of transformed categorical data was assessed using the McNamara test. The time point changes were evaluated using ANOVA for normally distributed variables and Wilcoxon's test for other variables. The significance level for all data was set at  $p = 0.05$ .

## RESULTS

The mean patient age at inclusion was  $56.9 \pm 11.9$  years in the study group and  $52.1 \pm 18.8$  years in the OPG ( $p = 0.13$ ). All patients were treated with at least one drug ( $\beta$ -blocker: 36 patients; calcium channel blocker: 12 patients;  $\beta$ -blocker and amiodarone: five patients). Baseline characteristics of both groups were similar apart from the peak gradient assessed by TTE (Table 1).

### Alcohol septal ablation procedure

During ASA the mean volume of absolute alcohol administered into the first or second septal branch was  $1.9 \pm 0.5$  mL. The creatine kinase-MB fraction (CK-MB) activity determined six and 12 h after ASA was  $107 \pm 55.9$  U and  $96.9 \pm 49$  U, re-

spectively, while troponin I (TnI) levels were  $33 \pm 32.8$  ng/mL and  $38.9 \pm 37$  ng/mL, respectively.

The LVOT peak gradient, assessed by TTE, was reduced from  $122.7 \pm 32.8$  mmHg at baseline, to  $54.8 \pm 37$  mmHg ( $p < 0.0001$ ) immediately after the procedure,  $51.8 \pm 37$  mmHg ( $p < 0.0001$ ) at month three, and  $37.2 \pm 27.8$  mmHg ( $p < 0.0001$ ) at month six.

In the OPG, the peak LVOT gradient was  $72.5 \pm 29$  mmHg at baseline,  $65.5 \pm 28.6$  mmHg at month three, and  $65.3 \pm 33$  mmHg at six months ( $p = 0.44$ ).

Procedural success (peak LVOT gradient below 50 mmHg or a 50% reduction in peak LVOT gradient) at six-month follow-up was achieved in 26 out of 30 (87%) ASA patients. A meaningful improvement in clinical status expressed as New York Heart Association (NYHA) class was also noted. Before ASA three patients were in NYHA class II, eight patients were in NYHA class II/III, and 19 patients were in NYHA class III. At six-month follow-up, 19 patients were in NYHA class I or I/II, six patients were in NYHA class II, and six patients were in NYHA class II/III or III (Table 2).

There was no significant improvement in clinical status at six months in the OPG (Table 2).

Six months after the ASA procedure the NT-proBNP serum level decreased from  $2174.4 \pm 819.8$  pg/mL to  $1103.4 \pm 618$  pg/mL ( $p < 0.0001$ ) (Fig. 1). NT-proBNP remained unchanged in the OPG, the levels were  $2133.9 \pm 1982.8$  pg/mL and  $2091.1 \pm 1601.2$  pg/mL ( $p = 0.18$ ) at baseline and at six months, respectively (Table 2).

### Echocardiographic evaluation

A trend toward a reduction in LA end-systolic diameter was observed in the group of ASA recipients (from  $47.4 \pm 6.4$  mm before ASA to  $45.2 \pm 5.4$  mm at month six;  $p = 0.06$ ). A reduction in MR severity was also noted in this group. On TTE evaluation before ASA, mild MR was noted in nine patients, moderate MR in 17 patients, and significant MR in four patients. After six months, the respective numbers of patients were 24 (mild MR), four (moderate MR), and two (significant MR). IVS thickness decreased from  $23.6 \pm 3.5$  mm at baseline to  $19.3 \pm 4$  mm ( $p < 0.0001$ ) and  $19.4 \pm 0.4$  mm ( $p < 0.0001$ ) at three- and six-month follow-up, respectively. Lateral wall thickness decreased from  $15.9 \pm 3.2$  mm to  $14.9 \pm 2.9$  mm ( $p = 0.046$ ) and  $14.2 \pm 2$  mm ( $p = 0.007$ ) at the same time points (Table 3).

In the OPG, all of the above TTE parameters remained unchanged after six months (Table 4).

### CMR evaluation

Due to the necessity of implanting a cardiac pacemaker (seven patients) or an automatic cardioverter-defibrillator (three patients) in some of the ASA patients, the CMR evaluation at six months could only be carried out in 20 out of 30 subjects in this group. On CMR evaluation, the MR volume decreased

Table 1. Baseline characteristics of both groups

	Study group (n = 30)	Pharmacotherapy group (n = 20)	p
Baseline characteristics:			
Age [years]	56.9 ± 11.9	52.1 ± 18.8	0.13
Male sex	15 (50)	8 (40)	0.49
NT-proBNP [pg/mL]	2174.4 ± 819.8	2133.9 ± 1982.8	0.31
NYHA II	3	4	
NYHA II/III	8	7	
NYHA III	19	9	
β-blocker	24	12	
Calcium channel blocker	7	5	
Amiodarone	3	2	
Echocardiographic data:			
PG max [mmHg]	122.7 ± 32.8	72.5 ± 29	0.02
EF [%]	71.0 ± 7.6	71.8 ± 8.2	0.36
LA size [mm]	47.4 ± 6.4	49 ± 6.4	0.19
LVEDD [mm]	44.5 ± 5.7	41.7 ± 9.6	0.1
LVEDD [mm]	24.6 ± 4.7	24.3 ± 4.0	0.39
IVSD [mm]	23.6 ± 3.5	24.6 ± 3.2	0.13
LWD [mm]	15.9 ± 3.2	14.8 ± 3	0.09
Mild MR	10	5	
Moderate MR	17	15	
Significant MR	3	0	
Cardiac magnetic resonance data:			
EF [%]	74.2 ± 5.6	72.4 ± 7.9	0.6
LV mass [g]	224.6 ± 59.3	198.8 ± 68	0.09
Aorta diameter [mm]	33.4 ± 4.9	33.2 ± 4.6	0.44
LA size [mm]	45.7 ± 8	46.6 ± 8.6	0.89
LVEDD [mm]	42.4 ± 7.4	44.5 ± 7.6	0.32
LVESD [mm]	21.2 ± 4.5	25.1 ± 7.4	0.06
IVSD [mm]	23.7 ± 2.8	24.4 ± 3.9	0.79
LWD [mm]	13.2 ± 3.4	12.5 ± 2.8	0.47
MR volume [mL]	31.9 ± 17	38 ± 13	0.17
Ergospirometric data:			
Exercise time [min]	9 ± 4.0	11.3 ± 4.0	0.06
METS	5.1 ± 1.7	6.1 ± 1.1	0.07
VO <sub>2</sub> /kg	17.4 ± 5.9	21.5 ± 6.9	0.03
% predicted VO <sub>2</sub> /kg	65 ± 18.2	69.8 ± 17	0.2

Data are shown as number (percentage) or mean ± standard deviation. EF — ejection fraction; IVSD — intraventricular septum diameter; LA — left atrium; LV — left ventricle; LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-systolic diameter; LWD — lateral wall diameter; METS — the metabolic equivalent of task; MR — mitral regurgitation; NT-proBNP — N-terminal pro-B-type natriuretic peptide; NYHA — New York Heart Association; PG max — maximal pressure gradient; VO<sub>2</sub> — the maximum rate of exercise oxygen consumption

from 31.9 ± 17 mL before ASA to 22 ± 9.5 mL after the procedure (p = 0.045). Using this imaging tool, we observed a non-significant LA diameter reduction in the study group at month six (from 45.7 ± 8 mm to 43.8 ± 8 mm; p = 0.16). The thickness of the basal part of the IVS decreased from

23.7 ± 2.8 mm to 18.0 ± 4 mm (p < 0.0001), while LW thickness decreased from 13.2 ± 3.4 mm to 12.2 ± 2.4 mm (p = 0.02) six months after ASA. There was also a significant reduction in LV ejection fraction, from 74.2% ± 5.6% to 71.4% ± 5.6% (p = 0.04) (Table 5).

**Table 2.** Cardiac failure symptoms in both groups, expressed as New York Heart Association (NYHA) class and serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels at baseline and at six-month follow-up

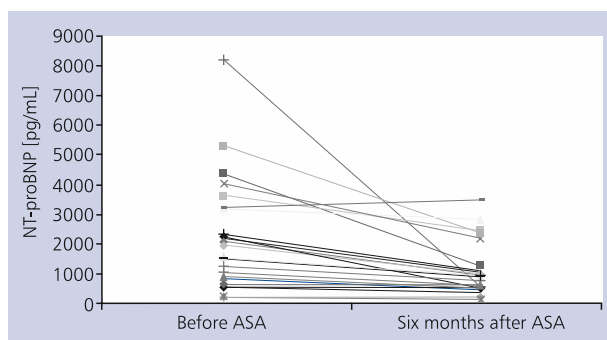
	Study group		Pharmacotherapy group	
	Baseline	Six-month follow-up	Baseline	Six-month follow-up
NT-proBNP [pg/mL]	2174.4 ± 819.8	1103.4 ± 618	2133.9 ± 1982.8	2091.1 ± 1601.2
NYHA I	0	11	0	0
NYHA I/II	0	8	0	0
NYHA II	3	6	4	5
NYHA II/III	8	3	7	8
NYHA III	19	2	9	7

Data are shown as number or mean ± standard deviation.

**Table 3.** Echocardiographic data of the study group before and six months after the alcohol septal ablation (ASA) procedure

	Echocardiographic data — study group			
	Baseline	Three months after ASA	Six months after ASA	p (baseline vs. six months)
PG max [mmHg]	122.8 ± 33	51.8 ± 37	37.2 ± 27.8	0.0001
EF [%]	71.0 ± 7.6	70.7 ± 6.6	63.3 ± 8.5	0.04
LA size [mm]	47.4 ± 6.4	45.9 ± 5.1	45.2 ± 5.4	0.06
LVEDD [mm]	44.5 ± 5.7	46.1 ± 4.6	47 ± 5.3	0.05
LVESD [mm]	24.6 ± 4.7	25.3 ± 4	25.5 ± 5.5	0.29
IVSD [mm]	23.6 ± 3.5	19.3 ± 4	19.4 ± 0.4	0.0001
LWD [mm]	15.9 ± 3.2	14.9 ± 2.9	14.2 ± 2	0.007
AWD [mm]	17.6 ± 3.4	15.8 ± 2.4	15.3 ± 2.8	0.06
Mild MR	9		24	
Moderate MR	17		4	
Significant MR	4		2	

Data are shown as number or mean ± standard deviation. AWD — anterior wall diameter; other abbreviations — see Table 1

**Figure 1.** Serum concentration of N-terminal pro-B-type natriuretic peptide (NT-proBNP) [pg/mL] before and six months after the alcohol septal ablation (ASA) procedure

In the OPG there was no difference between the above CMR parameters measured at baseline and at six-month follow-up (Table 6).

On CMR examination six months after the procedure, an area of late contrast enhancement corresponding to the post-ASA scar was observed. Mean infarct size was  $14.2 \pm 4$  g, which corresponded to  $8.0\% \pm 4.0\%$  of the total LV mass and  $16.2\% \pm 4.6\%$  of the IVS mass.

There was no correlation between the amount of alcohol injected, scar size, or CK-MB/Tnl level increase, and the necessity of pacemaker implantation.

Compared to the initial magnetic resonance image, none of the patients had a new area of fibrosis apart from the post-ASA scarring.

#### **LV muscle mass assessment in CMR in patients undergoing ASA compared to the OPG**

Intraventricular septum mass in ASA patients decreased from  $108.9 \pm 20.2$  g before the procedure to  $91.5 \pm 28.9$  g at six months ( $p = 0.01$ ), reflecting a 16% mass reduction. The decrease of the LV mass at six months was not significant ( $224.6 \pm 59.3$  g at baseline and  $183.8 \pm 77.9$  g at six months;

**Table 4.** Echocardiographic data of the optimal pharmacotherapy group at baseline and after sixth months of optimal pharmacotherapy

	Echocardiographic data — pharmacotherapy group		
	Baseline	After six months of optimal pharmacotherapy	p
PG max [mmHg]	72.5 ± 29	65.3 ± 33	0.44
EF [%]	71.8 ± 8.2	70.8 ± 8.1	0.35
LA size [mm]	49 ± 6.4	49.1 ± 7.9	0.48
LVEDD [mm]	41.7 ± 9.6	44.05 ± 7.0	0.18
LVESD [mm]	24.3 ± 4.0	25.8 ± 8.7	0.25
IVSD [mm]	24.6 ± 3.2	24.8 ± 3.8	0.8
LWD [mm]	14.8 ± 3	14.7 ± 2.8	0.47
Mild MR	5	5	
Moderate MR	15	15	
Significant MR	0	0	

Data are shown as number or mean ± standard deviation. Abbreviations — see Table 1

**Table 5.** Cardiac magnetic resonance data of the study group before and six months after the alcohol septal ablation (ASA) procedure

	Cardiac magnetic resonance data — study group		
	Baseline	Six months after ASA	P
EF [%]	74.2 ± 5.6	71.4 ± 5.6	0.04
LV mass [g]	224.6 ± 59.3	183.8 ± 77.9	0.18
Aorta diameter [mm]	33.4 ± 4.9	33.8 ± 3.8	0.45
LA size [mm]	45.7 ± 8	43.8 ± 8	0.16
LVEDD [mm]	42.4 ± 7.4	46.3 ± 5.8	0.02
LVESD [mm]	21.2 ± 4.5	27.6 ± 9.5	0.03
IVSD [mm]	23.7 ± 2.8	18.0 ± 4	0.0001
LWD [mm]	13.2 ± 3.4	12.2 ± 2.4	0.02
IVS mass [g]	108.9 ± 20.2	91.5 ± 28.9	0.01
Mass rest [g]	96.2 ± 34.6	92.8 ± 60	0.38
MR volume [mL]	31.9 ± 17	22 ± 9.5	0.045

Data are shown as mean ± standard deviation. Mass rest — total LV mass minus intraventricular septum (IVS) mass; other abbreviations — see Table 1

–18%;  $p = 0.18$ ). In the OPG neither the IVS mass nor the LV mass changed (Table 6).

#### ***The relation between outflow gradient reduction and the degree of LV remodelling and functional changes***

We observed a linear relationship between the LVOT peak gradient and LA diameter at six-month follow-up in the study group ( $p = 0.03$ ;  $r = 0.32$ ; Fig. 2A). A similar relationship was found between LVOT peak gradient and NT-proBNP level at six months ( $p = 0.005$ ;  $r = 0.4$ ; Fig. 2B, nonlinear regression).

There were no such relationships observed in the OPG.

## **DISCUSSION**

The aim of the study was to confirm whether a successful gradient reduction in patients with HOCM improves selected parameters related to LV overload.

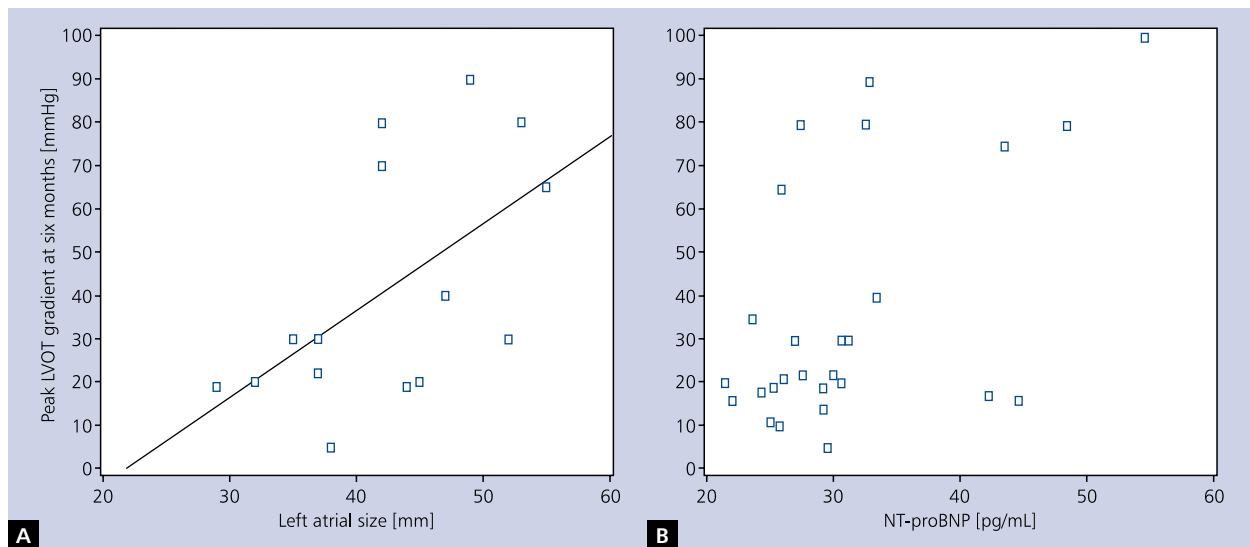
We found that successful ASA reduces LVH and serum NT-proBNP levels. There was also a trend toward LA size reduction, although statistical significance was not achieved.

In patients with HOCM, LA enlargement is a common finding, usually secondary to diastolic LV dysfunction and resultant LA overload. Diastolic heart failure often seen in patients with HOCM is the reason for elevated end-diastolic LV pressure and LV filling pressure, leading to LA enlargement [18]. An additional

**Table 6.** Cardiac magnetic resonance data of the optimal pharmacotherapy group at baseline and at six-month follow-up

	Cardiac magnetic resonance data — pharmacotherapy group		
	Baseline	After six months of optimal pharmacotherapy	p
EF [%]	72.4 ± 7.9	72.6 ± 4.7	0.46
LV mass [g]	198.8 ± 68	204.9 ± 56.8	0.39
Aorta diameter [mm]	33.2 ± 4.6	32.3 ± 6.2	0.36
LA size [mm]	46.6 ± 8.6	44.1 ± 7.6	0.25
LVEDD [mm]	44.5 ± 7.6	44.2 ± 4	0.44
LVESD [mm]	25.1 ± 7.4	23.4 ± 4.8	0.28
IVSD [mm]	24.4 ± 3.9	25.6 ± 3.6	0.22
LWD [mm]	12.5 ± 2.8	12.1 ± 2.6	0.37
MR volume [mL]	38 ± 13	36.9 ± 14.7	0.43

Data are shown as mean ± standard deviation. Abbreviations — see Table 1



**Figure 2.** The relation between left ventricular outflow tract (LVOT) gradient at six months post alcohol septal ablation procedure and left atrial size (**A**), as well as N-terminal pro-B-type natriuretic peptide (NT-proBNP) level (**B**). In the case of panel B, linear regression analysis could not be performed due to non-normal data distribution

detrimental factor increasing LA overload and, in effect, LA size is MR observed in patients with HOCM and SAM. In cases of significant MR there is additional volume overload of LA leading to its enlargement [18, 19]. ASA modifies the Venturi effect, partly responsible for anterior mitral leaflet movement toward the outflow tract, decreasing or even eliminating SAM and MR.

In the group of patients who underwent ASA, a trend toward LA size reduction was observed. Additionally, in this group we found significant linear relations between the mean LA size assessed in TTE and: (1) mean LW thickness evaluated by CMR; (2) mean LV mass excluding the IVS assessed by CMR; (3) mean LW thickness on TTE measurement.

The above data confirm some earlier observations suggesting that successful ASA leads to partial regression of LVH and improves LV diastolic function, thereby decreasing LA size [19, 20].

Nagueh et al. [19] investigated LV remodelling and causes for LA volume changes in HOCM patients after ASA. The authors confirmed that six months after ASA the LA volume decreases, and so does the severity of MR. Also, they showed a parallel improvement of LV filling parameters.

Based on CMR measurements, in a group of 52 patients at one week and one year after a successful ASA, Yuan et al. [21] also observed a significant reduction in LA size.

In another study assessing the effect of ASA and gradient reduction on LA size, the authors used three-dimensional (3D) TTE [20]. They performed ASA in a group of 12 patients who underwent 3D TTE, in which the end-diastolic and end-systolic LA volumes were measured. Consequently, the LA ejection fraction (LAEF) was calculated. These measurements were done before ASA and three months after. Significant LA size reduction and LAEF increase were noted. Moreover, the LAEF increase was correlated with LVOT gradient reduction [20]. Although the primary objective of the paper was to validate 3D TTE as a precise modality of LA assessment, proving that it is superior to standard TTE in this respect and offers similar precision to CMR, the authors also underscored the utility of LA volume assessment as a marker of chronic diastolic LV dysfunction.

As muscle relaxation during the phase of isovolumetric diastole improves, so does the elasticity of the LV during diastole. In effect, LV filling pressures decrease, and volumes increase, thereby leading to LA size reduction [22]. At the same time, reduced degree of MR after ASA decreases LA preload, which is an additional mechanism leading to LA size reduction [23–25].

Our study supports the view that successful LVOT gradient reduction leads to at least some regression of LVH. Furthermore, by improving the diastole and reducing the degree of MR, a successful ASA procedure may reduce LA size. An interesting observation made in this study is a linear correlation of LA size assessed by CMR and NT-proBNP concentration at six months after ASA.

Several studies have raised the problem of elevated BNP levels in patients with HOCM [9, 10]. This was particularly noticeable in patients with HOCM and LVOT obstruction, diastolic LV dysfunction, and massive muscle hypertrophy [9–11, 26].

Impaired relaxation of the LV in HOCM patients has been mostly held responsible for muscle wall strain and increased BNP synthesis and release [27]. In the investigated group of patients after successful ASA, the LVOT gradient decrease and LVH regression were accompanied by a significant reduction in NT-proBNP levels [27, 28].

Based both on published data and the results of this study, LVH regression extending also beyond the septal region is the most stable marker documenting the improvement of LV haemodynamics [28, 29]. It is much more reliable than the LVOT gradient itself. The latter varies widely by nature and seems an inadequate measure of subaortic outflow obstruction [30–33]. Possibly, other parameters, easier to assess and more stable, may hold a similar value. These may be the LA size, which we have failed to satisfactorily demonstrate in this study, and, more likely, serum NT-proBNP level reduction. According to data presented in this paper, measurement of NT-proBNP level should complement the assessment of LVH reduction and may also be used as an independent parameter of ASA efficacy due to its accessibility.

For a single-centre study the group of enrolled patients was limited. This was by necessity a non-randomised study, which may be the reason for the insignificant total/lateral wall mass reduction on CMR. The number of parameters assessed could have been more extensive; we did not assess tissue Doppler, 3D echo examination, and strain echo parameters, which may have added some more valuable information. However, we primarily attempted to assess the value of easily accessible parameters reflecting haemodynamic improvement in patients after ASA.

In conclusion, successful ASA leads to partial regression of LVH, also beyond the septal region itself, and improves LV diastolic function. This is reflected by serum NT-proBNP level reduction. Assessing these parameters as part of routine follow-up in patients after ASA may help to precisely evaluate the efficacy of the procedure, more reliably, perhaps, than the measurement of the LVOT gradient alone.

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#### WHAT IS NEW?

This single-centre, prospective, observational analysis is one of the largest studies confirming the efficacy of alcohol septal ablation in direct comparison to optimal pharmacotherapy. Magnetic resonance imaging data on the assessment of left ventricular wall remodelling as a result of a successful alcohol ablation procedure are still limited. The study confirms that significant left ventricular outflow tract (LVOT) gradient reduction leads to the regression of diffuse left ventricular hypertrophy and improves parameters of left ventricular overload. The new finding is that alcohol septal ablation also results in the reduction of in N-terminal pro-B-type natriuretic peptide level. The above parameters may be as useful in assessing the efficacy of alcohol septal ablation as the LVOT gradient itself, and they can be more stable markers of significant and permanent LVOT gradient reduction.