Original article

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Implementation of Guidelines for Secondary Prevention of Acute Myocardial Infarction in Clinical Practice

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After acute myocardial infarction (MI) patients are at high risk of recurrent cardiovascular events. Even though contemporary guidelines recommend intensive monitoring of modifiable risk factors, actual clinical practice has shown a substantial gap between guidelines and their application.

Objective of this study was assessment of achieving target values of individual and simultaneous risks in patients after MI, as well as analysis of their changes over time in actual clinical setting.

Research was conducted in the form of observation cross-sectional study for three time periods (2019, 2023 and 2025) and implied 128 patients who were included in cardiac rehabilitation. Clinical parameters, risk factors and applied therapy were analyzed. Target achievement assessment was carried out in compliance with valid guidelines.

High prevalence of traditional risk factors was recorded in all groups, especially with reference to hypertension, dyslipidemia and abdominal obesity. Considerable progress in lipid profile and

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glycemia management was recorded in 2025, as a result of application of combined antilipidemic therapy. However, simultaneous monitoring of all modifiable risk factors remained low: 2,7% in 2019, 2,5% in 2023 and 5,9% in 2025. During rehabilitation, medical therapy was optimized in more than half of patients.

Despite significant improvements of pharmacotherapy and partial advancement of individual risk factor monitoring strategies, comprehensive management of cardiovascular risk after MI is still insufficient. Results point to the need for more intensive, integrated and multidisciplinary approach to secondary prevention for reducing residual cardiovascular risk.

Key words: acute myocardial infarction, secondary prevention, risk factors, cardiac rehabilitation, actual clinical practice

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Implementacija preporuka za sekundarnu prevenciju u kliničkoj praksi kod pacijenata nakon akutnog infarkta miokarda

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Pacijenti nakon akutnog infarkta miokarda (AIM) imaju veoma visok rizik od ponovnih kardiovaskularnih događaja. Iako savremene smernice preporučuju intenzivnu kontrolu svih modifikabilnih faktora rizika, podaci iz realne kliničke prakse ukazuju na značajan jaz između preporuka i njihove primene.

Cilj ovog rada bila je procena stepena dostizanja ciljnih vrednosti pojedinačnih i istovremenih faktora rizika kod pacijenata nakon AIM, kao i analiza njihovih promena kroz vreme u realnim kliničkim uslovima.

Metode: Istraživanje je sprovedeno kao opservaciona studija preseka u tri vremenska perioda (2019, 2023. i 2025. godina) i obuhvatilo je 128 pacijenata uključenih u program kardiološke rehabilitacije. Analizirani su klinički parametri, faktori rizika i primenjena terapija. Procena dostizanja ciljnih vrednosti vršena je u skladu sa važećim smernicama.

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Rezultati: Visoka prevalencija tradicionalnih faktora rizika zabeležena je u svim grupama, posebno hipertenzije, dislipidemije i abdominalne gojaznosti. U 2025. godini uočen je značajan napredak u kontroli lipidnog statusa i glikemije, što je povezano sa većom primenom kombinovane antilipemijske terapije. Ipak, istovremena kontrola svih promenljivih faktora rizika ostala je izrazito niska: 2,7% u 2019, 2,5% u 2023. i 5,9% u 2025. godini. Tokom rehabilitacije terapija je optimizovana kod više od polovine pacijenata.

Zaključak: Uprkos napretku u farmakoterapiji i delimičnom poboljšanju kontrole pojedinačnih faktora rizika, sveobuhvatna kontrola kardiovaskularnog rizika nakon AIM i dalje je nedovoljna. Rezultati ukazuju na potrebu za intenzivnijim, integrisanim i multidisciplinarnim pristupom sekundarnoj prevenciji u cilju smanjenja rezidualnog kardiovaskularnog rizika.

Ključne reči: akutni infarkt miokarda, sekundarna prevencija, faktori rizika, kardiološka rehabilitacija, realna klinička praksa.

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Introduction

Globally speaking, cardiovascular diseases are the leading cause of mortality, with acute myocardial infarction (MI) assuming a central role among atherosclerosis diseases (1,2). Developments in acute therapy, including reperfusion strategies and modern pharmacotherapy, significantly reduced early mortality and improved survival after initial event for large number of patients (2,3). However, MI survivors are still at extremely high cardiovascular risk which implies risk of subsequent events, including recurrent MI, acute heart failure and sudden cardiac death (3,4).

Secondary prevention after MI implies multidisciplinary approach i.e., monitoring of modifiable risk factors (hypertension, dyslipidemia, diabetes, smoking), pharmacotherapy (antiplatelet medications, statins, ACE inhibitors) and lifestyle changes (3,5). Achieving objectives will reduce the risk of recurrent MI and improve long-term mortality (5).

Despite availability of efficient medical therapy and clearly defined guidelines, substantial number of patients fail to meet target values, especially in terms of lipid profile and blood pressure (4). Major factors for such failure imply poor patient adherence, low drug titration, clinical inertia and systemic limitations in patient monitoring (4,5).

Moreover, the concept of residual cardiovascular risk implies that, even at optimal therapy, patients can face cardiovascular events, which makes post-MI management even more complicated (5). Even though individual studies have assessed risk factor target achievement, data on simultaneous achievement of multiple targets and identification of failure-related factors are still limited, especially in regional populations (4).

Research objectives

Research objective is to assess the level of achieved targets for individual and simultaneous modifiable risk factors in patients with acute myocardial infarction, as well as to analyze their trend over time and correlation with applied therapy in actual clinical practice.

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Materials and methods

The study protocol was presented and approved by the Medical Ethical Committees of the Institute for Therapy and Rehabilitation “Niška Banja” in Serbia (decision number: 03-4307/1 from June 2015) and the Faculty of Medicine, University of Niš (Niš, Serbia). Informed consent was obtained from all patients before the commencement of the study.

The cross-sectional study included patients after acute myocardial infarction in three time periods (first group- 2019, second group- 2013 and third group- 2025). There were 128 patients (37 patients from 2019, 40 patients from 2023 and 51 patients from 2025) with acute myocardial infarction who were referred to cardiovascular rehabilitation.

The same data collection methodology was used for all three groups of patients. Data on demographic features, clinical parameters, risk factors and medical therapy before rehabilitation treatment were collected based on case history and available medical records. Parameters analyzed during rehabilitation involved arterial blood pressure (average values during rehabilitation, excluding day one), lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides) and glycemia. The application of standard pharmacotherapy, including beta blockers, ACE inhibitors, statins, anticoagulants and other relevant cardiovascular medications, was evaluated. Therapy changes during 21-day rehabilitation were recorded in compliance with valid guidelines.

The target values of arterial blood pressure for all three time periods are defined as values < 140 mmHg for systolic and < 90 mmHg for diastolic. The target value for LDL cholesterol (2019 ESC/EAS Guidelines) was considered to be < 1.4 mmol/L, for triglycerides < 1.7 mmol/L (2). Given that HbA1c was not routinely performed, the target value for glycemia was < 6.1 mmol/L. Limit values for partially successful reduction of abdominal obesity were taken, for men < 102 cm, and for women < 88 cm of waist circumference. Smoking cessation was defined as the patient not having smoked at all since the acute coronary event. A physically active patient is considered a person who has moderate physical activity for at least 5 days a week, lasting at least 30 minutes.

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Statistical analysis

All data were processed in the statistical program IBM Statistical Package for the Social Sciences version 18.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± SD, and categorical variables were reported as a count with percentages. Categorical variables were compared using a Chi-squared or Fischer's exact test, depending on the group size. Normal distribution of continuous variables was confirmed by the Kolmogorov-Smirnov test. All tests were considered two-sided. A two-sided $p<0.05$ was considered to be statistically significant.

Results

Basic characteristics of tested subjects

Table 1 shows basic features of the tested groups. Male patients were statistically more prevalent in all groups. Applying the Bonferroni correction for three comparisons, the significance threshold is $p<0.0167$. Then there remains a statistically significant difference in terms of gender representation only between 2019 and 2023. Average age of tested subjects at rehabilitation increased during the observed period. Average waist circumference was higher in both genders, with mild increase in female patients over time and variable values in male patients. Mean values of systolic and diastolic blood pressure were relatively stable in all three groups, without significant oscillations. Left ventricle ejection fraction was insignificantly reduced in 2025 group. Total number of risk factors was statistically highest in 2023, while data for 2025 indicated RF reduction. Number of blood vessels with stenosis >50% was recorded in third group, while time period between infarction and rehabilitation was the longest in 2025 group.

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Table 1. Basic characteristics of tested groups

Parameters		2019	2023	2025
Gender	Female (n/%)	5/13.51	17/42.5$^{*1:2}$	11/21.57
	Male (n/%)	32/86.49	23/57.5$^{*1:2}$	40/78.43
Waist circumference (cm)	Female (x±SD)	107.0±21.85	93.88±14.64$^{+1:2}$	94.73±13.96$^{+1:3}$
	Male (x±SD)	107.1±10.54	100.17±12.69$^{+1:2}$	103.4±10.04$^{+1:3}$
Age (years) (x±SD)		60,39±8,95	68,45±8,50$^{§1:2}$	69,67±8,27$^{§1:3}$
Time to rehabilitation (months) (x±SD)		3,75±1.4$^{§1:3}$	4,75±1,8	5,26±1,77
SBP (mmHg) (x±SD)		122±17,23	126,37±10,19	122,55±12,94
DBP (mmHg) (x±SD)		74±12,82	77,37±5,66	75,98±7,87
EF of left ventricle (x±SD)		48,95±9.41	50,64±9,30	46,34±9,61
Total RF (x±SD)		5,3±1,59$^{§1:3}$	$^{+1:2}$5,67±1,64$^{§2:3}$	3,55±1,06
Blood vessels with stenosis >50% (x±SD)		1,54±0,91$^{§1:3}$	1,49±0.93$^{§2:3}$	2.2±0.81

SBP, systolic blood pressure; DBP, diastolic blood pressure; EF, ejection fraction; RF, risk factor; *, p<0,05; $^{+}$, p < 0.01; §, p<0.01; ^{1} group from 2019; ^{2} group from 2023; ^{3} group from 2025. Comparison between groups is shown as 1:2, 1:3 and 2:3 with corresponding statistical significance.

Risk factor distribution

Table 2 indicates distribution of risk factors for cardiovascular diseases by tested groups. Hypertension and hyperlipidemia were most prevalent risk factors in all groups, with upward trend for 2025 group. Abdominal obesity was present in more than half of tested subjects in all groups, without any significant improvements over time. Diabetes prevalence was different, depending on a group. Smoking was predominant in 2019 group. In terms of statistical significance, physical inactivity was different for each group.

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Table 2. Risk factor distribution in tested groups

Risk factors for cardiovascular diseases	**2019**	**2023**	**2025**
Age (M > 55, F > 65) (n/%)	28/60,87$^{+1:3}$	32/80	44/86,27
Male patients (n/%)	37/80,43	23/57,5*	40/78,43
Abdominal obesity (M > 102cm, F > 88cm) (n/%)	36/78,26	22/55$^{*1:2}$	29/56,86$^{*2:3}$
Hypertension (n/%)	35/76,09$^{+1:3}$	38/95$^{*1:2}$	49/96,08
Hyperlipidemia (n/%)	31/67,39$^{§1:3}$	33/82,5$^{+2:3}$	50/98,04
Diabetes (n/%)	12/26,09	11/27,5	18/35,29
Hereditary factor (n/%)	20/43,48	21/52,5	25/49,02
Smoking (n/%)	37/80,43	19/47,5$^{*1:2}$	31/60,78
Physical inactivity (n/%)	7/15,21	20/50$^{§1:2}$	10/19,61$^{+2:3}$
Alcohol (n/%)	2/5,40	2/5	5/9,80

M, male patients, F, female patients; *, p<0,05; $^{+}$, p < 0.01; §, p<0.01. Comparison between groups is shown as 1:2, 1:3 and 2:3 with corresponding statistical significance.

Pharmacotherapy

The application of medical therapy was shown in table 3. Distribution of specific medications was statistically equivalent in all tested groups. There were no data on combined use of statins and Ezetimibe for 2019 group. Additionally, the stated medications were not present in 2023 group of subjects who were referred to rehabilitation. To achieve target value of this parameter, 9 patients (22,5%) were prescribed additional combination of Rosuvastatin and Ezetimibe at rehabilitation discharge. The use of the stated medications was recorded in 2025 group i.e., 35.3% of patients came to rehabilitation treatment with combined therapy.

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Table 3. Medical therapy

Medications	**2019** N (%)	**2023** N (%)	**2025** N (%)
Beta blockers	43/93,48	37/92,5	46/90,20
ACE inhibitors /ARB	36/78,26	33/82,5	42/82,35
Aspirin	38/82,61	36/90	41/80,39
Statins	43/93,48	35/87,5	45/88,23
Statin + Ezetimibe	/	0	18/35,29
Calcium channel blockers	6/16,22	11/27,5	12/23,53
Thiazide diuretic / Indapamide	7/15,21	5/12,5	10/19,61
Loop diuretics	16/34,78	15/37,5	25/49,02
Spironolactone / Eplerenone	/	11/27,5	20/39,21
P2Y12 receptor inhibitors	36/78,26	29/72,5	39/76,47
OAT	7/15,21	4/10	7/13,72

ACE, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; OAT, oral anticoagulation therapy.

Achieving target values

Figure 1 demonstrates percentage overview of reaching targets for most important risk factors for cardiovascular diseases. Blood pressure targets were similar in all three groups. Statistically significant percentage increase of glycemia target ($p<0.001$) and lipid parameter target was achieved in 2025. The lowest percentage of achieved LDL-cholesterol target was recorded in 2023, which was, in terms of statistics, significantly lower ($p<0.01$) compared to 2019 and extremely statistically lower than in 2025 ($p<0.001$). The highest percentage of triglyceride targets were achieved in the third group, which was statistically higher ($p<0.05$) than in two other groups.

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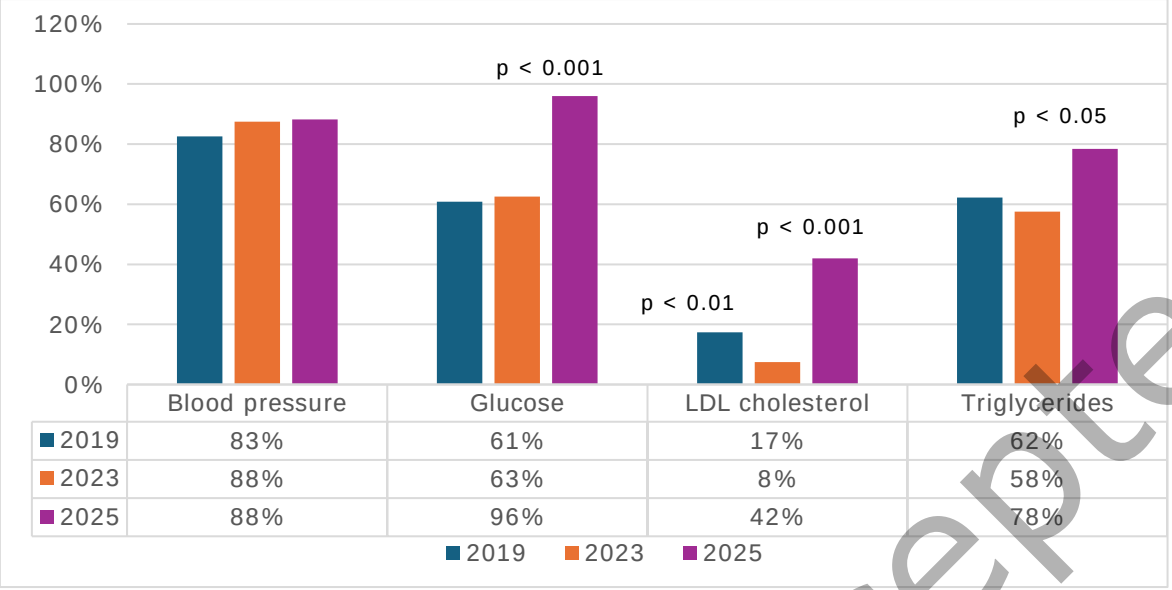


Figure 1. Percentage of achieved target values for variable risk factors. The year 2025 differed significantly from 2019 and 2023 in terms of glycemia, LDL-cholesterol and triglycerides. In addition, in 2023, the percentage of the achieved target value of LDL cholesterol was statistically lower than in 2019.

Analysis of laboratory parameters

Table 4 indicates glycemia and lipid parameter values for 2025 patients. The parameters refer to the period before rehabilitation (previously performed laboratory analyses) in relation to the rehabilitation period, when laboratory analyzes were performed. The records showed statistically significant reduction of glycemia and lipid parameter values, except for HDL-cholesterol values, which remained statistically unchanged.

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Table 4. Laboratory analysis results before rehabilitation and during 2025 rehabilitation.

Parameters	**Before rehabilitation**	**During rehabilitation**
Glycemia (mmol/L)	6,91±2,37	5,03±0,63[§]
Cholesterol (mmol/L)	4,58±1,47	3,67±1,18[+]
HDL-cholesterol (mmol/L)	1,13±0,35	1,04±0,27
LDL-cholesterol (mmol/L)	2,51±1,22	1,92±1,15[*]
Triglycerides (mmol/L)	1,99±1,19	1,55±0,63[*]

Legend: *, p<0,05; [+], p < 0.01; [§], p<0.01

Change of therapy during rehabilitation

Analysis of therapy change during 2025 institute rehabilitation showed therapy correction or intensification in 27 (54%) patients. In 2023, combined antilipidemic therapy (statin + Ezetimibe) was introduced in 9 (22.5%) patients, while changes during 2019 referred to medication dose change only. Most important changes implied intensification of antilipidemic therapy, primarily by introducing Ezetimibe as addition to statin therapy, as well as optimizing statin dose or replacing statin by another, more potent statin. Moreover, hypertension therapy correction, including introduction or titration of ACI/ARB, beta blockers and diuretics, was carried out in a number of patients. Specific number of tested subjects received Mineralocorticoid receptor antagonists (MRA), accompanied by correction of their hypertension therapy in line with clinical indications. To summarize, the change of therapy was carried out in more than half of patients, which emphasized the importance of active therapeutic approach during rehabilitation.

Detailed analysis of therapy changes during 2025 rehabilitation showed that most important interventions were focused on antilipidemic therapy. Seven (13,7%) patients started taking Ezetimibe, while 3 patients used more potent statin- Rosuvastatin, instead of Atorvastatin. Moreover, 3 (5,9%) patients started using statin therapy, which was not integral part of their previous medical therapy. Overall, the change of antilipidemic therapy was implemented in 13 (25,5%) patients, which represented an important element of total therapy interventions during rehabilitation.

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Simultaneous management of all variable risk factors

Simultaneous management of all modifiable risk factors in one patient is defined as achieving target values of arterial blood pressure, glycemia, LDL cholesterol and triglycerides, accompanied by quitting smoking and regulating body mass. In 2019, simultaneous achievement of all target values of modifiable risk factors was recorded in only one (2,7%) among 37 tested patients. Similar pattern was noted during 2023, where only one out of 40 (2,5%) patients managed to manage all modifiable risk factors simultaneously. Slight improvement was recorded in 2025, with three out of 51 patients (5,9%) who reached target values of all variable risk factors.

Discussion

Research results demonstrated the change of structure of patients included in cardiovascular rehabilitation, especially in 2023, when tested subjects were older and had more risk factors than patients in 2019. This discrepancy could be explained by outburst of COVID-19, which resulted in suspension of rehabilitation programs and changes in patient structure.

One of the most important aspects referred to prolonged waiting time between acute myocardial infarction and rehabilitation, which was more than 5 months in 2025. Such a long waiting period significantly deviated from guidelines which recommended 2-4 weeks between MI and rehabilitation initiation (2). As a rule, postponing reduces the possibility of improving functional capacity by approximately 1% per day (6), while early rehabilitation improves clinical outcome (7). Consequently, rehabilitation delay is an important, but potentially modifiable factor which has a negative impact on the outcome.

High prevalence of traditional risk factors, especially hypertension, dyslipidemia, obesity and diabetes, was recorded in all groups, which pointed to suboptimal management in both primary and secondary prevention. These findings were in accordance with data recorded in EUROASPIRE V study, where LDL-cholesterol target was achieved in 29% of patients, blood pressure target in approximately 58%, and glycemia target in 54% of patients (8). Similar results were recorded by American Association, where, despite high level of therapy application, less than half of patients managed to achieve LDL-cholesterol target (9).

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Although total application of pharmacotherapy did not significantly fluctuate, the change in dyslipidemia treatment was more than obvious. At early stage, statin monotherapy was predominant, while later on, therapy included combination with Ezetimibe, which resulted in significant improvement in reaching target values of LDL-cholesterol (42% in 2025). Similar results were noted in literature, where Ezetimibe was added to statin therapy, resulting in additional lowering of LDL-cholesterol and higher target achievement rate (10). Failure to achieve targets could be ascribed to insufficient therapy intensification, therapeutic inertia and poor adherence, whereas adequate adherence reduced mortality by 20–25% (11).

Improvement of lipid and glycose profile during 2025 rehabilitation was of special importance, as it confirmed importance of organized rehabilitation programs for therapy optimization. Therapy was adjusted in more than half of patients, which emphasized the relevance of active approach during rehabilitation. However, despite improvements in specific risk factors, simultaneous control of all modifiable risk factors was still extremely low (2,7% in 2019, 2,5% in 2023 and 5,9% in 2025). The stated results were in compliance with EUROASPIRE V study in which less than 10% of patients achieved adequate control of all risk factors (8), which proved limited efficiency of the existing strategies.

The above stated results could be explained by complexity of simultaneous control of multiple risk factors which required combination of intensive pharmacotherapy and long-term lifestyle changes, accompanied by high level of patient adherence (3). Lifestyle factors, such as smoking and obesity, require continuous motivation and long-term support, which makes them extremely challenging (12). Research results indicate that rehabilitation programs need to be improved through individualized approach, multidisciplinary interventions and long-term patient monitoring, to continue meeting therapy objectives.

Taking everything into account, despite therapy improvement, results confirmed the gap between guidelines and actual clinical practice. Secondary prevention enhancement requires early rehabilitation, intensive therapy optimization and improved adherence management.

Study limitations

During result interpretation, one should bear in mind that the research has several relevant limitations.

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First of all, the study was conducted in the form of cross-sectional study at one center, with relatively small number of tested subjects, which limited the possibility of applying results to general population. Additionally, research included only patients who were referred and admitted to cardiac rehabilitation, which could result in selection bias, having in mind that these patients had stronger motivation and better adherence than general population of patients after myocardial infarction.

Moreover, risk factor and therapy assessment were based on data obtained at admittance and during rehabilitation, which excluded long-term monitoring and restricted evaluation of continuity of achieved results and their impact on clinical outcome. Furthermore, the degree of patients' adherence to therapy, as one of the key factors of secondary prevention, could not be determined with precision.

Another limitation referred to the lack of detailed analysis of therapy intensity and titration, as well as reasons for failing to reach targets (e.g., adverse effects, side effects or therapeutic inertia). In addition, the study did not analyze socioeconomic and healthcare system factors, which could have a substantial impact on therapy availability and treatment success.

It is important to note that valid guidelines for secondary prevention were changed during the research period, especially with reference to target values of LDL-cholesterol, which could make direct comparison of analyzed time points even harder.

Finally, potential effects of COVID-19 on healthcare protection, patient structure and referral to treatment waiting time represented confusing factors which could not be fully quantified.

Conclusion

Despite advancements in pharmacotherapy and implementation of contemporary guidelines, simultaneous control of modifiable risk factors in patients with acute myocardial infarction has remained extremely low, with only 6% of patients achieving simultaneous control.

Even though individual factor management has shown progress, especially with reference to lipid profile, gap between guidelines and actual clinical practice is still substantial.

The above results indicate that partial control of risk factors is insufficient, and that approach to risk factor control should be based on aggressive treatment optimization, adherence improvement and early inclusion in cardiac rehabilitation. management.

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