

Original article ■

Attainment of Target Blood Pressure Values in Patients with Survived Myocardial Infarction and Diabetes Mellitus

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SUMMARY

Although arterial hypertension is an important factor contributing to cardiovascular complications in coronary patients with and without diabetes mellitus (DM), target values of blood pressure are rarely achieved in practice.

The aim of the study was to compare the attainment of target blood pressure in patients with DM who survived myocardial infarction (MI) (group A) with that in patients without DM (group B).

A group of 118 patients (both genders, with confirmed diagnosis of MI) was followed for three years, out of which 34 belonged to group A, and 84 to group B.

After three years of secondary prevention measures, in group B patients target blood pressure values (TA<140/90mmHg) were registered more often compared to the beginning of the study (84.8% vs 28.6%) ($p<0.0001$). Group A patients did not have statistically significant higher percentage of target blood pressure values (TA<130/80 mmHg) at the end of the study (11.8% vs 24.2%) ($p>0.05$), but the percentage of those with TA<140/90mmHg was significantly higher (57.6% vs 18.2%) ($p<0.0005$). Our analysis of secondary prevention indicated that 21.3% of group A and 12.7% of group B patients did not take β -blockers, but the difference was not statistically significant ($p>0.05$). In addition, there were no statistically significant differences in the use of ACE inhibitors between group A (84.8%) and group B (89.8%) ($p>0.05$).

Our study of the evaluation of secondary prevention measures in achieving target blood pressure values in patients with and without DM who survived MI demonstrated high prevalence of higher blood pressure values, especially in patients with DM, and still insufficient use of β -blockers and ACE inhibitors. Secondary prevention of cardiovascular events thus has to be intensified, particularly in patients with diabetes.

Key words: target values of blood pressure, diabetics and myocardial infarction, non-diabetics and myocardial infarction, secondary prevention

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder of multiple etiology, characterized by chronic hyperglycaemia and disturbed metabolism of carbohydrates, fats, and proteins, as the result of a defect in the secretion of insulin, action of insulin or a combination of the two.

The disease possesses the characteristics of a modern epidemics. The number of DM patients have been constantly rising in our country and worldwide. It is predicted that, in our country, the number of people affected with DM will rise from 422.000 (5.6%) in 2003 to 483.000 (6.3%) in 2025 (1).

Cardiovascular complications, especially coronary disease, are an important cause of morbidity and mortality of DM patients.

In individuals with acute myocardial infarction (MI) diabetes is found in about 20-25% of cases (2-4). Moreover, in this patient population, without previous data of history of diabetes, about 65% have abnormal glucose regulation found on oral glucose tolerance test (OGTT) (25% have previously undiagnosed diabetes, while 40% have glucose intolerance) (5,6).

Diabetes and arterial hypertension are commonly associated, increasing the risk of coronary heart disease. The PROCAM study (7) has shown that among middle-aged men MI was three times more common in DM patients during the four-year follow-up than in those without DM. Since diabetes and hypertension were present together, the incidence of MI was eight times higher than in the absence of these risk factors.

Hypertension is two times more common in patients with DM. Many patients with type 2 DM are already hypertensive at the moment of DM diagnosis. Patients with type 1 DM usually have normal values of blood pressure until the development of initial nephropathy, with microalbuminuria of 30-300mg/24h. With the development of clinically relevant nephropathy and proteinuria of over 300mg/24h blood pressure abruptly rises. Advanced renal insufficiency is associated with substantially elevated blood pressure values.

The risk of coronary disease is increased in both type 1 and 2 DM patients (8). MI is 2-3 times more common in DM patients compared to those without DM. According to the data of INTERHEART study (9), 15% of MIs in the West and 9% in the Central and Eastern Europe are the consequence of DM. The risk of MI in DM patients is similar to the risk in those with earlier MI with the risk of repeated MI (10). From these reasons, DM is defined as an equivalent of cardiovascular disease.

Moreover, individuals with type 2 DM have a higher mortality rate in acute MI and worse prognosis afterwards (11). The GRACE study (3) has shown that DM patients with acute coronary syndrome (ACS) have markedly higher hospital mortality than those without DM. Many studies have also shown that after survived

ACS, DM patients have significantly higher follow-up mortality rates compared to DM-free cases (2,12-14).

Since DM increases the absolute risk of coronary disease independently of other factors, the presence of other conventional risk factors leads to even higher absolute risk compared to DM-free patients; that is why we try to achieve still lower target blood pressure values in DM patients via risk factor modifications (15). In the treatment of hypertension we seek to achieve a blood pressure below 130/80mmHg (in DM-free patients below 140/90mmHg), and in those with compromised renal function and proteinuria of >1g/24h, blood pressure should be below 125/75mmHg (16).

Although modern medicine has at its disposal many antihypertensive drugs, and hypertension is an important contributor to cardiovascular complications in patients with and without DM, target blood pressure values often cannot be achieved in practice.

AIM

This study aims to compare the achievement of target blood pressure values in diabetics and non-diabetics with survived MI.

EXAMINEES AND METHODS

For the purpose of this study, we formed a group of subjects from the basis of the multicentric, prospective interventional study „Secondary prevention of coronary disease and cerebrovascular disease“ conducted in 38 health care centres in Serbia with 1.189 examinees in the first half of 2005.

The group was composed of patients of both genders under 80 years of age, with confirmed survived MI in the previous three years, based on the diagnosis summary devised by way of medical documentation analysis. The patients with the diagnosis of first MI in whom revascularization (percutaneous transluminal angioplasty - PTCA or by-pass) had not been done were considered eligible; excluded were those with postinfarction angina or reinfarction, since these were new coronary events. The study thus enrolled 118 patients in total, with survived MI in the period 2003-2005. All the patients were divided into two comparable groups - the group with DM (group A) (n=34) and group without DM (group B) (n=84).

The data were collected from the questionnaires, medical histories, and by physical examination. The follow-up poll list contained the items based on which the information could be obtained on systolic and diastolic blood pressure at the start of the study and during the period of secondary prevention after two, four, six, eighteen, and thirtysix months after the enrollment (2005-2008). In addition to other elements, we monitored pharmacologic therapy with β -blockers and ACE

inhibitors and the incidence of possible adverse coronary events (death, reinfarction, myocardial revascularization).

The study was designed in the way that there was no statistically significant difference between genders regarding diabetes diagnosed with survived MI (Fisher's exact probability test: $p=0.418$; $p>0.05$). DM was thus diagnosed in 27 (32.1%) men and 7 (20.6%) women.

Regarding the MI site, both men and women were equally enrolled and there was no statistically significant difference between genders in the numbers of inferior ($\chi^2=0.12$; $p=0.726$; $p>0.05$) and anteroseptal MI ($\chi^2=0.12$; $p=0.726$; $p>0.05$).

At the beginning of the study, there were no statistically significant differences in the observed parameters among 84 (71.2%) men and 34 (28.8%) women, which was in accordance with the study design. Among women there were 23.5% and among men 25.0% patients with familial DM ($\chi^2=0.95$; $p=0.329$; $p>0.05$). There were no statistically significant differences in the average values of systolic ($t=0.844$; $p=0.401$; $p>0.05$) and diastolic blood pressure ($t=1.376$; $p=0.171$; $p>0.05$).

Blood pressure measurement was performed using the auscultatory method and mercury manometer, abiding by the recommendations of the Joint National Committee of the American Medical Association

(17) and the European Society of Hypertension (18), both from 2003.

Classification of blood pressure values was done based on the classification of adult arterial hypertension by the European Society of Hypertension from 2003 (19) and 2007 (20) (Table 1). If the values of systolic or diastolic blood pressure could be classified in different categories, recommendations for more serious degrees were used.

All the patients were orally advised at the beginning of the study about required lifestyle changes and got written instructions on their diet, measures to be taken before blood pressure measurements and adverse effects of cardioprotective drugs. Blood pressure measurements were taken in out-patient conditions, with the same blood pressure monitor and measurement technique.

The effects of secondary prevention measures were assessed based on the latest European recommendations for secondary prevention of coronary disease (15).

Pearson's χ^2 -test and McNemar's test were used for data analysis.

Univariate logistic regression was used at first checkup to analyze the factors (variables) related to adverse coronary events. The variables were considered as numeric (y) or categorical (1 - presence of risk; 0 - absence of risk).

Table 1. Classification of adult arterial hypertension of the European Society of Hypertension from 2003 and 2007

Blood pressure categories	Systolic	Diastolic
Optimal	< 120 mmHg	< 80 mmHg
Normal	120-129 mmHg	80-84 mmHg
Highly normal	130-139 mmHg	85-89 mmHg
I° hypertension	140-159 mmHg	90-99 mmHg
II° hypertension	160-179 mmHg	100-109 mmHg
III° hypertension	≥ 180 mmHg	≥ 110 mmHg
Isolated systolic hypertension	≥ 140 mmHg	< 90 mmHg

RESULTS

After secondary prevention measures, group B patients had statistically significant higher proportion of target blood pressure values (TA<140/90mmHg) compared to the situation at the study start (84.8% vs 28.6%) (McNemar test: $\chi^2=39.2$; $p=0.0000000004$; $p<0.0001$) (Figure 1).

In group A, target blood pressure values (TA<130/80mmHg) were present in 11.8% of patients at

the study onset and in 24.2% at its end (Figure 2), but the difference was not statistically significant (McNemar χ^2 test: $p=0.219$; $p>0.05$).

However, the percentage of patients with DM (who were alive at the end of the study) and TA<140/90mmHg was statistically significantly higher after three years of secondary prevention measures (57.6% vs 18.2%) (McNemar χ^2 test: $p=0.0002$; $p<0.0005$) (Table 2).

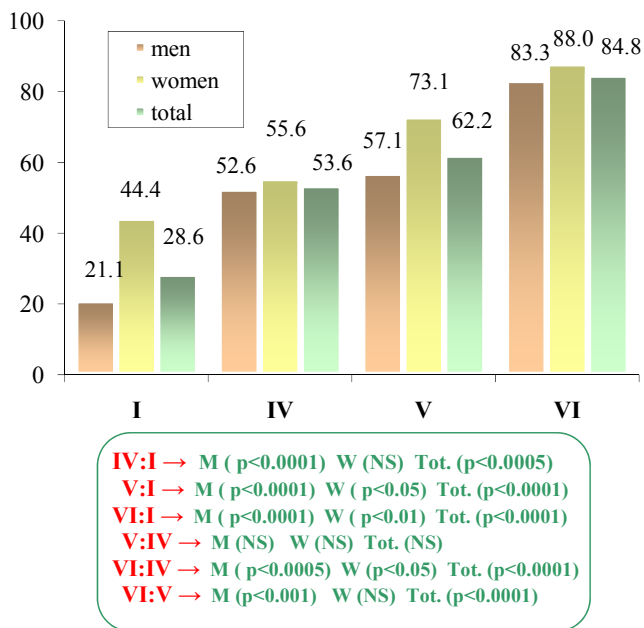


Figure 1. Proportion (%) of blood pressure <140/90mmHg in DM-free group

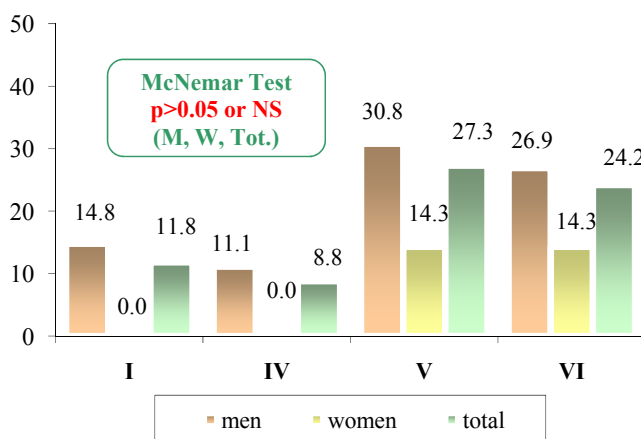


Figure 2. Proportion (%) of blood pressure <130/80mmHg in group with DM

Table 2. Proportion of TA <140/90mmHg in the group of patients with DM at the onset and end of the study

TA<140/90mmHg	Onset		End		McNemar Test (n=33)
	N _o	%	N _o	%	
Yes	6	18.2	19	57.6	p=0.0002 p<0.0005
No	27	81.8	14	42.4	
Total	33	100.0	33	100.0	

At the beginning of the study, a larger proportion of patients without DM (84.5%) than those with DM (70.7%) regularly took β -blockers, but the difference was not statistically significant ($\chi^2=0.5838$; $p>0.05$) (Table 3).

After three years of secondary prevention, 21.3% of patients with DM and 12.7% of those without DM did not use β -blockers, and the difference was not statistically significant ($\chi^2=0.2008$; $p>0.05$) (Table 4).

There was no statistically significant difference in the regularity of drug treatment with ACE inhibitors between groups A and B (85.3% vs 85.7%) at the study onset ($\chi^2=0.0005$; $p>0.05$) (Table 5).

At the end of the study, a slightly higher percentage of group B patients (89.8%), compared to group A subjects (84.8%), regularly took ACE inhibitors, but the difference was not statistically significant ($\chi^2=0.0665$; $p>0.05$) (Table 6).

Univariate logistic regression analysis demonstrated that in the examinees of our study, in addition to other factors (variables), both systolic and diastolic pressure constituted the risk of death or reinfarction of those with survived MI (Table 7).

Table 3. Use of β -blockers in patients with/without DM at the onset of the study

β-blockers	With DM		Without DM	
	N_e	%	N_e	%
Never used	3	8.8	7	8.3
Not used - contraindicated	6	17.6	1	1.2
Not used - adverse side effects	1	2.9	5	6.0
Regularly taken	24	70.7	71	84.5
Total	34	100.0	84	100.0

Table 4. Use of β -blockers in patients with/without DM at the end of the study

β-blockers	With DM		Without DM	
	N_e	%	N_e	%
Never used	3	9.1	3	3.8
Not used - contraindicated	2	6.1	1	1.3
Not used - adverse side effects	2	6.1	6	7.6
Regularly taken	26	78.7	69	87.3
Total	33	100.0	79	100.0

Table 5. Use of ACE inhibitors in patients with/without DM at the onset of the study

ACE inhibitors	With DM		Without DM	
	N_e	%	N_e	%
Never used	2	5.9	12	14.3
Not used - contraindicated	2	5.9	0	0
Not used - adverse side effects	1	2.9	0	0
Regularly taken	29	85.3	72	85.7
Total	34	100.0	84	100.0

Table 6. Use of ACE inhibitors in patients with/without DM at the end of the study

ACE inhibitors	With DM		Without DM	
	N _e	%	N _e	%
Never used	2	6.1	6	7.6
Not used - contraindicated	0	0	0	0
Not used - adverse side effects	3	9.1	2	2.6
Regularly taken	28	84.8	71	89.8
Total	33	100.0	79	100.0

Table 7. Risk factors for adverse coronary events (death and reinfarction) in patients with survived myocardial infarction

Characteristics	B*	SE**	P***	OR(95%CI)****
Gender	0.442	0.516	0.392	1.55 (0.56-4.27)
Age, y	0.080	0.026	0.002	1.08 (1.03-1.13)
Heredity (0,1)	0.042	0.446	0.925	1.04 (0.43-2.50)
Number of invariable risk factors, y	0.571	0.302	0.059	1.77 (0.98-3.20)
Body mass index (BMI), y	-0.004	0.060	0.947	0.996 (0.89-1.12)
Body mass index (BMI) (0,1)	0.721	0.544	0.185	2.06 (0.71-5.97)
Systolic blood pressure, y	0.039	0.012	0.0008	1.04 (1.02-1.06)
Systolic blood pressure (0,1)	1.370	0.652	0.036	3.93 (1.10-14.11)
Diastolic blood pressure, y	0.037	0.019	0.0511	1.04 (0.999-1.08)
Diastolic blood pressure (0,1)	1.089	0.585	0.063	2.97 (0.94-9.35)
Total cholesterol, y	-0.009	0.143	0.950	0.99 (0.75-1.31)
Total cholesterol (0,1)	-0.125	0.848	0.883	0.88 (0.17-4.64)
LDL-cholesterol, y	-0.136	0.161	0.398	0.87 (0.64-1.20)
LDL-cholesterol (0,1)	-0.765	0.766	0.318	0.46 (0.10-2.09)
HDL-cholesterol, y	0.613	0.565	0.277	1.85 (0.61-5.58)
HDL-cholesterol (0,1)	-1.193	0.779	0.125	0.30 (0.07-1.39)
Triglycerides, y	-0.208	0.183	0.255	0.81 (0.57-1.16)
Triglycerides (0,1)	-0.093	0.503	0.853	0.91 (0.34-2.44)
Glycaemia, y	0.196	0.088	0.025	1.22 (1.02-1.44)
Glycaemia (0,1)	0.686	0.443	0.122	1.98 (0.83-4.73)
Smoking (0,1)	-0.034	0.501	0.946	1.03 (0.39-2.76)
Physical inactivity (0,1)	0.938	0.448	0.036	2.56 (1.06-6.15)
Number of variable risk factors, y	0.207	0.121	0.086	1.23 (0.97-1.56)
Number of invariable risk factors	0.936	0.659	0.156	2.55 (0.70-9.29)
Angina pectoris	0.670	0.545	0.219	1.95 (0.67-5.69)
Arterial hypertension	1.259	0.777	0.105	3.52 (0.77-16.15)
Diabetes mellitus	0.709	0.460	0.123	2.03 (0.82-5.03)
Poststroke status	1.474	0.561	0.009	4.37 (1.45-13.12)
Arteriosclerotic disease of peripheral arteries	0.421	0.515	0.414	1.52 (0.55-4.18)
Symptomatic stenosis of carotid arteries	0.130	0.706	0.854	1.14 (0.28-4.54)
Aspirin (0,1)	-0.043	0.619	0.945	0.96 (0.28-3.22)
β-blockers (0,1)	0.081	0.561	0.884	1.08 (0.36-3.26)
ACE inhibitors (0,1)	0.901	0.787	0.252	2.46 (0.53-11.51)
Hypolipemics (0,1)	1.082	0.475	0.023	2.95 (1.16-7.49)
Metphormin (0,1)	0.718	0.797	0.367	2.05 (0.43-9.78)
Total number of unused drugs, y	-0.013	0.268	0.960	0.99 (0.58-1.67)
Treatment regularity (0,1)	0.590	0.656	0.368	1.80 (0.50-6.53)

* Coefficient of logistic regression ** Standard error *** Cross ratio

**** Confidence interval (95%)

y - variables considered to be numeric

0,1 - variables considered to be categorical (1 - presence of risk; 0 - absence of risk)

DISCUSSION

During the study, target blood pressure values were reached by 84.8% of patients with survived MI and without DM. In an American study, a far smaller number of patients without DM (65%) have reached target blood pressure values (21). Comparative analysis performed within the EUROASPIRE I and II study has produced even poorer results - only 51% of patients without DM had TA<140/90mmHg (22). On the other hand, in a study performed from 2003 to 2005 in Germany, patients without DM reached target blood pressure values in a percentage similar to our study (82.9%) (23).

In the group of patients with survived MI and DM, target blood pressure (TA<130/80mmHg) was achieved during the study in about a quarter of the examinees (24.2%). However, interventional measures of secondary prevention have markedly elevated the percentage of diabetics with TA<140/90mmHg (57.6%). These unsatisfactory results obtained in spite of increased use of a wide palette of antihypertensive drugs, can be ascribed to a higher percentage of overweight and obese patients, prescription of lower doses of drugs, inadequate increase of doses, and poor patient compliance. Moreover, target blood pressure values are achieved by only a small number of diabetics, both in the USA and Europe. According to the data of the NHANES study from 1999-2000 (24), only 35.8% of diabetics have TA<130/80mmHg, and 40.4% have TA<140/90 mmHg, which is lower than the percentages achieved in our study. The European Survey on Diabetes and the Heart from 2003 has yielded even poorer results, with as low as 30% of diabetics with TA<140/90mmHg (25). In the EUROASPIRE I and II study there were 43% of diabetics with TA<140/90mmHg (22), fewer than in our study. On the other hand, some studies have demonstrated much better results compared to our study. In a study in Spain (26), twice as many diabetics (48%) have achieved target blood pressure values (TA<130/80 mmHg). In a study in Germany, 45.5% of patients with DM had TA<130/80mmHg, and TA<140/90mmHg was found in even 78.4% (23).

By way of analysis of the data from large clinical studies, it has been found that the treatment with both β -blockers and ACE inhibitors in secondary prevention could reduce the rate of major coronary events in both diabetics and non-diabetics. Additionally, the therapy in secondary prevention has also supplementary beneficial effects (27).

The first choice of drugs for the patients with survived MI are β -blockers. A large number of studies have shown that β -blockers reduce the size of infarction, incidence of spread of infarction, recurrent ischemia, reinfarction, and sudden death rates, as well as morbidity and mortality in patients with or without DM who survived MI (28, 29). In our study, 78.9% of patients with DM and slightly more patients without DM (87.3%) regularly took β -blockers. According to the

data from similar studies, patients with DM tend to use β -blockers to a much lesser extent compared to those without DM. In the EUROASPIRE I and II study, β -blockers were used by 63% of patients without DM and by 62% of those with DM, which was markedly lesser than in our study (22). Other studies have shown even lesser use of β -blockers by both diabetics and non-diabetics. In an English study (30), β -blockers were used by 26.7% of patients with DM and 34.4% of those without DM, and in one study from Saudi Arabia 43% of patients with DM and 44% of those without DM (31).

The use of ACE inhibitors after MI reduces infarct size, limits ventricular remodelling, and reduces mortality. The patients at high risk, where those with DM belong too, have the greatest benefit from early use of ACE inhibitors (32, 33).

In our study, approximately the same number of patients with and without DM regularly took ACE inhibitors (84.8% vs 89.8%). Our results are better than the results obtained in other studies. In the EUROASPIRE I and II study slightly more patients with DM than those without DM have regularly taken ACE inhibitors (49% vs 35%) (22). A study from Saudi Arabia (31) has shown slightly better use of ACE inhibitors by the patients with DM (67% vs 51%). On the other hand, in an English study (30), 73.6% of patients without DM and 61% of those with DM have used ACE inhibitors, which is also below the results obtained in our study.

Our study has shown a very ample use of β -blockers and ACE inhibitors in secondary prevention if MI in patients with and without DM, even better than in some developed countries, but still with significant potentials for their wider use in the future. In addition to the use of antihypertensive drugs, non-pharmacologic measures too can reduce blood pressure values, and strong insistence is required regarding even better use of these secondary prevention measures.

The results of many studies in the field of secondary prevention have clearly demonstrated that increased blood pressure after acute MI is associated with increased risk of reinfarction and death from coronary disease in both diabetics and non-diabetics (34-36). These results were confirmed by our study as well. Modification of variable risk factors, arterial hypertension being one of them, substantially contributes to diminished risk of adverse coronary events (37). Education of individuals with survived MI about their continued treatment and prevention of risk factors in order to avoid secondary complications is therefore indispensable. It is not an easy goal to achieve, and the task of every physician is to repeatedly animate the patient regarding the prevention or, if already present, the treatment of risk factors.

CONCLUSION

Our study of the evaluation of secondary prevention in attaining target blood pressure values in patients

with and without DM and survived MI has shown a high prevalence of increased blood pressure values particularly in the group of patients with DM, and still insufficient use of β -blockers and ACE inhibitors. In patients with DM the attainment of blood pressure values TA<140/90mmHg was significant, while for the pressure ranges TA<130/80mmHg it was unsatisfactory. In DM-

free patients, target blood pressure values have been achieved in a significant degree. However, our results lag behind when compared to other studies' results mentioned in the discussion. The measures of secondary prevention of cardiovascular events should therefore be intensified, particularly in DM patients.

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DOSTIZANJE CILJNIH VREDNOSTI KRVNOG PRITISKA KOD BOLESNIKA SA PRELEŽANIM INFARKTOM MIOKARDA I ŠEĆERNOM BOLEŠĆU

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Sažetak

Iako je arterijska hipertenzija važan faktor koji doprinosi kardiovaskularnim komplikacijama kod koronarnih bolesnika sa i bez dijabetesa mellitusa (DM), dostizanje ciljnih vrednosti krvnog pritiska se u praksi retko ostvaruje.

Cilj ove studije bio je da se uporedi dostizanje ciljnih vrednosti krvnog pritiska kod bolesnika sa preživelim infarktom miokarda (IM) koji imaju DM (grupa A) sa onima koji nemaju DM (grupa B) .

Tokom istraživanja praćena je u trogodišnjem periodu grupa od 118 bolesnika, 34 pripadalo je grupi A i 84 grupi B, oba pola sa potvrđenom dijagnozom IM.

Posle trogodišnjeg sprovođenja mera sekundarne prevencije bolesnici grupe B imali su veću zastupljenost ciljnih vrednosti krvnog pritiska (TA<140/90mmHg) u odnosu na početak istraživanja (84.8% prema 28.6%) (p<0.0001). Bolesnici grupe A nemaju statistički značajno veću zastupljenost ciljnih vrednosti krvnog pritiska (TA<130/80mmHg) na kraju istraživanja (11.8% prema 24.2%) (p>0.05), ali je zato njihov procenat sa vrednostima TA<140/90mmHg statistički značajno veći (57.6% prema 18.2%) (p<0.0005). Analiza primene mera sekundarne prevencije pokazala je da 21.3% bolesnika grupe A i 12.7% grupe B nije uzimalo β-blokatore, ali razlika nije statistički signifikantna (p>0.05). Takođe, u pogledu uzimanja ACE inhibitora nema statistički signifikantne razlike između grupe A (84.8%) i grupe B (89.8%) (p>0.05).

Naša studija o evaluaciji mera sekundarne prevencije u pogledu dostizanja ciljnih vrednosti krvnog pritiska kod bolesnika sa/bez DM i preležanim IM, pokazala je visoku prevalencu povišenih vrednosti krvnog pritiska, naroćito u grupi sa DM, kao i još uvek nedovoljnu upotrebu β-blokatora i ACE inhibitora. Stoga treba intenzivirati mere sekundarne prevencije kardiovaskularnih događaja, naroćito kod bolesnika sa dijabetesom.

Ključne reći: ciljne vrednosti krvnog pritiska, dijabetičari i infarkt miokarda, nedijabetičari i infarkt miokarda, sekundarna prevencija