

Original article

Acute Myocardial Infarction in Patients under Forty-Five Years of Age: What Has Changed in Ten Years?

Danijela Đorđević Radojković^{1,2}, Miodrag Damjanović¹, Svetlana Apostolović^{1,2},
Jelena Milošević¹, Dragana Stanojević¹, Goran Koraćević^{1,2}, Ružica Janković Tomašević¹,
Tomislav Kostić^{1,2}, Sonja Dakić^{1,2}, Jelena Cvetković², Jovana Šarić²

¹University Clinical Center Niš, Cardiology Clinic, Niš, Serbia

²University of Niš, Faculty of Medicine, Niš, Serbia

SUMMARY

Introduction/Aim. The incidence of acute myocardial infarction (AMI) is declining in developed countries due to better prevention and more effective treatment of risk factors, however, the proportion of younger patients with AMI is increasing. The aim of the research was to compare patients under the age of 45 years with acute myocardial infarction at a ten-year interval, to detect changes in frequency and risk factors of AMI.

Material and methods. The retrospective study included patients under the age of 45 years, hospitalized at the Cardiology Clinic, University Clinical Center Niš, with a diagnosis of AMI during 2023 and 2013. The frequency of AMI, risk factors for coronary artery disease, the way of presentation and prevalence of coronary artery disease in both groups were compared.

Results. During the ten-year period, the total number of patients annually hospitalized with AMI increased (985 vs 1691). The proportion of younger patients increased significantly from 18 (1.7%) in 2013 to 57 (3.4%) in 2023, $p = 0.008$. The youngest patient with AMI in 2013 was 31 years old and in 2023, 25 years. The groups differed significantly in average age (43.3 years in 2013 vs 33.2 years in 2023, $p = 0.02$). Significantly more patients had dyslipidemia (89.8% vs 47.1%) and positive family history (87.8% vs 47.1%) in the 2023 group. The majority of patients in both groups presented with ST-segment elevation myocardial infarction (STEMI) and the majority had single-vessel disease. During 2023, the number of younger patients with three-vessel disease increased (5.3% vs 0%).

Conclusion. The proportion of patients aged up to 45 years among patients with AMI in our community has increased over the last ten years, and the average age and the minimum age of this patient group have decreased, with a higher frequency of dyslipidemia, heredity, and three-vessel coronary disease.

Keywords: myocardial infarction, young patients, risk factors

Corresponding author:

Jelena Milošević

e-mail: jelena.milosevic95@gmail.com

INTRODUCTION

The incidence of acute myocardial infarction (AMI) is declining in developed countries due to better prevention and more effective treatment of risk factors, nevertheless, cardiovascular and cerebrovascular diseases are still the leading cause of death, more than malignancies and chronic respiratory diseases combined (1 - 3). However, the proportion of younger patients with AMI is increasing, which may lead to long-term serious socioeconomic consequences (4).

Based on the observation that the number of younger patients with AMI is increasing in our community, the aim of the study was to compare younger patients with AMI in a ten-year interval to show whether the incidence of AMI has really increased and whether there are changes in risk factors that we could influence.

PATIENTS AND METHODS

The retrospective study included 1,691 patients hospitalized at the Cardiology Clinic, University Clinical Center Niš, with a diagnosis of myocardial infarction in 2023, and 985 patients who were hospitalized with the same diagnosis in 2013. We considered younger patients to be patients aged up to 45 years. Patients up to 45 years of age were selected from both calendar years and then the frequency of myocardial infarction, risk factors for coronary disease, the way of presentation, and prevalence of coronary disease were compared in both groups. We investigated traditional risk factors: age (we included patients up to 45), sex, history of smoking, family history (this parameter was considered positive if a patient's male first-degree relative developed cardiovascular disease-myocardial infarction, coronary revascularization or stroke before the age of 55, or if their female first-degree relative had developed it before the age of 65), history of hypertension (this parameter was considered positive if a patient had already been on antihypertensive therapy), diabetes mellitus (this parameter was considered positive if a patient had already been taking antidiabetic medications), dyslipidemia (this parameter was considered positive if a patient knew that he had elevated blood fats or has already been on antilipemic therapy or they had elevated lipid values an admission) and BMI (this was calculated by Quetelet formula, by dividing an individual's

weight in kilograms by their height in meters squared). The absolute values of blood pressure, blood glucose, and lipid levels were not taken into consideration because some patients controlled those values with regular therapy.

The collected data was processed in SPSS (Statistical Package for Social Science), Statistics for Windows, Version 13 (SPSS Inc., Chicago, Ill., USA). The normality of the distribution of the continuous variables was tested using the Shapiro-Wilk test. Parameter values between groups with normal distribution were compared using a Student's t-test for independent samples and ANOVA analysis of variance - Kruskal Wallis and Post Hoc Test. In case of deviation from normal distribution, Mann-Whitney test was used. The values of $p < 0.05$ were considered statistically significant.

RESULTS

Out of 985 patients hospitalized for acute myocardial infarction in 2013, 18 (1.7%) were under the age of 45. Out of 1,691 patients hospitalized for acute myocardial infarction in 2023, 57 of them (3.4%) were under the age of 45 years. Over the 10-year period, the total number of patients who are annually hospitalized with AMI increased. The proportion of younger patients in the total population of AMI patients increased significantly from 1.7% to 3.4%, $p = 0.008$, Figure 1.

The demographic characteristics of the examined groups are shown in Table 1.

The youngest patient with AMI in 2013 was 31 years old, and in 2023, 25 years old. The groups differed significantly in average age, 2013 - 43.3 years, 2023 - 33.2 years, $p = 0.02$. (Figure 2, 3 and 4).

The statistical results of comparing the groups according to the investigated parameters are shown in Table 1.

The groups did not differ significantly by gender (men 83.3% vs 87.7%, NS).

A high percentage of smokers was observed in both groups (82.4% vs 89.2%).

In the group of younger patients from 2023, the frequency of hypertension is almost twice as high (42.1% vs. 23.5%), but statistical significance was not reached.

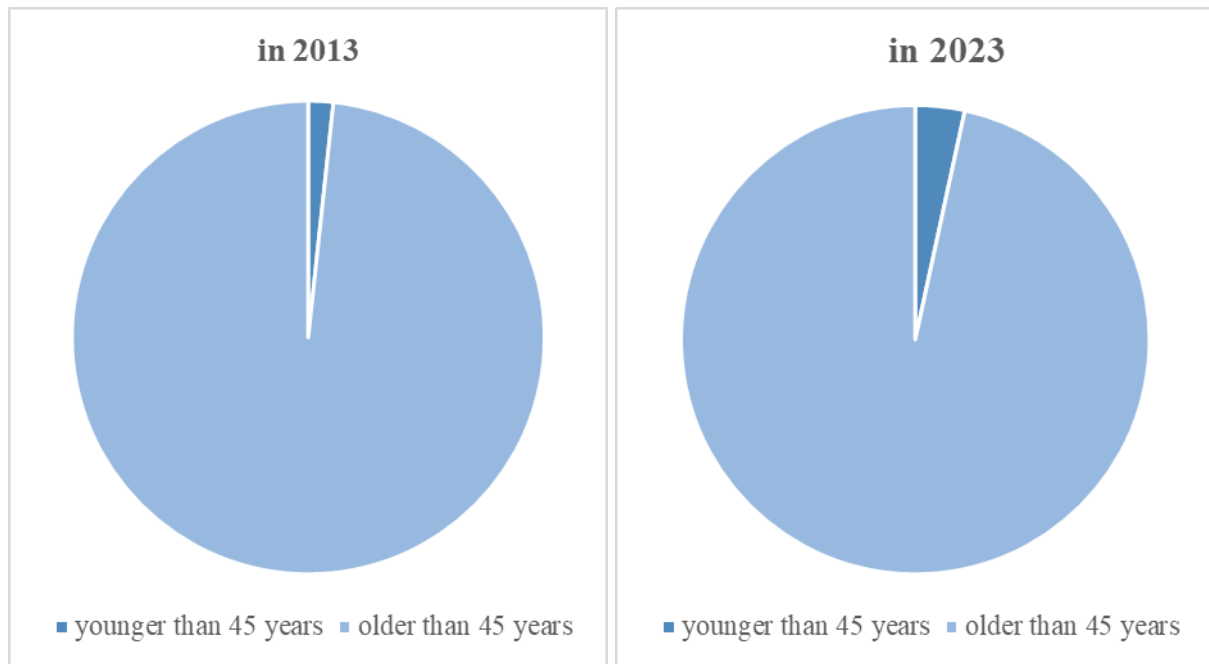


Figure 1. The proportion of younger patients in the total population of AMI patients in 2013 and 2023

Table 1. The demographic characteristic and statistical results of the comparison of the groups according to the investigated parameters

Parameters	In 2013 (N = 18)	In 2023 (N = 57)	Significance p value
Men	15 (83.3%)	50 (87.7%)	0.146
Age	43.3 ± 4.1 Min 31 Max 45	33.2 ± 5.24 Min 25 Max 45	0.002*
ACS presentation			0.008*
STEMI	15 (82.4%)	45 (78.9%)	1.000
NSTEMI	3 (17.6%)	12 (21.1%)	0.383
Diabetes mellitus	NA	Type 1 -2 (3.5%) Type 2 - 4 (7%)	0.668
Hypertension	4 (23,5%)	24 (42,1%)	0.534
Smoking	Current smokers 12 (70.6%) Non-smokers 6 (17.6%)	Current smokers 47 (82.1%) Non-smokers 6 (10.8%)	0.768
Dyslipidemia	8 (47.1%)	52 (89.8%)	0.001*
Family history	8 (47.1%)	50 (87.8%)	0.009*
BMI	27.15	27.46	0.749
Vessel involved (number)			
MINOCA	0 (0%)	11 (19.3%)	0.002*
1	11 (57.9%)	34 (57.9%)	
2	7 (47.1%)	8 (12.3%)	
3	0 (0%)	4 (5.3%)	

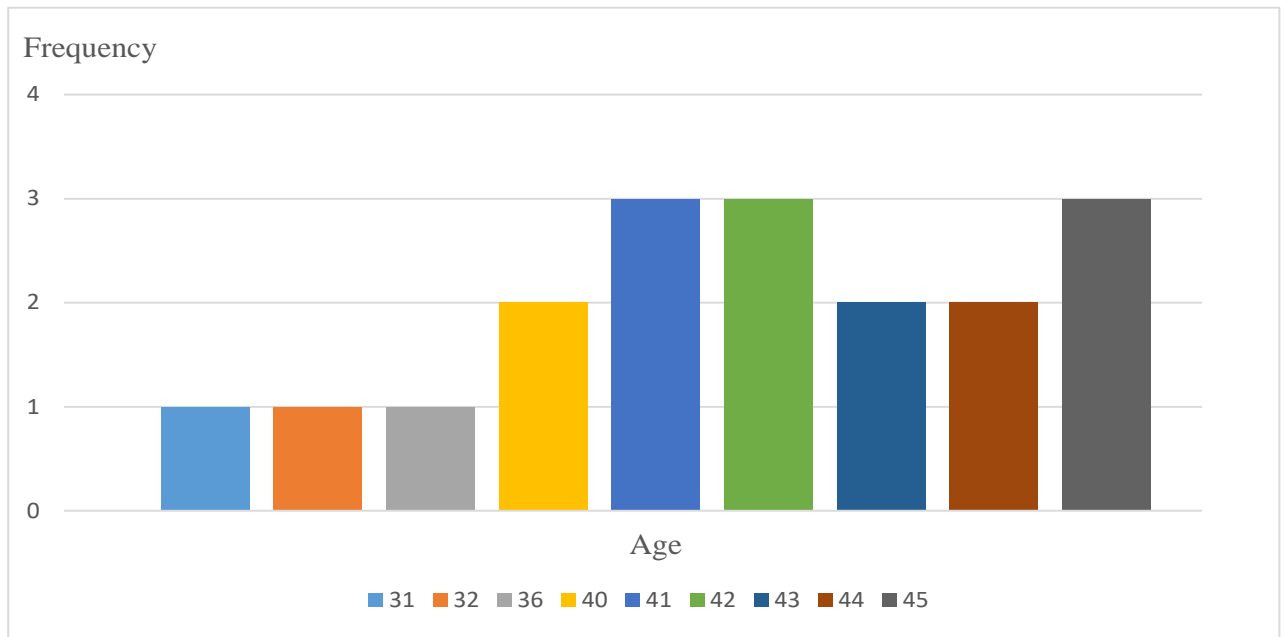


Figure 2. The frequency of age in which patients had myocardial infarction in 2013

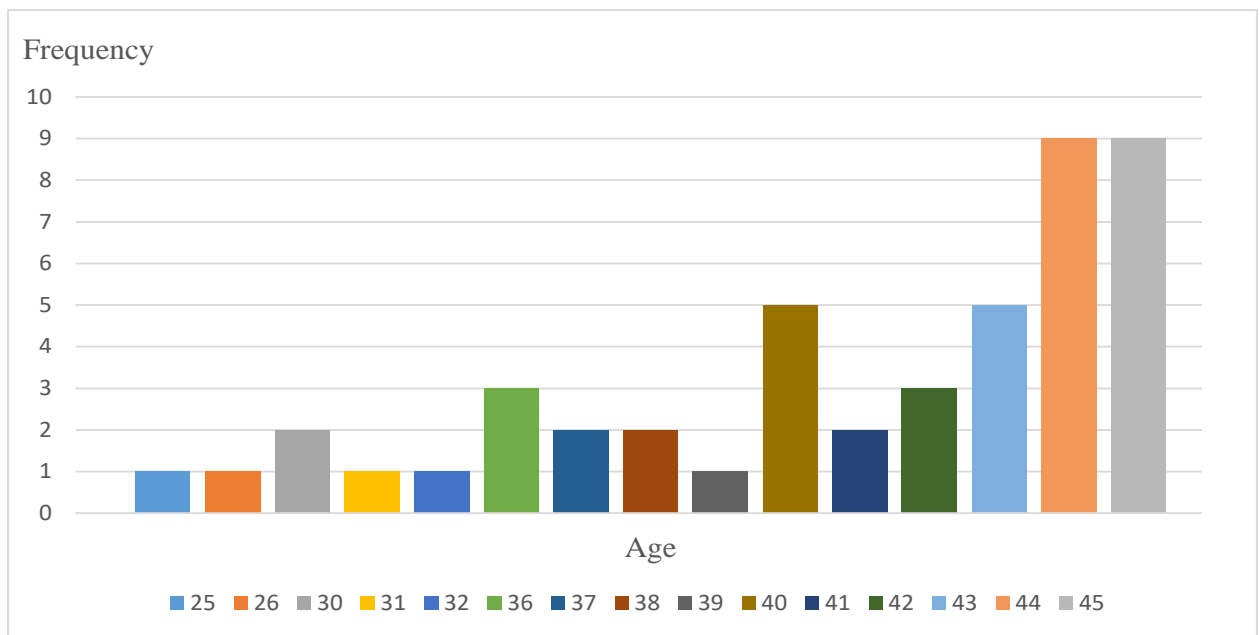


Figure 3. The frequency of age in which patients had myocardial infarction in 2023

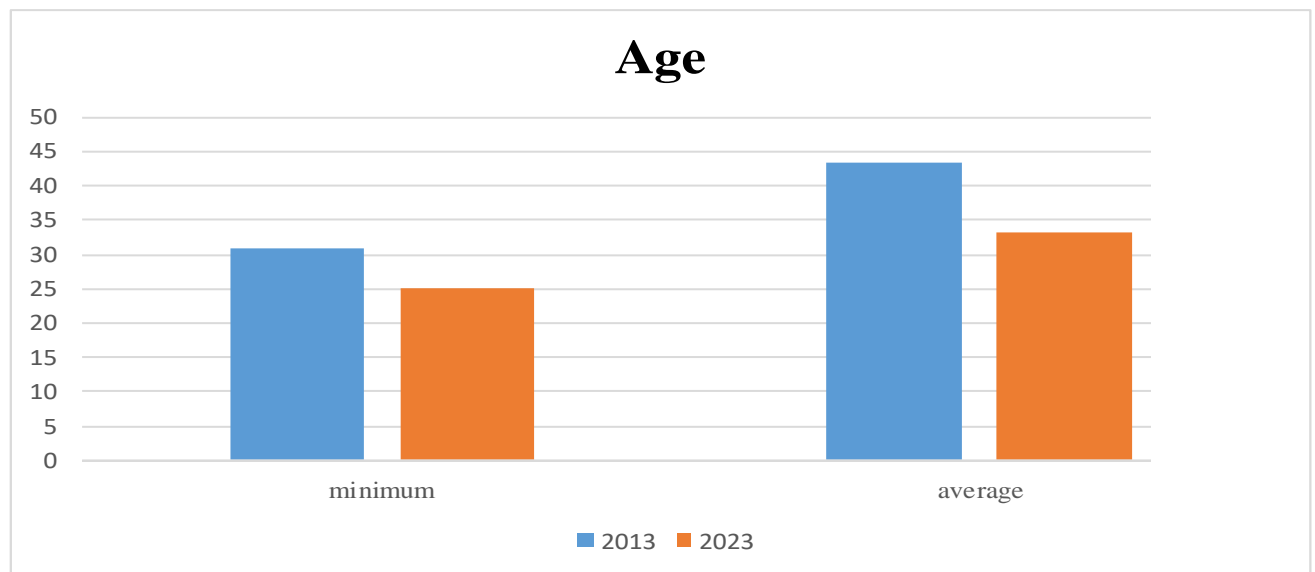


Figure 4. Minimum and average age in which patients had myocardial infarction in 2013 and in 2023

In the 2023 group, significantly more patients had dyslipidemia (89.8% vs 47.1%) and a positive family history (87.8% vs 47.1%).

Although there was no significant difference in BMI between the groups (27.15 vs 27.46, NS), the majority of patients in both groups were overweight but not obese.

The majority of patients in both groups presented with ST-segment elevation myocardial infarction (STEMI) (82.4% vs. 78.9%, NS) and the majority had single-vessel disease (57.9% in both groups). In 2023, the number of younger patients with three-vessel disease increased (5.3% vs 0%), but there were also patients with myocardial infarction non-obstructive coronary artery (MINOCA), which was not diagnosed in 2013.

DISCUSSION

It used to be an encouraging fact that mortality from AMI is decreasing. Now the frequency of AMI in the world is also decreasing. In the USA, the number of heart attacks has been continuously decreasing since 2002 until today (1-3). However, in our community, the overall incidence is still growing, and the increase in the proportion of younger patients proportional to the total number of patients with AMI is even more worrying. In the majority of previous studies, younger heart attack patients were considered to be those under 50 years of age (5, 6). In research by Chinese and Japanese authors, a pre-

mature heart attack was considered to be one under the age of 55 in men and under 65 in women (7, 8). The increase in the number of patients under the age of 45 with AMI is alarming data (9), which is why we also decided to single out this category of patients as younger.

The average age of patients in our research decreased over a 10-year period (from 43.3 to 33.2 years), which indicates that coronary atherosclerosis develops earlier and faster. It used to be referred to as a premature coronary disease, but is now referred to as a rapidly progressing form of the disease (10). In addition to smoking, dyslipidemia and diabetes, alcohol and cocaine use, obesity, level of lipoprotein a and homocysteine, oral contraceptive use, hypercoagulable states, systemic connective tissue disease, and hereditary factors are increasingly identified as contributing factors (10). Emotional stress is an insufficiently studied factor. MSIMI2 study has shown that psychological and physical stress is twice as likely to lead to myocardial ischemia in women after myocardial infarction (MI) than in men, in the age group up to 61 years, which is explained by more frequent microvascular dysfunction and peripheral vasoconstriction (11). Our respondents included a significant number of individuals with severe emotional and physical stress, depression, and steroid abuse during exercise. This is not shown in the results because these data were collected in 2023, but not in 2013, so we could not compare them. Other authors have come to similar conclusions (9).

Among the younger patients with AMI, more than 80% are men in both groups studied, which is similar to data from the literature (6) and corresponds to the well-known fact that coronary disease occurs 7 – 10 years later in women than in men. In the USA, the average age of men at their first heart attack is 65.6 years, while women are 72 years old. (1) Data from a three-year analysis of over 875,000 MI patients in Germany shows that women are 7 – 12 years older at the time of AMI, but also that the total number of patients with AMI is decreasing (12), which is not the case in our study. However, in a study by Chinese authors of over 9,000 patients under the age of 45 with AMI, 93.9% were male (13), which means that in our community there are still slightly more women suffering of premature AMI compared to the data from the literature, although there are some similar results to ours (4). Women are increasingly exposed to the same risk factors as men and at an earlier age.

The groups did not differ significantly in the percentage of smokers, but smoking was the dominant and unchanged risk factor in the younger AMI patient population in both 2013 and 2023. A study by Palmer et al. showed that male smokers aged 18 – 49 years have a 9-fold increased risk of MI compared to non-smokers of the same age. For female smokers, the risk is even 13 times higher (14). The prevalence of smoking as a risk factor in our younger respondents is over 80% of current and former smokers and is much higher than in other similar studies in the world, where it ranges from only 12% in Germany in the total population of patients with MI to 65.7% in China and 67.6% in Japan in younger patients (7, 8, 12). In New Zealand, the prevalence of smokers in patients up to 50 years of age with AMI is about 47%, and in the USA 52.5% (6, 15). In all studies, the percentage of smokers in the group of younger patients with AMI is significantly higher than in the group of older patients. Smoking accelerates the progression of atherosclerosis as it leads to endothelial dysfunction and increases the risk of thrombosis (16, 17). Smokers experience their first MI more than ten years earlier than non-smokers (18).

In our study, the incidence of dyslipidemia is increasing significantly in younger patients with AMI. In 2023, 89.8% of patients up to 45 years of age with AMI have dyslipidemia. Furthermore, data from the literature shows that dyslipidemia is a risk factor prevalent in patients with premature myocardial infarction in the range of 45%-82% (7, 8, 13).

This tells us that it is necessary to start treating dyslipidemia earlier, especially considering that our country belongs to the category of countries with a very high risk of cardiovascular morbidity and mortality, according to the ten-year risk tables for fatal or non-fatal cardiovascular events (19, 20). In the European recommendations for the prevention of cardiovascular disease, patients under the age of 50 are classified as younger (21).

Positive family history as a risk factor for premature AMI is widespread in our study, even in 87.8% of younger patients from 2023, in contrast to younger patients from 2013 (47.1%) as well as data from the literature, where it ranges from 7% (7) to over 20%-25% (13). This calls for more serious research into the genetic predisposition to premature AMI.

The prevalence of hypertension in the 2023 patient group is almost twice as high as in the 2013 group, although no statistical significance was achieved. According to our results, hypertension is a less significant risk factor for premature AMI than dyslipidemia, smoking and positive family history. Other authors have shown similar results (7, 13).

Diabetes rarely occurs in our patients with premature AMI and is consistent with data from the literature (7, 13). The explanation for this is that type 2 diabetes is a more common and significant risk factor for coronary disease than type 1 diabetes and that it occurs in the older population.

Excess body weight was found in both groups of our subjects, but the groups did not differ in terms of BMI. In some studies, obesity was identified as a risk factor for AMI in a higher percentage of younger patients than in older patients (6).

Overall, hypertension and diabetes are less common in patients with premature myocardial infarction than in older patients, and smoking, dyslipidemia, and a positive family history are more common risk factors.

We did not examine blood homocysteine levels, which could be a significant risk factor for premature MI (13).

In both groups of younger patients, the acute coronary event presented as STEMI in approximately 80% of patients, and angiographically, single-vessel coronary disease was predominant, which is similar to other studies (5, 13). The increase in the number of patients with three-vessel coronary disease in the younger patients in 2023 is concerning,

indicating a more aggressive progression of atherosclerosis.

In addition to the traditional risk factors present at the earlier age, the increasing number of younger patients with AMI may be influenced by substance abuse and hypercoagulable conditions (9, 10), indicating the need for this type of screening in the younger population.

CONCLUSION

The proportion of patients up to 45 years of age among patients with AMI in our community has increased over the ten-year period, and the minimum number of years in which the disease occurs and the average age of this patient group have decreased. The prevalence of smoking is consistently high, and dyslipidemia and heredity are significantly more common, as is coronary three-vessel disease in younger people in 2023. The results suggest that AMI is occurring in younger patients and that better and earlier primary prevention is needed – tackling smoking and starting treatment for dyslipidemia earlier, as well as screening for coronary disease in patients with positive family history and investigating and preventing many new less recognized risk factors.

Study limitations

Our single-center investigation included patients with acute myocardial infarction from Nišava county but also the southeast part of Serbia who were referred to our Cardiology Clinic in the acute/subacute phase of myocardial infarction from 2013 – 2023. Our Clinic is the only healthcare facility with a catheterization laboratory in this part of Republic of Serbia, and we have been accepting patients from other counties for decades now. We do not have precise information on the incidence of ACS regarding the whole country for this period and this was not the focus of our investigation. Regarding the prevalence of MINOCA in 2013, it is possible that patients were misdiagnosed as myocarditis, since this entity was recently introduced in clinical practice (increased awareness). It is undoubtful that those patients need to be screened for other non-traditional risk factors and this paper is a part of our endeavor to start investigating them as thrombophilia, homocysteine, and more.

Conflict of interest

The authors declare no conflict of interest in preparing this article.

References

1. Tsao CW, Aday AW, Almarzoq ZI, et al. Heart Disease and Stroke Statistics - 2023 Update: A Report From the American Heart Association. *Circ* 2023; 147(8): e93-e621.
<https://doi.org/10.1161/CIR.0000000000001123>
2. Reynolds K, Go AS, Leong TK, et al. Trends in Incidence of Hospitalized Acute Myocardial Infarction in the Cardiovascular Research Network (CVRN). *Am J Med* 2017; 130(3): 317-27.
<https://doi.org/10.1016/j.amjmed.2016.09.014>
3. Krumholz HM, Normand S-LT, Wang Y. Twenty-Year Trends in Outcomes for Older Adults With Acute Myocardial Infarction in the United States. *JAMA Netw Open* 2019; 2(3): e191938-e.
<https://doi.org/10.1001/jamanetworkopen.2019.1938>
4. Wu WY, Berman AN, Biery D, et al. Recent Trends in Acute Myocardial Infarction Among the Young. *Curr Opin Cardiol* 2020; 35(5): 524-30.
<https://doi.org/10.1097/HCO.0000000000000781>
5. Bauer D, Neuberg M, Nováčková M, et al. Pre-hospital delay, clinical characteristics, angiographic findings, and in-hospital mortality in young and middle-aged adults with acute coronary syndrome: a single-centre registry analysis. *Eur Heart J Suppl* 2023; 25 (Supplement E): E33-E39.
<https://doi.org/10.1093/eurheartjsupp/suad102>
6. Matsis K, Holley A, Al-Sinan A, et al. Differing Clinical Characteristics Between Young and Older Patients Presenting with Myocardial Infarction. *Heart Lung Circ* 2017; 26: 566-71.
<https://doi.org/10.1016/j.hlc.2016.09.007>
7. Liu Q, Shi RJ, Zhang YM, et al. Risk factors, clinical features, and outcomes of premature acute myocardial infarction. *Front Cardiovasc Med* 2022; 9: 1012095.
<https://doi.org/10.3389/fcvm.2022.1012095>
8. Yanase T, Sakakura K, Taniguchi Y, et al. Comparison of Clinical Characteristics of Acute Myocardial Infarction Between Young (< 55 Years) and Older (55 to < 70 Years) Patients. *Int Heart J* 2021; 62(1): 33-41.
<https://doi.org/10.1536/ihj.20-444>
9. Sood A, Singh A, Gadkari C. Myocardial Infarction in Young Individuals: A Review Article. *Cureus* 2023; 15(4): e37102.
<https://doi.org/10.7759/cureus.37102>
10. Klein LW and Nathan S. Coronary Artery Disease in Young Adults. *JACC* 2003; 41(4): 529-31.
[https://doi.org/10.1016/S0735-1097\(02\)02861-9](https://doi.org/10.1016/S0735-1097(02)02861-9)
11. Vaccarino V, Sullivan S, Hammadah M, et al. Mental Stress-Induced-Myocardial Ischemia in Young Patients With Recent Myocardial Infarction. *Circ* 2018; 137(8): 794-805.
<https://doi.org/10.1161/CIRCULATIONAHA.117.030849>
12. Kuehnemund L, Koeppe J, Feld J, et al. Gender differences in acute myocardial infarction - A nationwide German real-life analysis from 2014 to 2017. *Clin Cardiol* 2021; 44(7): 890-8.
<https://doi.org/10.1002/clc.23662>
13. Zhang D, Zuo H, Yang H, et al. Comparison of clinical profiles and associated factors for acute myocardial infarction among young and very young patients with coronary artery disease. *Coron Artery Dis* 2022; 33(8): 655-60.
<https://doi.org/10.1097/MCA.0000000000001183>
14. Palmer J, Lloyd A, Steele L, et al. Differential Risk of ST Segment Elevation Myocardial Infarction in Male and Female Smokers. *J Am Coll Cardiol* 2019; 73(25): 3259-66.
<https://doi.org/10.1016/j.jacc.2019.03.525>

15. Biery DW, Berman AN, Singh A, et al. Association of smoking cessation and survival among young adults with myocardial infarction in the Partners YOUNG-MI registry. *JAMA Netw Open* 2020; 3: e209649.
<https://doi.org/10.1001/jamanetworkopen.2020.9649>
16. Messner B and Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. *Arterioscler Thromb Vasc Biol* 2014; 34: 509-15.
<https://doi.org/10.1161/ATVBAHA.113.300156>
17. Csordas A and Bernhard D. The biology behind the atherothrombotic effects of cigarette smoke. *Nat Rev Cardiol* 2013; 10: 219-30.
<https://doi.org/10.1038/nrcardio.2013.8>
18. Weiner P, Waizman J, Weiner M, et al. Smoking and first acute myocardial infarction: age, mortality and smoking cessation rate. *Isr Med Assoc J* 2000; 2: 446-9.
19. SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. *Eur Heart J* 2021; 42: 2439-54.
<https://doi.org/10.1093/eurheartj/ehab309>
20. SCORE2-OP working group and ESC Cardiovascular risk collaboration. SCORE2-OP risk prediction algorithms: estimating incident cardiovascular event risk in older persons in four geographical risk regions. *Eur Heart J* 2021; 42: 2455-67.
<https://doi.org/10.1093/eurheartj/ehab312>
21. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2021; 42: 3227-337.
<https://doi.org/10.1093/eurheartj/ehab484>

Article info

Received: March 23, 2024

Revised: June 5, 2024

Accepted: June 10, 2024

Online first: November 13, 2024

Akutni infarkt miokarda kod bolesnika starosti do četrdeset pet godina: šta se promenilo za deset godina?

Danijela Đorđević Radojković^{1,2}, Miodrag Damjanović¹, Svetlana Apostolović^{1,2}, Jelena Milošević¹, Dragana Stanojević¹, Goran Koraćević^{1,2}, Ružica Janković Tomašević¹, Tomislav Kostić^{1,2}, Sonja Dakić^{1,2}, Jelena Cvetković², Jovana Šarić²

¹Univerzitetski klinički centar Niš, Klinika za kardiologiju, Niš, Srbija

²Univerzitet u Nišu, Medicinski fakultet, Niš, Srbija

SAŽETAK

Uvod/Cilj. Premda incidencija akutnog infarkta miokarda (AIM) u razvijenim zemljama opada zbog bolje prevencije i efikasnijeg lečenja faktora rizika, povećava se udeo mlađih bolesnika sa AIM-om. Cilj ovog istraživanja bio je da uporedi bolesnike starosti do 45 godina koji su doživeli akutni infarkt miokarda u razmaku od deset godina kako bi se pokazalo da li se učestalost AIM-a kod mlađih povećala i da li je došlo do promena u vezi sa faktorima rizika.

Materijal i metode. Retrospektivnim istraživanjem obuhvaćeni su bolesnici hospitalizovani na Klinici za kardiologiju Univerzitetskog kliničkog centra u Nišu sa dijagnozom AIM-a postavljenom u toku 2023. i 2013. godine. Izdvojeni su bolesnici starosti do 45 godina iz obeju kalendarskih godina, a potom su upoređeni učestalost infarkta, faktori rizika za pojavu koronarne bolesti, način prezentovanja i rasprostranjenost koronarne bolesti zabeleženi u pomenutim grupama.

Rezultati. Za deset godina povećao se ukupan broj bolesnika sa AIM-om koji se godišnje hospitalizuju (985 : 1691). Značajno je povećan udeo mlađih bolesnika, od 18 (1,7%) 2013. godine na 57 (3,4%) 2023. godine ($p = 0,008$) i smanjena njihova prosečna starost (43,3 godine 2013 : 33,2 godine 2023; $p = 0,02$). Najmlađi bolesnik sa AIM-om 2013. godine imao je 31 godinu, a 2023. 25 godina. Značajno je veći broj bolesnika iz grupe iz 2023. godine koji je imao dislipidemiju (89,8% : 47,1%) i pozitivnu porodičnu anamnezu (87,8% : 47,1%). Kod većine bolesnika u obema grupama prepoznat je infarkt miokarda sa elevacijom ST- segmenta (engl. *ST-elevation myocardial infarction* – STEMI). Takođe, većina je imala jednosudovnu bolest. U toku 2023. godine povećan je broj mlađih bolesnika sa trosudovnom bolešću (5,3% : 0%).

Zaključak. Udeo bolesnika starosti do 45 godina među bolesnicima sa AIM-om u našoj sredini povećao se u prethodnih deset godina, dok su se minimalni broj godina u kojima se bolest javila i prosečna starost ove grupe bolesnika smanjili. Takođe, zabeležena je veća učestalost dislipidemije, herediteta i trosudovne koronarne bolesti.

Ključne reči: infarkt miokarda, mlađi bolesnici, faktori rizika