*Original article*

# Patterns of post-MI left ventricular volume changes – clinical implications

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**Abstract**

**Background:** Left ventricular (LV) enlargement – the main discriminant of postinfarction remodelling – is dynamic and not necessarily progressive. The magnitude of the remodelling process is directly proportional to infarct size (IS), although it is significantly influenced by other factors.

**Aim:** To assess the clinical implications of different patterns of LV volume changes in 1-year echocardiographic follow-up after myocardial infarction (MI) and to determine early predictors of adverse remodelling.

**Methods:** The study group consisted of 132 patients (pts) (mean age 55.7±12 years) with their first MI (STEMI) (67% pts treated with fibrinolysis). In the consecutive ECHO examinations (S1, first day; S2, at discharge; S3, 6 months; and S4, one year after MI) the following parameters were assessed: WMSI, EDVI, ESVI, LVEF, LV sphericity index (WSF), index of infarct expansion (EXP), restrictive pattern of mitral flow (RP), grade of mitral regurgitation (MR). The criterion of significant LV dilatation was EDVI ≥85 ml/m$^2$ and/or ΔEDVI ≥20% between two succeeding ECHO. At S3 pts were classified into groups: group 1 with no LV dilatation (n=68), group 2 with early transient LV dilatation (S1 and/or S2) (n=26), group 3 with progressive (S1 – S2 – S3) LV dilatation (n=28). The prognostic value of the following parameters was assessed: anterior infarct location, Q-wave MI, Killip-Kimball class ≥2, lack of noninvasive assessed reperfusion R(–), EXP(+), CK ≥3000 IU, $WMSI_{S2}$ ≥1.5, $EDVI_{S2}$ ≥80 ml/m$^2$, $ESVI_{S2}$ ≥40 ml/m$^2$, $EF_{S2}$ <45%, $RP_{S2}$ and baseline LV hypertrophy (S1).

**Results:** Patients in group 3 had significantly larger IS (WMSI) than in group 1 (p <0.01) and group 2 (p <0.05). Infarct expansion was found only in group 3. One year after MI in group 3 compared to groups 1 and 2 adverse remodelling was observed: lower $EF_{S4}$ (p <0.001), more spherical LV ($WSF_{S4}$) (p <0.001), higher rate of $MR_{S4}$ ≥2 (p <0.001) and $RP_{S4}$ (p <0.001). Within each group $LVEF_{S1\text{-}S4}$ was stable in one-year follow-up. In group 3 incidence of heart failure (HF) was significantly higher than in groups 1 and 2 (respectively 57 vs. 2 vs. 4%; p <0.001). Cardiac death (CD) was observed only in group 3 (25% of pts). Increased EDVI ≥80 ml/m$^2$ at discharge was the most powerful independent predictor of progressive LV dilatation. Large IS (CK ≥3000 IU and/or WMSI ≥1.5) was not an independent predictor of adverse remodelling.

**Conclusions:** 1) During the first 6 months after MI the progression of LV dilatation was a useful sign identifying adverse remodelling, even in the absence of LVEF evolutionary changes. Progressive LV dilatation was associated with more spherical LV and higher rate of MR ≥2°. 2) Patients with progressive LV were at higher risks of HF and CD in one-year follow-up. 3) Increased EDVI ≥80 ml/m$^2$ at discharge was the most powerful independent predictor of adverse postinfarction remodelling. Large IS was not an independent predictor. 4) Echocardiographic monitoring after MI is of great clinical importance – it enables pts at higher risk of HF and CD to be identified.

**Key words:** postinfarction remodelling, echocardiography, prognosis after myocardial infarcion

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## Introduction

In 1986 McKay et al. introduced the term 'postinfarction remodelling' to describe the process of global enlargement of the left ventricle (LV) after transmural myocardial infarction (MI) and showed that the degree of such remodelling correlates with the size of the infarction [1]. Focal loss of myocardium leads to a sudden increase in LV loading and therefore initiates a number of compensatory changes that in unfavourable circumstances may lead to heart failure (HF) [1-4]. Global enlargement of the LV, the major sign of structural remodelling [1, 4-7], is a dynamic process [2, 7, 8]. One of the most important factors determining the scale of heart remodelling, along with the size of MI, is secure and

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maintained patency of the infarct-related artery (IRA) [2, 9]. In the era of fibrinolytic therapy it was shown that patients with long-term marked enlargement of the LV account for 16-20% of all post-MI patients [7, 8, 10]. In times of interventional treatment of acute MI, despite all the advances increasing reperfusion efficacy and survival, the percentage of patients with long-term enlargement of the LV is similar [11]. The clinical data indicate that the process of heart remodelling is heterogeneous. Its determinants have not been completely recognised and indicators of unfavourable prognosis are still being sought.

The aim of the study was to investigate, in an one--year observation, the dynamics of selected echocardiographic parameters of the structure and function of the LV after MI treated with fibrinolytic therapy, to identify different patterns of LV volume changes and to define their influence on the function of the ventricle as well as on the occurrence of adverse clinical events [HF and cardiac death (CD)]. An attempt was also undertaken to find which clinical and echocardiographic parameters, evaluated early post MI, help to predict the development of adverse cardiac remodelling.

## Methods

### The study group

The study group included 132 patients (99 men, 33 women) aged 27-80 years (average age 55.7±12) with the first ST elevation MI (STEMI) (67% treated with fibrinolysis; 33% with contraindications for fibrinolytic treatment). Patients with heart valve disease and those presenting with ischaemic mitral valve regurgitation (MR) >1° in the first echocardiographic examination were excluded. In the acute stage of MI, the Killip class was established in all patients and, based on the electrocardiogram, the type (Q, non-Q) and location (anterior, inferior) of MI were defined. The group of patients with inferior wall MI also included patients who failed to meet the criteria for anterior wall MI. In patients treated with fibrinolysis the reperfusion was assessed non-invasively – based on pain relief, ventricular arrhythmia, significant (>50%) reduction of ST segment elevation within 90 minutes from the onset of fibrinolysis, and early (<12 h) peak of creatine phosphokinase MB isoenzyme (CK-MB) activity.

### Echocardiography

Serial echocardiographic examinations were performed: in the first twenty-four hours of MI (examination 1), on discharge (examination 2), in 6 months (examination 3) and at one year after MI (examination 4). Echocardiogram consisted of recording M-mode and 2D images in all standard transthoracic views (according to ASE [12]) and Doppler examination. Hypertrophy of the LV was diagnosed on examination 1 if the interventricular septum and/or the LV posterior wall (PW) thickness was >11 mm. The LV end-diastolic volume (EDV) and end-systolic volume (ESV) as well as LV ejection fraction (LVEF) were calculated according to the modified Simpson's formula [12]. The LV volume index was calculated as the ratio of the volume to the body surface area. The reference values of the LV volume index, established on the basis of examination of 20 subjects without heart disease, at similar age and with comparable demographic characteristics were: for EDV index (EDVI) 63±10.6 ml/m$^2$, and for ESV index (ESVI) 23.5±9.4 ml/m$^2$. The criteria of significant enlargement of the LV were defined as EDVI ≥85 ml/m$^2$ and/or ΔEDVI ≥20% (ΔEDVI – presented as the relative increase of EDVI as a percentage between two consecutive examinations). The sphericity index (WSF[%]) was defined as a parameter of LV geometry and was calculated according to the formula WSF=($a$/$b$) × 100 ($a$ – mean transverse section area of the LV chamber during end-diastole in parasternal short axis view measured at the level of papillary muscles [cm$^2$]; $b$ – mean longitudinal section area of the LV during end-systole in apical 4C view [cm$^2$]). In the semi--quantitative assessment of LV contractility impairment, the division into 16 segments was used according to ASE [12] and the following scores of contractility abnormalities were adopted: 1 – normokinesis, 2 – hypokinesis, 3 – akinesis, 4 – dyskinesis. In order to estimate the size of MI by echocardiography, LV wall motion score index was calculated (WMSI) (summed scores of all segments divided by number of examined segments). As a biochemical criterion to estimate the size of MI, serum peak concentration of creatine phosphokinase was used (CK). The cut-off values to recognise large cardiac infarction were WMSI ≥1.5 and/or CK ≥3000 IU. Expansion of the infarction was identified in echocardiography using the expansion index (EXP) introduced by Jugdutt et al. [13]. Significant expansion was defined as an increase of EXP of at least 25% in the second examination compared to examination 1. Based on the Doppler examination two patterns of LV filling were distinguished: 1) restrictive (RP), when E/A ≥2 or E/A 1.5-2.0 and DT ≤140 ms; 2) non-restrictive, when these criteria were not met. Mitral valve regurgitation was assessed with the colour Doppler examination, using semi--quantitative methods (combined evaluation of the depth and width of the regurgitation jet, relative surface area of the wave as well as vena contracta with in at least two planes), with the following grading of regurgitation severity: level 0° – non-existent, 1° – mild, 2° – moderate, 3° – medium severe, 4° – severe. All analysed parameters are listed in Table I.

### Subgroups

At 6 months after MI (examination 3) the following groups of patients were identified: group 1 – without significant enlargement of the LV in examinations 1, 2 and 3 (n=68); group 2 – with transient enlargement of the LV (significant enlargement only in the early period of follow-up examination 1 and/or 2) (n=26); group 3 – with

**Table I.** Parameters assessed by echocardiography

| Parameter | Abbreviation [unit] |
|---|---|
| Thickness of LV posterior wall | PW [mm] |
| Thickness of interventricular septum | IVS [mm] |
| LV end-diastolic volume | EDV [ml$^3$] |
| LV end-systolic volume | ESV [ml$^3$] |
| LV ejection fraction | EF [%] |
| Peak flow velocity of early LV filling wave | E [m/s] |
| Peak flow velocity of late LV filling wave | A [m/s] |
| Ratio of E to A | E/A |
| Deceleration time of early LV filling wave | DT [ms] |
| LV end-diastolic volume index | EDVI [ml/m$^2$] |
| LV end-systolic volume index | ESVI [ml/m$^2$] |
| LV sphericity index | WSF |
| Infarct expansion index | EXP |
| Restrictive pattern of LV filling by Doppler | RP |
| Mitral valve regurgitation | MR [1°-4°] |
| LV muscle hypertrophy | mLV hypertrophy |

progressive dilatation of the LV (significant enlargement in consecutive examinations 1, 2 and 3) (n=28).

### Late observations

Between the 6$^{th}$ and 12$^{th}$ month post MI, echocardiographic follow-up of patients was continued and all adverse clinical events, such as HF and CD, were recorded. The symptoms of HF as well as date of CD were established based on clinical examination and available documents.

### Statistical analysis

In all study groups the mean values and standard deviations of all evaluated parameters were calculated. Hypotheses of mean values in each group being equal were verified using variance analysis or, in groups with heterogeneous variance, Wilcoxon's test (variance homogeneity was verified using Lavene's test). Discrete parameters were compared using $\chi^2$ test with Yates' correction or Fisher's test (depending on expected value) whereas continuous variables – using Student's t-test. To predict progressive enlargement of the LV, univariate analysis was carried out, using Mantel-Haenszel's test, and multivariable analysis was performed using a regression model of Cox proportional hazard. Values of $p \leq 0.05$ were considered statistically significant. To predict the occurrence of progressive LV dilatation, the prognostic value of the following (categorised) variables was analysed: age >60 years, anterior location of the MI, Q-wave infarct, absence of reperfusion [Rep(–)], Killip class ≥2, peak level of CK ≥3000 IU, presence of LV hypertrophy at baseline (examination 1), as well as of the following parameters at discharge from the hospital: $WMSI_2$ ≥1.5, $EDVI_2$ ≥80 ml/m$^2$, $ESVI_2$ ≥40 ml/m$^2$, $LVEF_2$ <45%, significant infarct expansion [EXP(+)], restrictive pattern of LV filling (RP). Statistical analysis was carried out using the computer package STATISTICA Ver.5.1.

## Results

**Clinical characteristics of examined groups of subjects with defined patterns of changes in LV volume.** Table II demonstrates the clinical characteristics of the groups: group 1 (without LV enlargement during the whole follow-up period), group 2 (with transient LV enlargement in the early period), and group 3 (with progressive LV enlargement). Patients who developed progressive LV dilatation (group 3) presented with significantly greater mean MI size compared with groups 1 and 2, assessed in both biochemical (CK) as well as in echocardiographic (WMSI) evaluation. This group also included a considerable proportion of patients with significant infarction expansion (39%), contrary to groups 1 and 2, in which MI expansion did not occur. Patients with progressive LV enlargement more frequently presented symptoms of heart failure in acute MI phase (Killip class ≥2). Of note, there were no significant differences in demographic, clinical and echocardiographic variables between groups 1 and 2.

**Analysis of dynamics of echocardiographic structural and functional parameters of LV changes as well as of the prevalence of adverse clinical events in groups with different LV enlargement patterns.** Figure 1 demonstrates trend graphs of the echocardiographic parameters of LV structure and function in groups with different patterns of LV volume changes. Table III presents mean values of parameters of LV geometry and function, recorded at the end of one-year follow-up, as well as prevalence of adverse clinical events. Significant differences of mean EDVI and ESVI between groups 1 vs. 2, 1 vs. 3, and 2 vs. 3 are obvious as LV enlargement – along with its evolution pattern – was a criterion for group identification. In the group with progressive LV dilatation (group 3) the increase of ventricle sphericity ($WSF_{1-4}$) was parallel with volume change (Figure 1).

Of note, even though throughout the entire follow-up period the mean value of LVEF was permanently significantly lower in group 3 than in all other groups, its value was relatively stable in all analysed groups, and did not significantly change during one-year follow-up ($EF_{1-4}$) (Figure 1). There were significant differences in mean LV volume between groups 1 and 2 only at discharge from hospital ($EDVI_2$, $ESVI_2$). Except for that moment, mean LV volume did not differ between the groups (Figure 1). No significant differences in LV sphericity between groups 1 and 2 were noted throughout the entire study period (Figure 1). At one year after MI, patients with progressive LV dilatation presented with increased sphericity and lower

**Table II.** Clinical characteristics of study groups: group 1 – without LV enlargement; group 2 – with transient LV enlargement; group 3 – with progressive LV enlargement

| Variable | Group 1 (n=68) | Group 2 (n=26) | Group 3 (n=28) | p |
|---|---|---|---|---|
| Age [years] | 56.5±12.0 | 53.9±12.2 | 55.4±12.4 | NS |
| Male gender | 47 (69%) | 21 (81%) | 22 (79%) | NS |
| Heart rate [beats/min] | 71.6±9.2 | 68.1±11.6 | 76.7±10.3 | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.05<br>group 2 vs. group 3: <0.01 |
| Killip class ≥2 | 1/67 (1.5%) | 1 (4%) | 9 (32%) | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.001<br>group 2 vs. group 3: <0.05 |
| CK [IU] | 1136±993 | 1482±1813 | 2775±2212 | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.01<br>group 2 vs. group 3: <0.05 |
| WMSI | 1.29±0.2 | 1.35±0.3 | 1.56±0.3 | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.01<br>group 2 vs. group 3: <0.05 |
| Anterior infarct | 22 (32%) | 14 (54%) | 15 (54%) | NS |
| Q wave MI | 54 (79%) | 18 (69%) | 28 (100%) | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.01<br>group 2 vs. group 3: <0.01 |
| EXP | 0 | 0 | 11 (39%) | |
| Hypertrophy $mLV_{bad.1}$ | 54 (79%) | 20 (77%) | 22 (79%) | NS |
| Diabetes | 10 (15%) | 3 (12%) | 1 (4%) | NS |
| Hypertension | 41 (60%) | 15 (58%) | 13 (46%) | NS |
| Cigarette smoking | 49 (72%) | 22 (85%) | 21 (75%) | NS |
| Hyperlipidaemia | 44 (65%) | 19 (73%) | 21 (75%) | NS |
| | | Used medications | | |
| Angiotensin-converting enzyme inhibitors | 52 (76%) | 19 (73%) | 24 (86%) | NS |
| Beta-blockers | 54 (79%) | 22 (85%) | 20 (71%) | NS |
| Statins | 34 (50%) | 18 (69%) | 12 (42%) | NS |
| Diuretics | 12 (18%) | 8 (31%) | 24 (86%) | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.001<br>group 2 vs. group 3: <0.001 |

*Abbreviations: see Table I*

**Table III.** Mean values of selected echocardiographic parameters and the rate of adverse clinical events in study groups. The mean values ± SD and numbers and percentages (in brackets) of patients are presented

| Parameter | Group 1 (n=68) | Group 2 (n=26) | Group 3 (n=28) | p |
|---|---|---|---|---|
| $WSF_4$ [%] | 36.9±7.6 | 37.9±7.8 | 51.8±9.3 | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.001<br>group 2 vs. group 3: <0.001 |
| $EF_4$ [%] | 62.2±7.2 | 63.5±6.0 | 48.6±9.4 | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.001<br>group 2 vs. group 3: <0.001 |
| $MR_4$ ≥2° | 2 (3%) | 0 | 13 (62%) | group 1 vs. group 3: <0.001 |
| $RP_4$ | 4 (6%) | 1 (4%) | 12 (57%) | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.001<br>group 2 vs. group 3: <0.001 |
| Cardiac death | 0 | 0 | 7 (25%) | |
| Heart failure in one-year follow-up | 1 (2%) | 1 (4%) | 16 (57%) | group 1 vs. group 2: NS<br>group 1 vs. group 3: <0.001<br>group 2 vs. group 3: <0.001 |

*Abbreviations: see Table I*

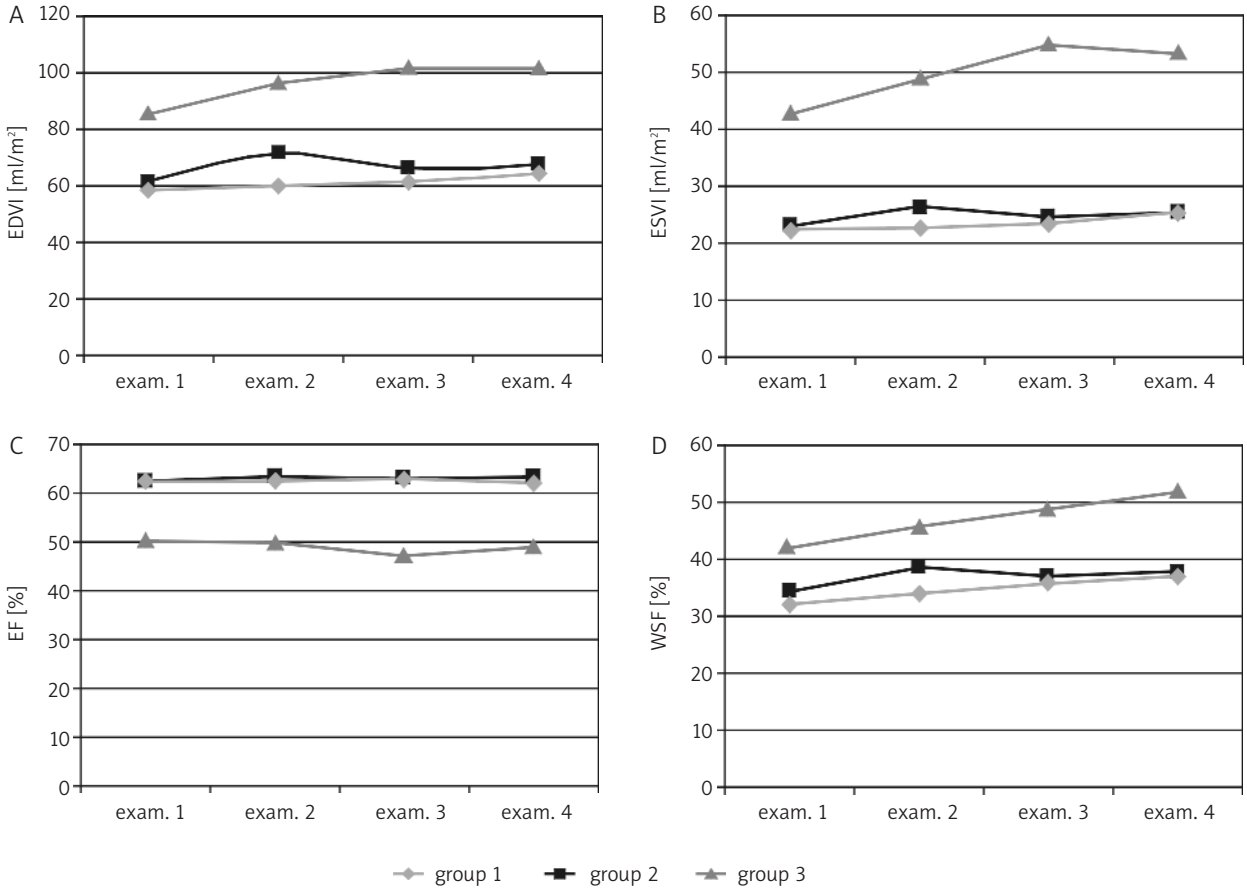


**Figure 1.** Changes of analysed echocardiographic parameters over the follow-up period. Examination 4: group 1 vs. group 2: NS; group 1 vs. group 3: p <0.001; group 2 vs. group 3: p 0.001 (for all four depicted parameters)

mean LVEF than patients in groups 1 and 2 (Table II). The percentage of patients with RP was higher in group 3 than in the other groups and MR ≥2° was more frequent as well (Table III). Patients with progressive LV enlargement significantly more frequently developed HF (57%) compared to patients from groups 1 (2%) and 2 (4%) (Table III). Between the 6th and the 12th month of observation, CD occurred in every fourth patient (25%) in group 3, while in groups 1 and 2 no deaths were observed (Table III). There were no significant differences between groups 1 and 2 in terms of adverse clinical events (HF, CD) (Table III). The groups also did not differ in terms of ACEI and beta-blocker therapy (Table II). The significantly greater percentage of patients treated with diuretics (Table II) in group 3 is not surprising, given the higher prevalence of HF in this group (Table III).

**Analysis of prognostic value of selected clinical and echocardiographic variables in predicting the development of progressive LV dilatation.** Tables IV and V demonstrate the results of analysis of the influence of the selected variables (categorised) on the occurrence of progressive LV dilatation. Univariate analysis confirmed the prognostic value of the majority of them (Table IV). Multivariable factor Cox's analysis revealed that only high EDVI value (≥80 ml/m²) noted at discharge from the hospital and no reperfusion signs (estimated non-invasively) independently predicted the development of LV dilatation (Table V).

## Discussion

Our observations confirmed the heterogeneous nature of post-infarction LV remodelling. Changes in LV volume were not unidirectional. In 21% of patients the increase of LV volume turned out to be progressive, while in 20% of patients early enlargement of LV regressed within 6 months. From a theoretical MI model it might be assumed that LV enlargement, allowing the restoration of ejection function, must occur if the contracting myocardium loss exceeds 20% of the ventricular mass [14]. This mechanism is therefore mainly compensatory. Degree of LV enlargement and the evolution of LV volume changes depend, however, on multifactorial interactions, such as the size of necrosis, infarct-related artery patency, haemodynamic factors, compensatory hypertrophy of myocardium, and intensity of neuron--hormone activation [1-4, 10, 15, 16]. Global LV enlargement is a dynamic process [2, 7, 8]. During the

**Table IV.** Univariate analysis of the effects of categorised variables on progressive LV dilatation occurrence

| Parameter | Progressive LV dilatation (+) | (–) | Relative risk [RR] | 95% CI for RR | p |
|---|---|---|---|---|---|
| Killip-class ≥2 | 9/19 | 10/94 | 2.82 | 1.51-5.27 | 0.00268 |
| Myocardial infarction | 15/13 | 42/62 | | | 0.213 |
| Q/n – Q | 28/0 | 82/22 | | | 0.00791 |
| CK ≥3000 IU | 9/17 | 5/69 | 3.25 | 1.83-5.80 | 0.00046 |
| WMSI ≥1.5 | 17/11 | 11/83 | 5.19 | 2.76-9.74 | 0.00000 |
| Reperfusion (–) | 14/4 | 18/52 | 6.13 | 2.20-17.03 | 0.00005 |
| EXP (+) | 11/17 | 0/94 | 6.53 | 4.22-10.11 | 0.00000 |
| $mLV_{exam.\,1}$ hypertrophy | 22/6 | 80/24 | | | 0.854 |
| EF2 <45% | 9/19 | 3/93 | 4.42 | 2.62-7.47 | 0.00001 |
| $EDVI_2$ ≥80 ml/m² | 23/5 | 9/85 | 12.94 | 5.37-31.2 | 0.00000 |
| $ESVI_2$ ≥40 ml/m² | 17/11 | 3/91 | 7.88 | 4.38-14.2 | 0.00000 |
| $RP_2$ | 13/15 | 1/103 | 7.3 | 4.45-11.98 | 0.00000 |

first few days following MI, early LV dilatation occurs, especially when the infarction expands. McKay et al. demonstrated that early global enlargement of the ventricle, based on the Frank-Starling mechanism being an important component of it, is mainly compensatory and can subsequently stabilise or regress [1].

Patterns of LV volume changes after MI have been the subject of very few studies. In the population of patients with MI treated with fibrinolysis studied by Gaudron et al., compensatory, transient LV enlargement occurred in 25% of patients; in 20% of patients LV dilatation was progressive in 3-year observation [7]. In a study by Warren et al. LV dilatation progressed within 6 months in 16% of patients [10]. Also in the GISSI-3 study, a significant, late (6 months) LV enlargement was observed in 16% of patients [8]. It seems that the differences in proportions of subpopulations presenting with late LV enlargement depend partially on adopted criteria of LV dilatation. They can also depend on factors associated with imaging technique and period of observation [7, 8, 10]. The type of administered treatment is also of significant importance. However, even in the era of interventional treatment of MI (high effectiveness of mechanical reperfusion) the percentage of patients with long-term LV enlargement reaches 27% [11].

Identified patterns of LV volume changes after MI demonstrate the division of patients into subgroups of different risk level of adverse clinical events. In the group of patients with progressive LV dilatation between the 6$^{th}$ and the 12$^{th}$ month of observation, every fourth patient died, while no deaths were seen in other groups. More than half of patients with progressive LV dilatation developed symptomatic HF, whereas in other groups HF was rare.

In our observation, the analysis of trends in echocardiographic changes of LV structure and function parameters revealed differences between the examined groups. A year after MI, patients with progressive LV enlargement presented with significantly worse parameters of systolic and diastolic LV function compared with other groups. It is of major importance that even though in the group of patients with progressive LV dilatation mean LVEF was still significantly lower than in other groups, it did not change significantly within the one-year follow-up period in any of the analysed groups. In the GISSI-3 population, patients with significant late LV dilatation were the only subgroup in which LVEF significantly deteriorated 6 months after MI [8]. The results of our study are consistent with the observations of Gaudron et al., who – also in patients with progressive LV enlargement – did not observe significant LVEF changes within 1.5 years after MI [7]. Our study therefore supports Gaudron's et al. thesis that the progression of LV enlargement reflects unfavourable LV remodelling better than the evolution of LVEF changes and precedes HF [7].

**Table V.** Multivariable analysis of the effects of categorised variables on progressive LV dilatation

| Parameter | Progressive LV dilatation (+) | (–) | β | Relative risk [RR] | p |
|---|---|---|---|---|---|
| $EDVI_2$ ≥80 ml/m² | 23/5 | 10/86 | 2.05 | 7.79 | 0.00050 |
| Reperfusion (–) | 14/4 | 18/52 | 1.42 | 4.16 | 0.0156 |

Our study demonstrates that progressive LV enlargement is accompanied by a significant increase in LV sphericity and more frequent occurrence of functional MR. According to one hypothesis, the change of LV shape is determined by haemodynamic principles [17, 18]. Spherical LV shape in an advanced stage of its enlargement, together with impaired myocardial contractility, allows – in the presence of decreased contraction amplitude – more effective ejection volume to be generated [17]. This potentially adaptive mechanism eventually intensifies LV dysfunction and accelerates the occurrence of

decompensated dilatation, as increased sphericity enhances wall tension (and therefore also progression of chamber dilatation) and leads to the development of MR [17]. Coghlan et al. showed that the myocardial fibres of damaged and enlarged LV are arranged more horizontally and therefore the ventricle exhibits none of the benefits of its originally oblique and spiral arrangement – the heart architecture changes from proper Gothic into Roman [19]. The 'Romanic' heart is more spherical, and presents with a decreased EF, high filling pressure and impaired ability to pump blood [19]. Unfavourable changes of the shape of the ventricle and higher proportion of patients with functional MR ≥2 noted in the group with progressive LV enlargement in our study reflect the mechanisms responsible for more frequent HF occurrence in this group.

**Early predictors of unfavourable heart remodelling.** McKay et al. showed that the degree of heart remodelling correlates with the size of necrosis [1]. Similarly, in the GISSI-3 study it was demonstrated that late indexes of LV volume was significantly greater in patients with extensive (assessed by echocardiography) MI area [8]. Gaudron et al. reported that the size of MI (evaluated on ventriculography) was a predictor of progressive LV dilatation [7]. In our study, the occurrence of extensive MI (assessed on echocardiography and in biochemical evaluation) was associated with significantly increased risk of progressive LV dilatation; the size of MI, however, was not an independent predictor. This observation indicates the importance of other factors that interact with the size of necrosis. Our study confirmed previous observations [1, 4, 6, 20, 21] that infarct expansion increases the risk of unfavourable long-term LV remodelling. This factor, however, did not have an independent prognostic value either. The lack of effective reperfusion turned out to be a strong and independent predictor of LV enlargement progression after MI. Despite significant methodological limitations (reperfusion evaluated non-invasively), this observation strongly supports the hypothesis of an open artery [10, 22, 23] as probably one of the most important factors determining the scenario of post-infarction heart remodelling.

**Prognostic significance of early LV enlargement after MI.** White et al. reported a key study in predicting outcomes after MI; it pointed out the significance of LV size evaluation – LV end-systolic volume estimated on ventriculography turned out to be the most powerful mortality predictor, even more powerful than the progression of coronary disease or any other clinical or demographic parameter [24]. In the studied population, high value of EDVI (≥80 ml/m$^2$) noted at discharge from the hospital was the most powerful independent predictor of progressive LV dilatation. This is consistent with the SAVE study results showing that early (average 11$^{th}$ day) LV enlargement after MI was an independent risk factor of late unfavourable clinical events, including death and LV dilatation progression [25]. Similarly, in the Assmann et al.'s study, EDVI assessed on ventriculography early after MI was – apart from biochemically estimated size of necrosis – the most powerful independent prognostic factor of late LV enlargement [26]. An echocardiographic GISSI-3 substudy showed, however, that LV enlargement in the early stage after MI (before discharge from hospital) was not a predictor of LV enlargement within 6 months after MI [8]. Similar observations were made by Sanchis et al. [27]. The results of our study add to the evidence suggesting that significant early dilatation of LV is a powerful predictor of LV enlargement progression after MI.

Our study suggests that a high proportion of patients presenting with progressive LV enlargement developed infarct expansion at an early stage (the phenomenon that causes dynamic LV volume increase). High EDVI value in early phase of remodelling reflects the forces increasing diastolic LV wall tension at the moment when it cannot be balanced well enough by compensating heart muscle hypertrophy, a reaction that occurs later and is less dynamic [1, 4]. According to the Laplace's formula in a mechanistic heart remodelling model the increase in LV wall tension is the most important factor of its dilatation progression [28, 29]. Clinical implications of early LV enlargement after MI, however, are still to be discussed. Our observations confirm the partially compensating character of LV volume changes after MI. On the other hand it is suggested that if the volume changes are dynamic and exceed a certain critical level, they might promote unfavourable LV remodelling. Echocardiographic monitoring of patients after MI is therefore of critical clinical importance. It allows selection of a subgroup with high risk of HF and CD development, who require aggressive treatment strategies.

## Study limitations

1) The study was limited by the use of non-invasive methods of reperfusion assessment after fibrinolysis. Early and late patency of the infarct-related artery was not assessed on angiography.
2) According to available reports, different biochemical methods are used to evaluate the size of MI. The CK peak was used as an MI extent marker in this study. Even though it is not a reference biochemical parameter reflecting the size of MI, it has been used to evaluate the extent of necrosis by many researchers.
3) The degree of MR was rated with semi-quantitative methods and it could have influenced the results.

## Conclusions

1) In the first 6 months after MI, the progression of LV enlargement was a sign identifying patients who would develop unfavourable LV remodelling, even in the absence of significant LVEF changes. In one-year

observation progressive LV enlargement was accompanied by significantly greater ventricle sphericity and more frequent occurrence of MR ≥2°.

2) During one-year follow-up in patients with the pattern of progressive LV enlargement, the incidence of adverse clinical events – HF and CD – was significantly higher.
3) High $EDVI_2$ value (≥80 ml/m$^2$) assessed at discharge from the hospital was the most powerful independent predictor of progressive LV dilatation after MI. The size of MI was not an independent predictor in that sense.
4) Echocardiographic monitoring of patients after MI allows early selection of a subgroup with high risk of CD and HF development.

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# Wzorce zmian objętości lewej komory po zawale serca – implikacje kliniczne

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## Streszczenie

**Wstęp:** Globalne powiększenie lewej komory (LV), główny wyznacznik pozawałowej przebudowy serca (PS), jest zjawiskiem dynamicznym. Skala PS koreluje z wielkością zawału (MI) przy istotnym wpływie innych czynników.

**Cel:** Ocena klinicznych implikacji różnych wzorców zmian objętości LV wyodrębnionych w trakcie jednorocznej obserwacji echokardiograficznej oraz określenie wczesnych predyktorów niekorzystnej przebudowy serca.

**Metodyka:** Grupę badaną stanowiło 132 chorych (średni wiek 56±12 lat) z pierwszym w życiu MI z uniesieniem odcinka ST (STEMI) (w tym 67% chorych leczonych fibrynolitycznie). W seryjnych badaniach echokardiograficznych (badanie 1.: pierwsza doba; badanie 2.: przy wypisie; badanie 3.: po 6 mies.; badanie 4.: rok po MI) określano: wskaźnik kurczliwości lewej komory (WMSI), wskaźnik objętości końcoworozkurczowej lewej komory (EDVI), wskaźnik objętości końcowoskurczowej lewej komory (ESVI), frakcję wyrzutową lewej komory (LVEF), wskaźnik sferyczności (WSF), wskaźnik ekspansji (EXP) zawału, doplerowski model restrykcji napełniania LV (mR), stopień niedomykalności zastawki mitralnej (MR). Jako kryterium istotnego powiększenia LV przyjęto: EDVI ≥85 ml/m$^2$ i/lub ΔEDVI ≥20% między dwoma kolejnymi badaniami. W 6 mies. po MI wyodrębniono 3 grupy: I – bez powiększenia LV (n=68); II – z przemijającym powiększeniem LV (badanie 1. i/lub badanie 2.) (n=26); III – z progresywnym powiększeniem LV (badanie 1. – 2. – 3.) (n=28). Ocenie poddano wartość prognostyczną zmiennych: lokalizacja przednia MI, zawał Q, klasa Killipa ≥2, brak reperfuzji oszacowanej nieinwazyjnie, EXP(+), kinaza kreatynowa (CK) ≥3000 IU, $WMSI_2$ ≥1,5, $EDVI_2$ ≥80 ml/m$^2$, $ESVI_2$ ≥40 ml/m$^2$, $EF_2$ <45%, $mR_2$ oraz obecność przerostu LV na starcie przebudowy serca (badanie 1.).

**Wyniki:** W grupie III rozmiar MI (WMSI) był znacząco większy niż w grupie I i II (odpowiednio: 1,56±0,3, 1,29±0,2, p <0,01; 1,35±0,3, p <0,05). Ekspansja zawału wystąpiła tylko w grupie III (39%). Po upływie roku od MI w grupie III wzorzec PS był niekorzystny w porównaniu z grupą I i II – niższa $LVEF_4$ (p <0,001), większy $WSF_4$ (p <0,001), częstsze występowanie $MR_4$ ≥2° (p <0,001) oraz $mR_4$ (p <0,001). Mimo różnic między grupami, w obrębie żadnej z nich LVEF nie zmieniała się znacząco w całym okresie obserwacji. W grupie III znamiennie częściej niż w grupie I i II pojawiła się niewydolność serca (HF), odpowiednio: 57 *vs* 2 *vs* 4% (p <0,001). Zgony sercowe wystąpiły jedynie w grupie III (25% chorych). Podwyższona wartość EDVI ≥80 ml/m$^2$ przy wypisie ze szpitala była najsilniejszym, niezależnym predyktorem progresywnego powiększenia LV. Duży rozmiar MI (CK ≥3000 IU i/lub WMSI ≥1,5) nie był niezależnym predyktorem niekorzystnej przebudowy serca.

**Wnioski:** 1. W okresie pierwszych 6 mies. po MI progresja powiększenia LV była objawem dobrze identyfikującym chorych rozwijających niekorzystną przebudowę serca, nawet w nieobecności istotnych zmian LVEF. Progresywnemu powiększeniu LV towarzyszył w rocznej obserwacji istotnie większy stopień sferyczności komory oraz częstsze występowanie MR ≥2°. 2. U chorych z wzorcem progresywnego powiększenia LV znamiennie częściej w rocznej obserwacji wystąpiły HF i zgon sercowy (CD). 3. Najsilniejszym, niezależnym wskaźnikiem przewidywania progresywnej dylatacji LV po MI była wysoka wartość EDVI (≥80 ml/m$^2$) stwierdzana przy wypisie ze szpitala. Wielkość MI nie była niezależnym wskaźnikiem prognostycznym. 4. Monitorowanie echokardiograficzne chorych po MI pomaga wcześnie wyodrębnić podgrupę wysokiego ryzyka CD i rozwoju HF.

**Słowa kluczowe:** pozawałowa przebudowa serca, echokardiografia, prognozowanie po zawale serca

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