

# ISPITIVANJE UTICAJA RAZLIČITIH DETERMINANTI NA SMRTNI ISHOD OD AKUTNOG KORONARNOG SINDROMA PACIJENATA LEČENIH U KORONARNOJ JEDINICI OPŠTE BOLNICE U VALJEVU I NJIHOVE RAZLIKE

ORIGINALNI RAD

ORIGINAL ARTICLE

## ASSESSING DIFFERENT DETERMINANTS INFLUENCING THE DEATH OUTCOME RESULTING FROM ACUTE CORONARY SYNDROME IN PATIENTS TREATED IN THE CORONARY UNIT OF THE GENERAL HOSPITAL IN VALJEVO, AND THEIR DIFFERENCES

Aleksandra Filipović<sup>1</sup>, Janko Janković<sup>2</sup>

<sup>1</sup> Zavod za javno zdravlje Valjevo, Valjevo, Srbija

<sup>1</sup> Institute of Public Health Valjevo, Valjevo, Serbia

<sup>2</sup> Univerzitet u Beogradu, Medicinski fakultet, Institut za socijalnu medicinu, Beograd, Srbija

<sup>2</sup> University of Belgrade, Faculty of Medicine, Belgrade, Institute of Social Medicine, Serbia

### SAŽETAK

**Uvod:** Kardiovaskularne bolesti su vodeći uzrok morbiditeta i mortaliteta u većini zemalja sveta i odgovorne su za smrt 17,9 miliona ljudi godišnje i 11,8% ukupnih DALY-ja. U Srbiji je akutni koronarni sindrom (AKS) glavni uzročnik smrtnog ishoda među ishemijskim bolestima srca, sa udelom od 49,9%.

**Cilj:** Cilj rada je da se ispita povezanost različitih determinanti (demografskih, antropometrijskih, bioloških markera, faktora rizika, prisustva komorbiditeta i farmakoterapijskog pristupa) sa smrtnim ishodom od akutnog koronarnog sindroma pacijenata lečenih u Koronarnoj jedinici, kao i njihove razlike.

**Materijali i metode:** Istraživanje je sprovedeno kao studija preseka i njime je obuhvaćeno 384 punoletnih lica sa AKS-om, koji su bili korisnici usluga Odeljenja kardiologije sa koronarnom jedinicom Opšte bolnice u Valjevu, 2020. godine. Kao instrument istraživanja korišćen je „Koronarni list“, koji su kreirali, prema nacionalnim potrebama, Institut za javno zdravlje Srbije „Dr Milan Jovanović Batut“, Institut za epidemiologiju i Udruženje kardiologa Srbije, u formi upitnika koji popunjavaju lekari zaposleni u Koronarnoj jedinici, a koji se potom dostavlja Zavodu za javno zdravlje Valjevo. Svi ispitanici su dali informisani pristanak za anonimno učesće u istraživanju. Dobijeni podaci su analizirani metodama deskriptivne i analitičke statistike, kao i metodama univarijantne i multivarijantne linearne regresije.

**Rezultati:** Ukupan uzorak činilo je 288 (75%) muškaraca i 96 (25%) žena. Prosečna starost pacijenata umrlih od AKS-a iznosila je  $72,9 \pm 9,8$  godina, dok je starost pacijenata koji nisu umrli iznosila  $65,0 \pm 12,0$  godina, i ova razlika se pokazala kao statistički značajna ( $p < 0,001$ ). Pacijenti kojima su prilikom prijema u bolnicu izmerene niže vrednosti i sistolnog i dijastolnog krvnog pritiska su statistički značajno više umirali od onih koji su imali nešto više vrednosti ( $p < 0,001$ ). Evidentna je manja smrtnost onih pacijenata sa AKS-om kojima je, tokom hospitalizacije, ordinirana sledeća farmakoterapija: acetylsalicylic acid ( $p < 0,001$ ), beta blokatori ( $p = 0,003$ ), ACE inhibitori ( $p < 0,001$ ) i statini ( $p < 0,001$ ), dok su smrtni ishod imali svi pacijenti koji su u propisanoj terapiji imali i inotropne, kao jedan od lekova ( $p < 0,001$ ).

**Zaključak:** Naše istraživanje ukazuje na postojanje povezanosti ispitivanih determinanti sa smrtnim ishodom pacijenata obolelih od akutnog koronarnog sindroma. Neophodno je poboljšanje kvaliteta podataka, relevantno i pravovremeno vođenje medicinske dokumentacije i evidencije, te kontinuirano unapređenje programa prevencije, sa ciljem smanjenja faktora rizika za nastanak AKS-a.

**Ključne reči:** akutni koronarni sindrom, smrtni ishod, faktori rizika

### ABSTRACT

**Introduction:** Cardiovascular diseases are the leading cause of morbidity and mortality in most countries of the world and are responsible for the death of 17.9 million people per year and for 11.8% of total DALYs. In Serbia, acute coronary syndrome (ACS) is the main cause of death among ischemic heart diseases, with a share of 49.9%.

**Aim:** The aim of the study is to examine the association of various determinants (demographic, anthropometric, biological markers, risk factors, presence of comorbidities, and the pharmacotherapeutic approach) with the death outcome resulting from ACS patients treated at the Coronary Unit, as well as their differences.

**Materials and methods:** This cross-sectional study included 384 adults with ACS, who were patients of the Cardiology Department with the Coronary Unit of the General Hospital in Valjevo, in 2020. The so-called Coronary Sheet was used as a research instrument. It was created, based on national needs, by the Institute of Public Health of Serbia "Dr. Milan Jovanović Batut", the Institute of Epidemiology, and the Cardiology Society of Serbia. This sheet is in the form of a questionnaire filled out by doctors working at the Coronary Unit, which is then submitted to the Institute of Public Health Valjevo. All respondents gave informed consent for anonymous participation in the research. The obtained data were analyzed using the methods of descriptive and analytical statistics, as well as the methods of univariate and multivariate linear regression.

**Results:** The total sample consisted of 288 (75%) men and 96 (25%) women. The average age of patients who died of ACS was  $72.9 \pm 9.8$  years, while the average age of patients who did not die of ACS was  $65.0 \pm 12.0$  years. The difference was statistically significant ( $p < 0.001$ ). Statistically significantly more patients who had lower values of both systolic and diastolic blood pressure, when admitted to hospital, died than those who had somewhat higher values of systolic and diastolic pressure at admission ( $p < 0.001$ ). The mortality rate was lower for patients with ACS who were prescribed acetylsalicylic acid ( $p < 0.001$ ), beta blockers ( $p = 0.003$ ), ACE inhibitors ( $p < 0.001$ ), and statins ( $p < 0.001$ ) during hospitalization, while all patients whose therapy included inotropes as one of the drugs died ( $p < 0.001$ ).

**Conclusion:** Our research indicates the existence of a link between the examined determinants and the death outcome in patients suffering from ACS. It is necessary to improve the quality of data, maintain relevant and timely medical documentation and records, and continuously improve prevention programs, with the aim of reducing risk factors for the occurrence of ACS.

**Key words:** acute coronary syndrome, death outcome, risk factors

Autor za korespondenciju:

Janko Janković

Institut za socijalnu medicinu, Medicinski fakultet, Univerzitet u Beogradu

Dr Subotića 15, 11000 Beograd, Srbija

Elektronska adresa: janko.jankovic@med.bg.ac.rs

Corresponding author:

Janko Janković

Institute of Social Medicine, Faculty of Medicine, University of Belgrade, Serbia

15 Dr Subotića Street, 11000 Belgrade, Serbia

E-mail: janko.jankovic@med.bg.ac.rs

Primljeno • Received: October 25, 2022; Revidirano • Revised: October 27, 2022; Prihvaćeno • Accepted: October 30, 2022; Online first: December 25, 2022

DOI: 10.5937/smlk3-40807

## UVOD

Bolesti srca i krvnih sudova su vodeći uzrok obolevanja i umiranja, kako u razvijenim zemljama sveta, tako i u zemljama u razvoju. U svetu, 17,9 miliona ljudi umre svake godine od ove patologije [1]. Glavni uzrok izgubljenih godina života, globalno i u svakom pojedinačnom regionu sveta, jeste ishemijska bolest srca (IBS), praćena cerebrovaskularnom bolešću (CVB). Kardiovaskularne bolesti (KVB) su odgovorne za 11,8% ukupnih DALY-ja (engl. *disability-adjusted life year*), a glavna bolest u grupi je IBS, sa 5,2% [2]. Najveći porast smrtnih slučajeva u svetu, u poslednje dve decenije, evidentiran je upravo po pitanju smrti od IBS-a, te je u 2019. godini od ove bolesti umrlo 8,9 miliona ljudi [3].

Ni u Srbiji nije drugačija situacija, pa su kardiovaskularne bolesti, u 2020. godini, bile vodeći uzrok umiranja, sa udelom od 47,3% [4]. U strukturi umiranja od kardiovaskularnih bolesti, IBS je imala udeo od 15,9%, u 2020. godini, dok je akutni koronarni sindrom (AKS) bio glavni uzrok među ishemijskim bolestima srca, odgovoran za 49,9% smrti. Standardizovane stope mortaliteta od AKS-a su iznosile više od 36,1 na 100.000 stanovnika, na teritoriji Kolubarskog okruga, i zajedno sa još tri okruga (Zlatiborski, Raški i Severnobanatski) zabeležile su najveće vrednosti u Srbiji, u 2020. godini [5]. U populaciji Srbije se godišnje izgubi 150.886 DALY-ja zbog IBS-a [6].

AKS, kao najkompleksnija forma ishemijske bolesti srca [7], predstavlja spektar kliničkih ispoljavanja uzrokovanih patofiziološkim procesom, u čijoj osnovi se nalazi ruptura ili erozija aterosklerotskog plaka u koronarnoj arteriji, koju prati stvaranje intravaskularnog koaguluma, koji uzrokuje akutno smanjenje ili potpuni prekid dotoka krvi. AKS može da se manifestuje kao: akutni infarkt miokarda sa elevacijom ST segmenta (engl. *ST-elevation myocardial infarction – STEMI*), akutni infarkt miokarda bez elevacije ST segmenta (engl. *non-ST-elevation myocardial infarction – NSTEMI*), nestabilna angina pectoris (AP) ili naprasna srčana smrt [5].

S obzirom da je opterećenje kardiovaskularnim bolestima veliko [8], posebna pažnja stručne javnosti je usmerena ka prevenciji faktora rizika, bar onih koje je moguće korigovati, a to su: prekomerna telesna težina, arterijska hipertenzija, *diabetes mellitus*, hiperlipoproteinemija [9]. Dosadašnja istraživanja ukazuju na to da različiti stepeni gojaznosti i sedalački način života učestvuju, kao značajni faktori rizika, u nastanku AKS-a, kao i u lošijoj prognozi bolesti [10]. Rizik od smrtnog ishoda od AKS-a je veći kod osoba normalne težine sa centralnim tipom gojaznosti [11]. Kada je reč o arterijskoj hipertenziji, ona je vodeći uzrok prevremenih neželjenih kardioloških događaja i nosi dva do tri puta veći rizik

## INTRODUCTION

Cardiovascular diseases are the leading cause of morbidity and mortality, both in developed and developing countries of the world. Globally, every year, 17.9 million people die due to this type of pathology [1]. The main cause of life years lost, both globally and in every individual region of the world, is ischemic heart disease (IHD), followed by cerebrovascular disease (CVD). Cardiovascular diseases (CVDs) are responsible for 11.8% of total disability-adjusted life years (DALYs), and the main disease in this group is IHD, with 5.2% [2]. In fact, the greatest increase in mortality in the world, in the last two decades, was recorded regarding deaths from IHD – in 2019, 8.9 million people died from this disease [3].

The situation in Serbia is no better. Thus, in 2020, cardiovascular diseases were the leading cause of death, with a share of 47.3% [4]. Within the structure of mortality from cardiovascular diseases, in 2020, IHD had a share of 15.9%, while acute coronary syndrome (ACS) was the main cause amongst ischemic heart diseases, and it was responsible for 49.9% of deaths. Standardized mortality rates from ACS were more than 36.1 per 100,000 population, in the territory of the Kolubara District, and together with the mortality rates for three more districts (the Zlatibor District, the Raška District, and the North Banat District), had the highest values in Serbia, in 2020 [5]. In the population of Serbia, 150,886 DALYs are lost yearly, due to IHD [6].

As the most complex form of ischemic heart disease [7], ACS represents a spectrum of clinical manifestations caused by a pathophysiological process, which stems from a rupture or erosion of atherosclerotic plaque in the coronary artery that is accompanied by the development of an intravascular coagulum, which causes acute reduction or complete blockage of blood flow. ACS can manifest as the following: ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), unstable angina pectoris (AP), or sudden cardiac death [5].

Since the burden of cardiovascular diseases is great [8], special attention of the professional community is directed towards preventing risk factors, at least the ones that can be modified, these being the following: excess body weight, arterial hypertension, diabetes mellitus, hyperlipoproteinemia [9]. Research up to date indicate that different levels of obesity and a sedentary lifestyle participate, as significant risk factors, in the development of ACS, as well as in poorer prognosis of disease [10]. Risk of the death outcome resulting from ACS is greater in persons with normal weight with central obesity [11]. As far as arterial hypertension is concerned, it is the leading cause of premature adverse cardiovascular events and carries a two to three times

od AKS-a, kod lica koja je imaju, u poređenju sa normotenzivnim osobama [12]. Studije pokazuju da osobe obolele od *diabetes mellitus*-a, koje su razvile AKS, imaju lošije, kako kratkoročne, tako i dugoročne ishode, u odnosu na lica bez ovog komorbiditeta [13]. S obzirom na to da su povišene vrednosti lipida u krvi jedan od najvažnijih aktera u procesu nastanka ateroskleroze, smanjenje njihovog nivoa doprinelo bi smanjenju morbiditeta i mortaliteta od IBS-a za čak 40% [14].

U etiopatogenezi AKS-a, posebnu ulogu imaju i nezdravi stilovi života, poput pušenja i izloženosti stresu [15,16]. Prema studiji slučaja i kontrole sprovedenoj u Siriji, mogućnost razvoja akutnog infarkta miokarda (IM) je osam puta veća kod osoba oba pola koje puše više od 25 cigareta dnevno, u odnosu na osobe koje nikada nisu pušile [17]. U prilog hipotezi da dugotrajni uticaj stresogenih faktora na osobu izaziva endotelnu disfunkciju, i posledično nastanak AKS-a, govori istraživanje koje pokazuje da su ispitanici sa većim kardiovaskularnim rizikom bili izloženiji stresu [18].

Nastanku akutnog koronarnog sindroma takođe doprinose i starosno doba, pol i genetsko opterećenje, kao nepromenljivi faktori svake individue [9]. Registrovani AKS u mlađem životnom dobu u porodičnoj anamnezi je važan predisponirajući faktor za nastanak AKS-a, naročito kada se radi o srođnicima muškog pola obolelih pre 55. godine života i srođnicima ženskog pola obolelih pre 65. godine života [19,20]. Studije pokazuju da 35 varijanti genetskog rizika povezanih sa koronarnom bolešću deluju nezavisno od drugih faktora rizika [21]. Posmatrano po polnoj strukturi, kod muškaraca je veći rizik za nastanak AKS-a nego kod žena u periodu premenopauze, dok se kod osoba ženskog pola evidentira nešto lošiji tok bolesti sa brojnijim komplikacijama i većom stopom mortaliteta od AKS-a [20,22]. Sagledavajući podatke Populacionog registra za AKS Srbije za 2020. godinu, najveći broj umrlih je među starijom populacijom, odnosno u dobnoj grupi >75 godina, što potvrđuje tezu o značaju starosnog doba kao nezavisnog faktora rizika za nastanak i ishod AKS-a [5].

Cilj rada je da se ispita uticaj različitih determinanti (demografskih, antropometrijskih, bioloških markera, faktora rizika, prisustva komorbiditeta i farmakoterapijskog pristupa) na smrtni ishod od akutnog koronarnog sindrom kod pacijenata lečenih u Koronarnoj jedinici Opšte bolnice u Valjevu, tokom 2020. godine, kao i njihove razlike. Prema našim saznanjima, istraživanja ovog tipa se sprovode uglavnom na nacionalnom nivou ili u većim medicinskim centrima, pa su podaci sa područja okruga oskudni, i upravo je motiv za izbor ove teme pokušaj da se donekle ispravi ta slika.

greater risk of ACS in persons suffering from it, as compared to normotensive persons [12]. Studies show that persons suffering from diabetes mellitus who develop ACS, have poorer short-term as well as long-term outcomes, as compared to persons without this comorbidity [13]. Since an elevated lipid blood level is one of the most important factors in the process of atherosclerosis development, decreasing it would contribute to the decrease in morbidity and mortality from IHD, by as much as 40% [14].

In the etiopathogenesis of ACS, unhealthy lifestyles, such as smoking and exposure to stress, play a particularly important role [15,16]. According to a case-control study carried out in Syria, the probability of the development of acute myocardial infarction (MI) is eight times greater in persons of both sexes who smoke more than 25 cigarettes a day, as compared to persons who have never smoked [17]. The hypothesis that the long-term impact of stressogenic factors on a person causes endothelial dysfunction, and, consequently, the development of ACS, is substantiated by a study showing that patients with higher cardiovascular risk were more exposed to stress [18].

Age, sex, and genetic burden, as unchangeable factors related to each individual, also contribute to the development of acute coronary syndrome [9]. Registered ACS at a younger age in the family anamnesis is an important predisposing factor for the development of ACS, especially when male relatives developing disease before the age of 55 years and female relatives developing disease before the age of 65 are concerned [19,20]. Studies show that 35 genetic risk variants connected with coronary disease act independently of other risk factors [21]. Observed by sex structure, men carry a higher risk of the development of ACS than women during menopause, while in female patients a somewhat less favorable development of disease with numerous complications and a higher mortality rate from ACS is registered [20,22]. The Serbia Acute Coronary Syndrome Registry for 2020 shows that the greatest number of deceased patients was amongst the elderly population, i.e., in the age group >75 years, which confirms the thesis regarding the significance of age as an independent risk factor for the development and outcome of ACS [5].

The aim of the study is to investigate the influence of different determinants (demographic, anthropometric, biological markers, risk factors, presence of comorbidities, and the pharmacotherapeutic approach) on the death outcome resulting from ACS patients treated at the Coronary Unit of the General Hospital in Valjevo, in 2020, as well as their differences. According to our understanding, studies of this type are carried

## MATERIJALI I METODE

### Tip studije i uzorak

Istraživanjem, koje je urađeno kao studija preseka, obuhvaćeno je 384 punoletna lica sa AKS-om, koja su koristila usluge sekundarne zdravstvene zaštite, odnosno usluge Odeljenja kardiologije sa koronarnom jedinicom Opšte bolnice u Valjevu, u periodu od 01. 01. 2020. do 31. 12. 2020. godine. Prema Uredbi o Planu mreže zdravstvenih ustanova [23], Opšta bolnica u Valjevu je jedina stacionarna zdravstvena ustanova na teritoriji Kolubarskog okruga, pa shodno tome, odsek Koronarne jedinice obezbeđuje zdravstvenu zaštitu pacijenata sa područja šest opština: Valjevo, Lajkovac, Ub, Mionica, Osečina i Ljig.

### Instrument istraživanja

Kao instrument istraživanja korišćen je obrazac za prijavu lica obolelih od akutnog koronarnog sindroma – „Koronarni list“, koji su kreirali, prema nacionalnim potrebama, Institut za javno zdravlje Srbije „Dr Milan Jovanović Batut“, Institut za epidemiologiju i Udruženje kardiologa Srbije. Ovaj list je kreiran u formi upitnika koji popunjavaju lekari zaposleni u Koronarnoj jedinici, a koji se potom dostavlja okružnom Zavodu za javno zdravlje zaduženom za vođenje Regionalnog registra za lica obolela od akutnog koronarnog sindroma, koji je deo sveobuhvatnog Populacionog registra za akutni koronarni sindrom u Srbiji [5]. Na taj način su evidentirani svi oboleli od AKS-a na teritoriji Kolubarskog okruga koji su lečeni u Koronarnoj jedinici Opšte bolnice u Valjevu, u 2020. godini. S obzirom na obavezu prijavljivanja lica obolelih od AKS-a, koja je regulisana Zakonom o zdravstvenoj dokumentaciji i evidencijama u oblasti zdravstva [24], stopa odgovora je iznosila 100%. Svi ispitanici su dali informisani pristanak za anonimno učešće u istraživanju i time dali dozvolu istraživačima da koriste podatke dobijene iz istraživanja.

### Varijable

U istraživanju je ispitivana povezanost demografskih i antropometrijskih varijabli, bioloških markera, faktora rizika i primene određene farmakoterapije sa smrtnim ishodom od AKS-a. Demografske odrednice koje su korišćene bile su: pol (muški/ženski), starost i tip naselja (urbano/ruralno). Varijabla starost je kategorizovana u tri uzrasne grupe: prva – mlađi od 65 godina, druga – od 65 do 74 godine i treća – 75 godina i stariji. Od antropometrijskih karakteristika, posmatrane su: visina, težina, indeks telesne mase (engl. *body mass index* – *BMI*); od bioloških markera posmatrani su: glukoza, hemoglobin, kreatin kinaza (engl. *creatine kinase* – *Max*

out mostly at the national level or at the level of larger medical centers, which is why data at the district level are limited. In fact, selecting this topic was motivated by an attempt to correct this situation.

## MATERIALS AND METHODS

### The study type and sample

The research, which was carried out as a cross-sectional study, included 384 adults with ACS, who received secondary healthcare services, i.e., who were treated at the Cardiology Department with the Coronary Unit of the General Hospital in Valjevo, in the period between January 1, 2020, and December 31, 2020. According to the Decree on the Health Care Institution Network Plan [23], the General Hospital in Valjevo is the only inpatient healthcare facility in the territory of the Kolubara District. Consequently, the Coronary Unit of this hospital provides health services for patients from six municipalities: Valjevo, Lajkovac, Ub, Mionica, Osečina, and Ljig.

### Research instrument

The form for reporting persons with acute coronary syndrome – the *Coronary Sheet*, was used as the research instrument. It was created, based on national needs, by the Institute of Public Health of Serbia "Dr. Milan Jovanović Batut", the Institute of Epidemiology, and the Cardiology Society of Serbia. This sheet is in the form of a questionnaire filled out by doctors working at the Coronary Unit, which is then submitted to the Institute of Public Health Valjevo. The Institute is in charge of maintaining the Regional Acute Coronary Syndrome Registry, which is a part of the comprehensive Serbian Acute Coronary Syndrome Registry [5]. In this way, all ACS patients in the territory of the Kolubara District, treated at the Coronary Unit of the General Hospital in Valjevo, in 2020, were recorded. As it is mandatory to report all ACS cases, as prescribed by the Law on Health Documentation and Records in the Field of Health [24], the response rate was 100%. All respondents gave informed consent for anonymous participation in the research, thus giving consent for the use of the data obtained from the survey.

### Variables

The study analyzed the association between demographic and anthropometric variables, biological markers, risk factors, and the application of certain pharmacotherapy with the lethal outcome resulting from ACS. The demographic determinants observed were the following: sex (male/female), age, and type of settlement (urban/rural). The age variable was categorized into the following three groups: I – patients younger than 65

CK) i troponin I; od farmakoterapije posmatrani su: acetylsalicina kislina, nitrati, inotropi, heparin, niskomolekularni heparini, beta blokatori, inhibitori angiotenzin konvertujućeg enzima (engl. *angiotensin-converting enzyme inhibitors – ACEI*), klopidogrel i statini. Kada je reč o faktorima rizika, korišćene su sledeće varijable: pušački status, hiperlipoproteinemija (HLP), hipertenzija (*hypertensio arterialis – HTA*), *diabetes mellitus* (DM), bol u grudima. Od prethodnih i sadašnjih bolesti posmatrani su: prethodni akutni infarkt miokarda (AIM), prethodni bajpas, prethodna perkutana transluminalna koronarna angioplastika (engl. *percutaneous transluminal coronary angioplasty – PTCA*), prethodni cerebrovaskularni insult (CVI), periferna arterijska bolest, bolesti pluća i anemije. Kao zavisna varijabla korišćena je smrt od AKS-a, sa dva ishoda (da/ne).

### Statističke metode obrade podataka

U ovoj studiji, dobijeni podaci su analizirani korišćenjem deskriptivnih i analitičkih statističkih metoda. Od deskriptivnih metoda korišćeni su: apsolutni i relativni brojevi (n,%), mere centralne tendencije (aritmetička sredina, medijana) i mere disperzije (standardna devijacija, percentili). Od analitičkih statističkih metoda korišćeni su testovi razlike – parametarski (t test) i neparametarski testovi (Pirsonov  $\chi^2$  test, Fišerov test tačne verovatnoće, Man-Vitnijev U test). Izbor testa za testiranje razlike zavisio je od tipa podataka i raspodele. Parametarski metodi korišćeni su u situaciji gde je raspodela bila normalna, dok su neparametarski testovi korišćeni u situaciji gde raspodela nije bila normalna. Normalnost raspodele ispitivana je na osnovu deskriptivnih parametara, pomoću testova normalnosti raspodele (Kolmogorov-Smirnov test i Šapiro–Vilksov test) i grafičkim metodama (histogram, boks plot, Q-Q plot). Za analizu povezanosti nezavisnih varijabli (starost, pušenje, BMI, HTA, bolesti pluća, Killip klasa, glukoza, Hgb, acetylsalicilna kiselina, beta blokatori, ACEI i statini) sa smrtnim ishodom od AKS-a, kao zavisnom varijablom, korišćena je logistička regresiona analiza – univarijantna i multivarijantna. U radu su prikazani unakrsni odnosi (UO) i 95-procentni intervali poverenja sa donjom i gornjom granicom (95% IP) kod logističkih modela. Valjanost modela je ispitivana pomoću *Nagelkerke R Squared*. Verovatnoća  $p < 0,05$  je uzeta kao minimalni nivo statističke značajnosti.

Svi podaci su obrađeni u SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) softverskom paketu i R 3.4.2 (R Core Team 2017. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria) softverskom paketu.

years, II – patients between the age of 65 and 74 years, and III – patients aged 75 years and above. The following anthropometric characteristics were observed: height, weight, and body mass index (BMI). The following biological markers were taken into account: the glucose level, the hemoglobin level, the creatine kinase (Max CK) level, and the level of troponin I. As far as pharmacotherapy is concerned, the following were observed: acetylsalicylic acid, nitrates, inotropes, heparin, low molecular weight heparin (LMWH), beta blockers, angiotensin-converting enzyme inhibitors (ACEI), clopidogrel, and statins. As far as the risk factors are concerned, the following variables were considered: smoking status, hyperlipoproteinemia (HLP), hypertension (*hypertensio arterialis – HTA*), diabetes mellitus (DM), chest pain. Of the previous and existing conditions, the following were observed: previous acute myocardial infarction (AMI), preexisting bypass, previous percutaneous transluminal coronary angioplasty (PTCA), previous cerebrovascular insult (CVI), peripheral artery disease (PAD), pulmonary diseases, and anemias. As the dependent variable, death from ACS was used, with two outcomes (yes/no).

### Statistical data processing methods

The data obtained in this study were analyzed using descriptive and analytical statistical methods. The following descriptive methods were applied: absolute and relative numbers (n, %), measures of central tendency (arithmetic mean, median), and measures of dispersion (standard deviation, percentiles). The following analytical statistical methods were used: tests of difference – parametric (t test) and non-parametric (Pearson's  $\chi^2$  test, Fisher's exact test, the Mann–Whitney U test). The choice of test for calculating difference depended on the type of data and type of distribution. Parametric methods were used when distribution was normal, while non-parametric tests were used when the distribution was not normal. Normality of distribution was tested on the basis of descriptive parameters, with tests of normality (the Kolmogorov-Smirnov test and the Shapiro–Wilk test) and with graphical tests (histogram, box plot, Q-Q plot). Logistic regression analysis (univariate and multivariate) was used for analyzing the association between independent variables (age, smoking, BMI, HTA, pulmonary disease, Killip class, glucose, Hgb, acetylsalicylic acid, beta blockers, ACEI, and statins) and the death outcome resulting from ACS, as the dependent variable. The study presents cross-section relationships and 95% confidence intervals, with lower and upper bounds (95% CP) in logistic models. The validity of the model was tested with the Nagelkerke R Squared. The probability value of  $p < 0.05$  was taken as the minimal level of statistical significance.

## REZULTATI

Ukupan uzorak u našem istraživanju bio je sastavljen od 288 (75%) muškaraca i 96 (25%) žena. Prosečna starost pacijenata iznosila je  $65,8 \pm 12,1$  godina, pri čemu je najmlađi pacijent imao 29 godina, a najstariji 95 godina. Sociodemografske karakteristike pacijenata, u odnosu na smrtni ishod, prikazane su u **Tabeli 1**.

Prosečna starost umrlih pacijenata iznosila je  $72,9 \pm 9,8$  godina, dok je starost pacijenata koji nisu umrli iznosila  $65,0 \pm 12,0$  godina, i ova razlika je statistički značajna ( $p < 0,001$ ). Na osnovu distribucije pacijenata po starosnim grupama (**Tabela 1**), evidentno je da su najstariji pacijenti bili najugroženiji, odnosno sa najvećim procentom smrtnog ishoda. Za razliku od

All data were processed with the SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) software and the R 3.4.2 (R Core Team 2017. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria) software.

## RESULTS

The total sample in our study was composed of 288 (75%) men and 96 (25%) women. The average age of the patients was  $65.8 \pm 12.1$  years, with the youngest patient aged 29 and the oldest aged 95 years. The sociodemographic characteristics of the patients, in relation to the lethal outcome, are presented **Table 1**.

**Tabela 1.** Sociodemografske karakteristike pacijenata u odnosu na smrt od AKS-a

		Smrtni ishod / Death outcome				p vrednost* / p value*
		Ne / No		Da / Yes		
		N	%	N	%	
Starost / Age	< 65 godina / < 65 years	157	95.7%	7	4.3%	0.001
	65 – 74 godine / 65 – 74 years	112	86.8%	17	13.2%	
	75+ godina / 75+ years	74	81.3%	17	18.7%	
Pol / Sex	Muški / Male	260	90.3%	28	9.7%	0.294
	Ženski / Female	83	86.5%	13	13.5%	
Tip naselja / Type of settlement	Gradsko/prigradsko / Urban/suburban	159	89.3%	19	10.7%	0.999
	Seosko / Rural	184	89.3%	22	10.7%	

\*Pirsonov  $\chi^2$  test  
AKS – akutni koronarni sindrom

**Table 1.** Patient sociodemographic characteristics, in relation to death from ACS

\*Pearson's  $\chi^2$  test  
ACS – acute coronary syndrome

**Tabela 2.** Antropometrijski podaci i vrednost arterijskog krvnog pritiska pacijenata u odnosu na smrtni ishod od AKS-a

	Smrtni ishod / Death outcome				p vrednost / p value
	Ne / No		Da / Yes		
	AS / AM	SD / SD	AS / AM	SD / SD	
Visina (cm) / Height (cm)	176.7	8.4	174.6	8.6	0.132 <sup>a</sup>
Težina (kg) / Weight (kg)	79.7	10.6	75.7	11.5	0.025 <sup>a</sup>
BMI (kg/m <sup>2</sup> ) / BMI (kg/m <sup>2</sup> )	25.4	2.2	24.7	2.4	0.056 <sup>a</sup>
TAs <sup>c</sup> / TAs <sup>c</sup>	134.9	25.7	111.9	31.0	< 0.001 <sup>a</sup>
TAd <sup>c</sup> / TAd <sup>c</sup>	82.7	13.0	70.4	14.8	< 0.001 <sup>a</sup>
	N	%	N	%	
Povišen pritisak na prijemu <sup>d</sup> / Elevated blood pressure at admission <sup>d</sup>	25	13.5	10	6.2	0.025 <sup>b</sup>

<sup>a</sup>t test za nezavisne uzorke; <sup>b</sup>Pirsonov  $\chi^2$  test; <sup>c</sup>Kontinuirani numerički podaci dobijeni merenjem sistolnog i dijastolnog krvnog pritiska prilikom prijema pacijenata sa AKS-om u bolnicu; <sup>d</sup>Vrednosti arterijskog krvnog pritiska  $\geq 140/90$  mmHg izmerene prilikom prijema pacijenata sa AKS-om u bolnicu  
AKS – akutni koronarni sindrom  
BMI – indeks telesne mase (engl. body mass index)  
AS – aritmetička sredina  
SD – standardna devijacija  
TAs – sistolni krvni pritisak (tensio arterialis systolis)  
TAd – dijastolni krvni pritisak (tensio arterialis diastolis)

**Table 2.** Anthropometric data and arterial blood pressure values in patients, in relation to the death outcome from ACS

<sup>a</sup>Independent-samples t-test; <sup>b</sup>Pearson's  $\chi^2$  test; <sup>c</sup>Continuous numerical data obtained by measuring systolic and diastolic blood pressure at hospital admission in patients with ACS; <sup>d</sup>Arterial blood pressure values  $\geq 140/90$  mmHg measured at hospital admission in patients with ACS  
ACS – acute coronary syndrome  
BMI – body mass index  
AM – arithmetic mean  
SD – standard deviation  
TAs – systolic blood pressure (tensio arterialis systolis)  
TAd – diastolic blood pressure (tensio arterialis diastolis)

starosti, nije bilo značajne razlike po pitanju mortaliteta među polovima, a kada je u pitanju tip naselja, distribucija po mortalitetu je bila identična i u gradskom/prigradskom i u seoskom tipu naselja.

U **Tabeli 2**, prikazani su antropometrijski podaci i vrednosti arterijskog krvnog pritiska pacijenata, u odnosu na smrtni ishod od AKS-a.

Na osnovu vrednosti prikazanih u **Tabeli 2**, evidentno je da su pacijenti u obe grupe bili slične konstitucije, te da su pacijenti koji su umrli imali čak i nešto manju telesnu težinu. Nasuprot ovome, vrednosti krvnog pritiska bile su značajno niže kod pacijenata koji su imali smrtni ishod.

U **Tabeli 3**, prikazana je distribucija faktora rizika pacijenata, u odnosu na umiranje od akutnog koronarnog sindroma.

Na osnovu pušačkog statusa, utvrđeno je da su pušači umirali u značajno manjem procentu. Ipak, treba napomenuti da ne postoji podatak o broju bivših pušača, koji je značajan u ovoj populaciji. Pacijenti koji su prethodno imali bol u grudima su takođe umirali u manjem procentu, ali ova razlika nije bila statistički značajna. Distribucija smrtnog ishoda u odnosu na HLP, HTA i DM je vrlo slična i ona je bez statističke značajnosti.

The average age of the deceased patients was 72.9 ± 9.8 years, while the age of the surviving patients was 65.0 ± 12.0 years, and this difference is statistically significant ( $p < 0.001$ ). Based on the distribution of patients by age groups (**Table 1**), it is evident that the oldest patients were most at risk, i.e., they had the highest percentage of lethal outcome. As opposed to age, there was no significant difference in mortality between the sexes. In relation to the type of settlement, the distribution in relation to mortality was identical in both the urban/suburban and rural type of settlement.

**Table 2** presents patient anthropometric data and values of arterial blood pressure, in relation to mortality from ACS.

Based on the values presented in **Table 2**, it is evident that the patients of both groups were of similar physical build, and that the deceased patients even had a somewhat lower body weight. On the other hand, blood pressure values were significantly lower in patients who died.

**Table 3** presents the distribution of risk factors in patients, in relation to mortality from acute coronary syndrome.

As far as smoking status is concerned, it was determined that the percentage of smokers who died was

**Tabela 3.** Faktori rizika pacijenata u odnosu na umiranje od AKS-a

		Smrtni ishod / Death outcome				p vrednost* / p value*
		Ne / No		Da / Yes		
		N	%	N	%	
Pušenje / Smoking	Ne / No	225	86.5%	35	13.5%	0.031
	Da / Yes	90	94.7%	5	5.3%	
Bol u grudima / Chest pain	Ne / No	263	88.0%	36	12.0%	0.111
	Da / Yes	79	94.0%	5	6.0%	
HLP / HLP	Ne / No	147	90.7%	15	9.3%	0.442
	Da / Yes	196	88.3%	26	11.7%	
HTA / HTA	Ne / No	65	90.3%	7	9.7%	0.765
	Da / Yes	277	89.1%	34	10.9%	
DM / DM	Ne / No	242	90.0%	27	10.0%	0.535
	Da / Yes	101	87.8%	14	12.2%	

**Table 3.** Risk factors in patients, in relation to death from ACS

\*Pirsonov  $\chi^2$  test

AKS – akutni koronarni sindrom

HLP – hiperlipoproteinemija

HTA – povišeni krvni pritisak (*hypertensio arterialis*)

DM – diabetes mellitus

\*Pearson's  $\chi^2$  test

ACS – acute coronary syndrome

HLP – hyperlipoproteinemia

HTA – elevated blood pressure (*hypertensio arterialis*)

DM – diabetes mellitus

**Tabela 4.** Laboratorijski parametri pacijenata u odnosu na smrtni ishod od AKS-a

**Table 4.** Patient laboratory parameters, in relation to death from ACS

		Smrtni ishod / Death outcome					p vrednost* / p value*
		AS / AM	SD / SD	Med / Med	P25 / P25	P75 / P75	
Glukoza / Glucose	Ne / No	7.8	3.8	6.6	5.7	8.3	<0.001 <sup>b</sup>
	Da / Yes	11.9	7.0	10.2	7.4	15.1	
Hgb / Hgb	Ne / No	137.1	21.9	141.0	127.0	151.5	0.022 <sup>a</sup>
	Da / Yes	124.2	28.6	130.0	111.0	145.0	
Max CK / Max CK	Ne / No	761.1	936.3	336.0	111.0	1,010.0	0.309 <sup>b</sup>
	Da / Yes	766.8	646.2	735.5	162.0	1,165.0	
Troponin I / Troponin I	Ne / No	1,624.4	4,265.8	18.5	2.0	797.0	0.751 <sup>b</sup>
	Da / Yes	1,164.2	3,940.1	15.0	3.5	45.5	

\*t test za nezavisne uzorke; <sup>b</sup>Man-Vitnjev U test

AKS – akutni koronarni sindrom

Hgb – hemoglobin

Max CK – maksimalna vrednost kreatin kinaze (engl. *creatin kinase*)

<sup>a</sup>Independent-samples t-test; <sup>b</sup>Mann-Whitney U test

ACS – acute coronary syndrome

Hgb – hemoglobin

Max CK – maximum creatine kinase

U Tabeli 4, prikazana je deskriptivna statistika laboratorijskih parametara pacijenata, u odnosu na smrtni ishod od AKS-a.

Prosečna vrednost glukoze je bila značajno veća kod pacijenata koji su imali smrtni ishod. Nasuprot tome, pacijenti sa smrtnim ishodom imali su značajno niže vrednosti hemoglobina. Medijana maksimalne vrednosti kreatin kinaze (*Max CK*) bila je veća kod pacijenata sa smrtnim ishodom, iako su prosečne vrednosti bile vrlo slične. Ipak, varijabilnost je bila dovoljno velika da nije bilo moguće potvrditi značajnost razlike. Isto je bilo i sa troponinom I, gde su medijane bile vrlo slične (prosečna vrednost je bila ekstremno velika zbog pojedinih ekstremnih vrednosti).

Distribucija anamnestičkih podataka o prethodnim i sadašnjim bolestima pacijenata, u odnosu na smrtni ishod od akutnog koronarnog sindroma, prikazana je u Tabeli 5.

Procenat pacijenata sa smrtnim ishodom se nije značajno razlikovao u odnosu na prethodne i sadašnje bolesti. Naime, pacijenti sa prethodnim akutnim infarktom miokarda i aortokoronarnim bajpasom, kao i prethodnim cerebrovaskularnim insultom, imali su vrlo sličan, odnosno gotovo identičan procenat smrtnog ishoda. Prethodnu *PTCA* kao i perifernu arterijsku bolest imalo je samo dva pacijenta, pa je razlika u procentima irelevantna. Pacijenti kod kojih su evidentirane bolesti pluća imali su dosta veći procenat smrtnog ishoda u odnosu na one koji su bili bez bolesti pluća, ali se radi o malom broju pacijenata, pa je i očekivan izostanak statističke značajnosti.

significantly smaller. However, it should be noted that data on the number of former smokers were not available, which is significant for this population. Patients who had previously experienced chest pain also had a smaller percentage of mortality, however, this difference was not statistically significant. The distribution of the death outcome in relation to HLP, HTA, and DM is very similar and is without statistical significance.

Table 4 presents descriptive statistics for patient laboratory parameters, in relation to mortality from ACS.

The average glucose level was significantly higher in patients who had a death outcome. On the other hand, patients with a lethal outcome had significantly lower levels of hemoglobin. The median maximum CK (*Max CK*) value was higher in patients with a lethal outcome, although the average values were very similar. Nevertheless, the variability was large enough to make it impossible to confirm the significance of the difference. The same happened with troponin I, where the median values were also very similar. (The average value was extremely large due to individual extreme values).

The distribution of anamnestic data on previous and existing patient diseases, in relation to the death outcome resulting from acute coronary syndrome, is presented in Table 5.

The percentage of patients with the death outcome did not significantly differ in relation to previous and existing diseases. Namely, patients with previous acute myocardial infarction and aortocoronary bypass, as well as patients with previous cerebrovascular insult had a very similar, i.e., almost identical percentage of



**Tabela 5.** Prethodne i sadašnje bolesti pacijenata u odnosu na smrtni ishod od AKS-a

**Table 5.** Previous and existing diseases in patients, in relation to the death outcome from ACS

		Smrtni ishod / Death outcome				p vrednost* / p value*
		Ne / No		Da / Yes		
		N	%	N	%	
Prehodni AIM / Previous AMI	Ne / No	292	89.8%	33	10.2%	0.383 <sup>a</sup>
	Da / Yes	49	86.0%	8	14.0%	
Prehodni aortokoronarni bajpas / Previous aortocoronary bypass	Ne / No	308	89.3%	37	10.7%	1.000 <sup>b</sup>
	Da / Yes	34	89.5%	4	10.5%	
Prehodni PTCA / Previous PTCA	Ne / No	340	89.2%	41	10.8%	1.000 <sup>b</sup>
	Da / Yes	2	100.0%	0	0.0%	
Prehodni CVI / Previous CVI	Ne / No	337	89.4%	40	10.6%	0.549 <sup>b</sup>
	Da / Yes	6	85.7%	1	14.3%	
Periferna bolest arterija / Peripheral artery disease	Ne / No	341	89.3%	41	10.7%	1.000 <sup>b</sup>
	Da / Yes	2	100.0%	0	0.0%	
Bolesti pluća / Pulmonary diseases	Ne / No	335	89.8%	38	10.2%	0.102 <sup>b</sup>
	Da / Yes	8	72.7%	3	27.3%	
Anemija / Anemia	Ne / No	331	89.2%	40	10.8%	1.000 <sup>b</sup>
	Da / Yes	12	92.3%	1	7.7%	

\*Pirsonov  $\chi^2$  test; <sup>b</sup>Fišerov test tačne verovatnoće

AKS – akutni koronarni sindrom

AIM – akutni infarkt miokarda

PTCA – perkutana transluminalna koronarna angioplastika (engl. *percutaneous transluminal coronary angioplasty*)

CVI – cerebrovaskularni insult

\*Pearson's  $\chi^2$  test; <sup>b</sup>Fisher's exact test

ACS – acute coronary syndrome

AMI – acute myocardial infarction

PTCA – percutaneous transluminal coronary angioplasty

CVI – cerebrovascular insult

Karakteristike pacijenata sa akutnim koronarnim sindromom, u odnosu na smrtni ishod, prikazane su u **Tabeli 6**.

Najveći broj pacijenata dovezen je u zdravstvenu ustanovu od strane službe za hitnu medicinsku pomoć, dok su u daleko manjem broju pacijenti došli samoinicijativno. Ostali načini dolaska u zdravstvenu ustanovu su bili u znatno manjem broju. Smrtnost je bila najveća kod *NSTEMI* i *STEMI* tipova infarkta, dok su nestabilna AP i IM sa blokom leve grane bili bez smrtnih ishoda. Pacijenti sa različitim lokalizacijama infarkta se nisu značajno razlikovali po smrtnom ishodu. Ono što je očekivano, pacijenti sa višim stepenom *Killip* klasifikacije imali su u većem procentu smrtni ishod, i ovaj trend je statistički značajan. Kada je reč o komplikacijama tokom hospitalizacije, poremećaj ritma je bio prisutan kod dva pacijenta, a postinfarktna angina, mehaničke komplikacije i reinfarkt se nisu javili u ispitivanom uzorku pacijenata. Gotovo svi pacijenti koji su zahtevali kardiopulmonalnu reanimaciju su umrli, i ova razlika je statistički značajna.

the death outcome. Previous PTCA and peripheral artery disease were present in only two patients, rendering the difference in percentage irrelevant. Patients in whom pulmonary diseases were recorded had a much higher percentage of lethal outcome, as compared to those without lung disease, however, the number of patients in question was small, which is why statistical significance was not recorded, as could be expected.

The characteristics of patients with acute coronary syndrome, in relation to the death outcome, are presented in **Table 6**.

The greatest number of patients was brought to hospital by emergency services, while a far smaller number of patients came in on their own. Other modes of arrival to hospital were significantly rarer. Mortality was the highest in *NSTEMI* and *STEMI* type of myocardial infarction, while unstable AP and MI with left bundle branch block did not result in death. Patients with different localizations of myocardial infarction did not differ significantly with regards to the death outcome. As expected, patients with a higher Killip class had a

**Tabela 6.** Karakteristike pacijenata sa AKS-om u odnosu na smrtni ishod

**Table 6.** Characteristics of patients with ACS, in relation to the death outcome

		Smrtni ishod / Death outcome				p vrednost* / p value*
		Ne / No		Ne / No		
		N	%	N	%	
Dolazak / Arrival to hospital	Samoinicijativno / Of their own accord	38	92.7%	3	7.3%	0.734 <sup>b</sup>
	Upućen iz doma zdravlja / Referred from the community health care center	1	100.0%	0	0.0%	
	Službom hitne pomoći / Brought in by emergency services	243	89.7%	28	10.3%	
	Iz druge zdravstvene ustanove / Transferred from another hospital	15	100.0%	0	0.0%	
	Prebačen sa drugog odeljenja / Transferred from another department	6	100.0%	0	0.0%	
ST elevacija / ST elevation	STEMI	167	88.8%	21	11.2%	0.008 <sup>b</sup>
	NSTEMI	119	85.6%	20	14.4%	
	IM sa blokom leve grane / MI with left bundle branch block	2	100.0%	0	0.0%	
	Nestabilna angina pectoris / Unstable angina pectoris	55	100.0%	0	0.0%	
Lokalizacija / Localization	Prednji / Anterior	46	86.8%	7	13.2%	0.457 <sup>a</sup>
	Zadnje-donji / Posteroinferior	107	90.7%	11	9.3%	
	Neoznačeni / Unspecified	49	84.5%	9	15.5%	
Killip* / Killip*	1	147	94.2%	9	5.8%	0.001 <sup>c</sup>
	2	40	81.6%	9	18.4%	
	3	10	76.9%	3	23.1%	
	4	0	0.0%	1	100.0%	
Poremećaj ritma / Rhythm disruption	Ne / No	340	89.5%	40	10.5%	1.000 <sup>b</sup>
	Da / Yes	2	100.0%	0	0.0%	
Kardiopulm. reanimacija / Cardiopulmonary resuscitation	Ne / No	341	93.2%	25	6.8%	<0.001 <sup>b</sup>
	Da / Yes	1	6.3%	15	93.8%	

<sup>a</sup>Pirsonov  $\chi^2$  test; <sup>b</sup>Fišerov test tačne verovatnoće; <sup>c</sup> $\chi^2$  – kvadratni test za trend  
\*Klasifikacija srčane insuficijencije u AIM prema Killip-u: 1 – bez znakova srčane slabosti; 2 – plućna kongestija, S3 galop, povišen jugularni venski pritisak; 3 – plućni edem; 4 – kardiogeni šok  
AKS – akutni koronarni sindrom  
STEMI – akutni infarkt miokarda sa elevacijom ST segmenta (engl. ST-elevation myocardial infarction)  
NSTEMI – akutni infarkt miokarda bez elevacije ST segmenta (engl. non-ST-elevation myocardial infarction)

<sup>a</sup>Pearson's  $\chi^2$  test; <sup>b</sup>Fisher's exact test; <sup>c</sup> $\chi^2$  – Chi square for trend  
\*Classification of heart failure in AMI according to the Killip classification: 1 – no evidence of heart failure; 2 – pulmonary congestion, S3 gallop, elevated jugular venous pressure; 3 – pulmonary edema; 4 – cardiogenic shock  
ACS – acute coronary syndrome  
STEMI – ST-elevation myocardial infarction  
NSTEMI – non-ST-elevation myocardial infarction  
MI – myocardial infarction

Distribucija pacijenata, sa farmakoterapijom koju su primali tokom hospitalizacije, u odnosu na smrtni ishod, prikazana je u **Tabeli 7**.

Postojala je značajno manja smrtnost pacijenata koji su koristili acetilsalicilnu kiselinu u odnosu na one koji nisu pili ovaj lek. Svi pacijenti koji su bili na inotropima su imali smrtni ishod, ali se i radi o težim pacijentima kojima su ovi lekovi bili indikovani. Pacijenti kojima su ordinirani beta blokatori, ACE inhibitori i statini su imali statistički značajno niži procenat smrtnosti, u odnosu na pacijente koji nisu uzimali ove lekove. Nije bilo statistički značajne razlike u vezi sa ostalim terapijskim modalitetima, u odnosu na smrtni ishod. Nijedan pacijent nije imao urgentnu bajpas hirurgiju, urgentnu PTCA ili urgentni pejsmejker.

higher percentage of mortality, and this trend is statistically significant. As far as complications during hospitalization are concerned, arrhythmia occurred in two patients, while postinfarct angina, mechanical complications, and reinfarction did not occur in the examined patient sample. Almost all patients who required cardiopulmonary resuscitation died, and this difference is statistically significant.

The distribution of patients with pharmacotherapy, in relation to the death outcome, is presented in **Table 7**.

The mortality of patients who took acetylsalicylic acid was significantly lower as compared to patients who did not take this medicine. All patients who were given inotropes died. However, these were severe cases where this medication was indicated. Patients who

**Tabela 7.** Farmakoterapija koju su pacijenti primali tokom hospitalizacije u odnosu na smrtni ishod od AKS-a

**Table 7.** Pharmacotherapy which the patients received during hospitalization, in relation to death outcome from ACS

		Smrtni ishod / Death outcome				p vrednost* / p value*
		Ne / No		Ne / No		
		N	%	N	%	
Acetil-salicilna kiselina / <i>Acetylsalicylic acid</i>	Ne / No	16	61.5%	10	38.5%	< 0.001 <sup>b</sup>
	Da / Yes	326	91.3%	31	8.7%	
Nitrati / <i>Nitrates</i>	Ne / No	312	89.7%	36	10.3%	0.403 <sup>b</sup>
	Da / Yes	30	85.7%	5	14.3%	
Inotropi / <i>Inotropes</i>	Ne / No	342	91.7%	31	8.3%	< 0.001 <sup>b</sup>
	Da / Yes	0	0.0%	10	100.0%	
Heparin / <i>Heparin</i>	Ne / No	340	89.2%	41	10.8%	1.000 <sup>b</sup>
	Da / Yes	2	100.0%	0	0.0%	
LMWH-i / <i>LMWHs</i>	Ne / No	79	84.9%	14	15.1%	0.119 <sup>a</sup>
	Da / Yes	263	90.7%	27	9.3%	
Beta blokatori / <i>Beta blockers</i>	Ne / No	143	84.1%	27	15.9%	0.003 <sup>a</sup>
	Da / Yes	199	93.4%	14	6.6%	
ACEI / <i>ACEI</i>	Ne / No	86	78.9%	23	21.1%	< 0.001 <sup>a</sup>
	Da / Yes	256	93.4%	18	6.6%	
Klopidogrel / <i>Clopidogrel</i>	Ne / No	116	88.5%	15	11.5%	0.734 <sup>a</sup>
	Da / Yes	226	89.7%	26	10.3%	
Statini / <i>Statins</i>	Ne / No	33	64.7%	18	35.3%	<0.001 <sup>a</sup>
	Da / Yes	309	93.1%	23	6.9%	

<sup>a</sup>Pirsonov  $\chi^2$  test; <sup>b</sup>Fišerov test tačne verovatnoće

AKS – akutni koronarni sindrom

LMWH – niskomolekularni heparin (engl. *low molecular weight heparin*)

ACEI – inhibitori angiotenzin konvertujućeg enzima (engl. *angiotensin-converting enzyme inhibitors*)

<sup>a</sup>Pearson's  $\chi^2$  test; <sup>b</sup>Fisher's exact test

ACS – acute coronary syndrome

LMWH – low molecular weight heparin

ACEI – angiotensin-converting enzyme inhibitors

U Tabeli 8, prikazani su univarijantni i multivarijantni modeli logističke regresije, sa smrtnim ishodom kao zavisnom varijablom.

Modelovanje je rađeno u nekoliko koraka. Prvo je urađen univarijantni model sa svim prediktorima koji su imali p vrednost manju od 0,1 u univarijantnim analizama, i za koje je bilo logično da budu dalje modelovani. Problem nedostajućih podataka kod Killip klasifikacije (43%), glukoze (11,7%) i hemoglobina (7,8%), prevaziđen je tako što date varijable nisu ušle u multivarijantni model. Naime, uključivanjem ovih varijabli bi se napravio problem prevelikog broja nedostajućih podataka, čime model bi model postao nevalidan. Glukoza i hemoglobin mogu varirati (glukoza na dnevnom nivou), pa su ove vrednosti u startu isključene. Time je finalni multivarijantni model bio sa 10% nedostajućih podataka.

Na osnovu rezultata univarijantne analize, starost, Killip klasa, glukoza i hemoglobin, predstavljaju značajne prediktore smrtnog ishoda. U multivarijantnom modelu (bez navedenih parametara, koji značajno

were prescribed beta blockers, ACE inhibitors, and statins had a statistically significantly lower percentage of mortality, as compared to patients who did not receive this medication. There was no statistically significant difference regarding other treatment modalities, in relation to the death outcome. None of the patients had emergency bypass surgery, emergency PTCA, or emergency pacemaker implantation.

Table 8 shows univariate and multivariate models of logistic regression, with the death outcome as the dependent variable.

Modeling was performed in several steps. The univariate model was designed first, with all the predictors whose p values was less than 0.1 in univariate analyses, and for whom it was logical that they should be modeled further. The problem of missing data in the Killip classification (43%), glucose levels (11.7%), and hemoglobin values (7.8%) was overcome by not entering these variables into the multivariate model. Namely, introducing these variables would create the problem of too many missing data, rendering the model invalid.

**Tabela 8.** Univarijantni i multivarijantni modeli logističke regresije sa smrtnim ishodom kao zavisnom varijablom

**Table 8.** Univariate and multivariate logistic regression models with death outcome as a dependent variable

Prediktori / Predictors	Analiza / Analysis			
	Univariate		Multivariate	
	OR (95% IP) / OR (95% CI)	p vrednost* / p value*	OR (95% IP) / OR (95% CI)	p vrednost* / p value*
<b>Starost / Age</b>				
< 65 godina / < 65 years	1		1	
65 – 74 godina / 65 – 74 years	3.40 (1.36 - 8.48)	0.009	3.43 (1.18 - 9.90)	0.023
75+ godina / 75+ years	5.15 (2.05 - 12.96)	< 0.001	4.33 (1.15 - 12.91)	0.008
<b>Pušenje / Smoking</b>	0.37 (0.14 - 0.94)	0.037	0.54 (0.17 - 1.77)	0.311
<b>BMI / BMI</b>				
< 25	1			
25 - 29.9	0.68 (0.35 - 1.32)	0.260		
30+	0.67 (0.08 - 5.56)	0.715		
<b>HTA (prijem) / HTA (at admission)</b>	0.42 (0.12 - 0.91)	0.028	0.56 (0.24 - 1.33)	0.190
<b>Bolesti pluća / Pulmonary diseases</b>	3.31 (0.84 - 12.99)	0.087	2.23 (0.40 - 12.35)	0.358
<b>Killip</b>				
1	1			
2	3.67 (1.37 - 9.87)	0.010		
3+4	6.53 (1.71 - 24.97)	0.006		
<b>Glukoza / Glucose</b>	1.15 (1.07 - 1.23)	< 0.001		
<b>Hgb / Hgb</b>	0.98 (0.96 - 0.99)	0.004		
<b>Acetilsalicilna kiselina / Acetylsalicylic acid</b>	0.15 (0.06 - 0.36)	< 0.001	0.92 (0.22 - 3.81)	0.912
<b>Beta blokatori / Beta blockers</b>	0.37 (0.19 - 0.74)	0.004	0.54 (0.24 - 1.19)	0.125
<b>ACEI / ACEI</b>	0.26 (0.13 - 0.51)	< 0.001	0.44 (0.19 - 1.03)	0.057
<b>Statini / Statins</b>	0.14 (0.07 - 0.28)	< 0.001	0.33 (0.12 - 0.91)	0.033

OR – odnos verovatnoće (engl. odds ratio)

IP – interval poverenja

BMI – indeks telesne mase (engl. body mass index)

HTA – povišeni krvni pritisak (hypertensio arterialis)

Hgb – hemoglobin

ACEI – inhibitori angiotenzin konvertujućeg enzima (engl. angiotensin-converting enzyme inhibitors)

OR – odds ratio

CI – confidence interval

BMI – body mass index

HTA – elevated blood pressure (hypertensio arterialis)

Hgb – hemoglobin

ACEI – angiotensin-converting enzyme inhibitors

smanjuju uzorak), značajni prediktori su: starost, ACE inhibitori i statini. Objasnjena varijabilnost modela (Nagelkerke R Squared) iznosi 0,215.

## DISKUSIJA

Ovim radom je ispitivana povezanost između demografsko-antropometrijskih varijabli, faktora rizika, prisustva komorbiditeta, primenjene farmakoterapije i smrtnog ishoda od AKS-a, kod korisnika zdravstvene zaštite Opšte bolnice u Valjevu, kao i njihove razlike. Na osnovu dobijenih rezultata, utvrđeno je da postoji povezanost između određenih starosnih grupa i smrtnog

Glucose and hemoglobin levels may vary (glucose may vary on a daily basis), which is why these values were excluded at the very beginning. Thereby, the final multivariate model was lacking 10% of the data.

Based on the results of univariate analysis, age, Killip class, glucose and hemoglobin levels are significant predictors of the death outcome. In the multivariate model (without the above stated parameters, which significantly reduce the sample), the significant predictors are age, ACE inhibitors, and statins. The described variability of the model (Nagelkerke R Squared) is 0.215.

ishoda od AKS-a, odnosno da procenat korisnika sa smrtnim ishodom raste sa starošću, pa je i udeo umrlih najveći u najstarijoj dobnoj grupi (> 75 godina). Prema podacima iz literature, pacijenti starijeg životnog doba sa AKS-om imaju lošije bolničke ishode u odnosu na mlađe pacijente. Više je razloga za to: smanjen preostali kapacitet organizma uslovljen starenjem kao fiziološkim procesom, prisustvo više pridruženih bolesti, češća atipična prezentacija bolesti, kao i nemogućnost primene svih farmakoterapijskih modela. Razlike u zbrinjavanju starijih pacijenata sa AKS-om, odnosno razlike u izboru terapije, najčešće se ogledaju u tome što se stariji pacijenti ređe podvrgavaju reperfuzionim terapijama – trombolizi i primarnoj perkutanoj koronarnoj intervenciji, i u manjem procentu im se prepisuju lekovi za sekundarnu prevenciju, nakon otpusta iz bolnice, u odnosu na pacijente mlađeg uzrasnog doba [25]. Kohortna studija, koja je sprovedena na uzorku od 10.253 pacijenata sa AKS-om, iz 25 evropskih zemalja, potvrđuje da je starost značajan prediktor povećane bolničke smrtnosti od AKS-a. Udeo pacijenata koji su podvrgnuti koronarografiji je bila u obrnutoj korelaciji u odnosu na povećanje starosnog doba, tj. kod samo 13% pacijenata starosti  $\geq 85$  godina je primenjena ova dijagnostička procedura [26].

U našem istraživanju, grupi pacijenata sa AKS-om koji su imali smrtni ishod, pripadali su i pacijenti koji su imali nešto niže vrednosti telesne težine ( $p = 0,056$ ). Ono što je važno naglasiti je da su podaci o telesnoj težini dobijeni anamnestičkim putem, pa treba uzeti u obzir i subjektivnost ispitanika prilikom davanja odgovora. Postoji mogućnost da bi se dobili nešto drugačiji rezultati da su antropometrijski podaci obezbeđeni merenjem.

U studiji, koja je obuhvatila 8.680 azijskih pacijenata različite etničke pripadnosti sa akutnim infarktom miokarda, u periodu od 2011. do 2021. godine, analizirane su ishodne varijable na mesečnom nivou: kardiovaskularni mortalitet, mortalitet svih uzroka, ponovne hospitalizacije, razvoj kardiogenog šoka, razvoj srčane insuficijencije, te pojava moždanog udara, kod pacijenata bez standardnih promenljivih faktora rizika, u odnosu na one koji su ih imali. Neočekivano, među pacijentima bez modifikujućih faktora rizika (pušenje, hipertenzija, hiperholesterolemija i DM), bile su veće stope kardiovaskularnog mortaliteta, kardiogenog šoka, kao i veća smrtnost od svih uzroka, u petogodišnjem periodu nakon akutnog infarkta miokarda. Identifikovanje ove neuobičajeno rizične grupe pacijenata zahteva posebnu pažnju u pristupu njihovom lečenju, naročito zato što se radi o osobama mlađeg životnog doba [27].

Pacijenti sa AKS-om, kojima su, prilikom prijema u Opštu bolnici Valjevo, izmerene niže vrednosti ar-

## DISCUSSION

This study analyzes the association between demographic and anthropometric variables, risk factors, the presence of comorbidities, and the applied pharmacotherapy with the lethal outcome resulting from ACS, in patients treated at the General Hospital in Valjevo, as well as their differences. Based on the results obtained, an association was determined between certain age groups and the lethal outcome resulting from ACS, i.e., it was established that the percentage of patients with the lethal outcome rose with age, which is why the percentage of deceased patients is the highest in the oldest age group (> 75 years). According to data found in literature, older patients with ACS have less favorable hospital outcomes as compared to younger patients. There is a number of reasons for this: decreased remaining capacity of the body resulting from ageing as a physiological process, the presence of multiple comorbidities, more frequent atypical presentation of the disease, as well as limitations in the application of all pharmacotherapeutic models. The differences in treating older patients with ACS, i.e., the differences in the selection of therapy, are most commonly reflected in the fact that older patients less frequently undergo reperfusion therapies – thrombolysis and primary percutaneous coronary intervention, and in the fact that these patients are less frequently prescribed drugs for secondary prevention, after they are dismissed from hospital, as compared to younger patients [25]. A cohort study carried out on a sample of 10,253 patients with ACS, from 25 European countries, confirms that old age is a significant predictor of increased inhospital mortality resulting from ACS. The percentage of patients undergoing coronarography was in inverse correlation with the increase in age, i.e., this diagnostic procedure was applied in only 13% of patients aged  $\geq 85$  [26].

In our study, patients with somewhat lower values of body weight ( $p = 0.056$ ) belonged to the group of patients with ACS with a lethal outcome. It is important to stress that the data on body weight were obtained through anamnesis, which is why the subjectivity of the patients in their responses should be taken into consideration. There is a possibility that somewhat different information would have been obtained had anthropometric data been obtained with measurement.

A study, which included 8,680 multiethnic Asian patients with acute myocardial infarction, in the period between 2011 and 2021, analyzed the following outcome variables on a monthly basis – cardiovascular mortality, all-cause mortality, repeated hospitalization, development of cardiogenic shock, development of cardiac insufficiency, the occurrence of stroke, in patients without standard variable risk factors, as com-

terijskog krvnog pritiska, statistički su značajno više umirali od onih koji su imali nešto više vrednosti. Niže vrednosti arterijskog krvnog pritiska prilikom prijema su uglavnom u korelaciji sa težom kliničkom slikom pacijenata sa AKS-om i neretko su manifestacija ulaska pacijenta u kardiogeni šok, što sledstveno vodi lošijem zdravstvenom ishodu. Muat i saradnici [28] su pratili vrednosti sistolnog arterijskog pritiska izmerenih u prvih 48 sati nakon prijema, kod pacijenata sa akutnim infarktom miokarda starijih od 75 godina. Pacijenti kojima je izmeren sistolni pritisak < 125 mmHg imali su dva puta veći rizik od kardiovaskularnog mortaliteta u periodu od jedne godine nakon AIM-a.

Sagledavanjem samo pušačkog statusa utvrđeno je da su pušači u značajno manjem procentu imali smrtni ishod. Ovaj paradoks se može objasniti činjenicom da među pacijentima koji su dali podatak da ne puše nedostaju informacije o tome da li su u prošlosti ili nedavno bili pušači, i ukoliko jesu, vremenski koliko dugo i koji broj cigareta su pušili dnevno. Kreiranju kompletne slike doprineo bi podatak o dužini pušačkog staža i broju popušanih cigareta dnevno, kod aktuelnih pušača. U literaturi se takođe nailazi na pojam pušačkog paradoksa. Prema metaanalizi sprovedenoj u Kini, koja je brojala 2.188 pacijenata sa akutnim infarktom miokarda, uzrasta  $\leq 45$  godina, nisu evidentirane razlike u pogledu neželjenih kardiovaskularnih ishoda između pušača i nepušača [29].

Kod pacijenata sa AKS-om koji su imali smrtni ishod, zabeležene su značajno veće vrednosti glukoze u odnosu na one koji su preživeli, što je u skladu sa podacima iz literature. Prema podacima prospektivne longitudinalne opservacione kohortne studije, sprovedene na uzorku od 3.576 pacijenata sa AKS-om, na području Meksičkog zaliva [13], uočeno je da je kod pacijenata sa DM-om bio značajno veći bolnički mortalitet, tridesetodnevni mortalitet i jednogodišnji mortalitet nego kod pacijenata bez ovog komorbiditeta. Jednogodišnji mortalitet je bio za 13,7% veći kod pacijenata koji su imali dijabetes. Zajednička studija Američkog udruženja za srce i Kineskog kardiološkog društva [30], koja je obuhvatila 63.450 pacijenata sa AKS-om, pokazala je da je kod pacijenata sa istovremeno prisutnim dijabetesom ili suspektim dijabetesom, bio dvostruko veći rizik od smrti bilo kog uzroka i jedan i po puta veći rizik od velikih neželjenih kardiovaskularnih i cerebrovaskularnih događaja.

U našem istraživanju, pacijentima sa AKS-om, koji su bili u grupi onih koji su imali smrtni ishod, zabeležene su značajno niže vrednosti hemoglobina. Ovi rezultati su u skladu sa prospektivnom randomizovanom kontrolisanom studijom, koja je obuhvatila 7.781 pacijenta sa AKS-om [31]. Kod ovih pacijenata su, prilikom

pared to those patients who had them. Unexpectedly, amongst patients who were without modifying risk factors (smoking, hypertension, hypercholesterolemia, and DM), the rates of cardiovascular mortality and cardiogenic shock were higher, as was all-cause mortality, in the five-year period after acute myocardial infarction. Identifying this unusually risky group of patients requires particular attention with respect to the approach to their treatment, especially because of the younger age of these patients [27].

Patients with ACS, in whom lower values of arterial blood pressure were measured at admission to the General Hospital in Valjevo, died statistically significantly more frequently than those patients whose blood pressure values were somewhat higher. Lower values of arterial blood pressure at admission were mostly in correlation with a more severe clinical presentation in patients with ACS. They are often the manifestation of cardiogenic shock in the patient, which consequently leads to a less favorable health outcome. Mouhat et al. [28] monitored the values of systolic arterial blood pressure measured in the first 48 hours upon admission, in patients with acute myocardial infarction older than 75 years. The risk of cardiovascular mortality in the one-year follow-up period after AMI was twice higher in patients whose systolic pressure was < 125 mmHg.

When observing only smoking status, it was determined that smokers had a significantly smaller percentage of lethal outcome. This paradox can be explained by the fact that, with regards to patients who stated that they were non-smokers, there was a lack of data on whether they were former smokers or recent smokers, and if they were, how long they had smoked and how many cigarettes they smoked a day. The data on the length of smoking status and the number of cigarettes smoked per day in smokers would also contribute to a clearer understanding. Data found in literature also describes the concept of the smoker's paradox. According to a meta-analysis carried out in China, which included 2,188 patients with acute myocardial infarction, aged  $\leq 45$  years, differences regarding adverse cardiovascular outcomes between smokers and non-smokers were not recorded [29].

In patients with ACS who had a death outcome, significantly higher values of blood glucose were recorded, as compared to the survivors, which is in keeping with data from literature. According to the data published in a prospective longitudinal observational cohort study, carried out on a sample of 3,576 patients with ACS, in the Mexican Gulf area [13], significantly higher in-hospital mortality, thirty-day mortality, and one-year mortality were recorded in patients with DM, as compared to patients without this comorbidity. One-year mortality

bolničkog lečenja, smanjene vrednosti hemoglobina ( $\geq 3$  g/dL) bile nezavisno povezane sa povećanim rizikom od smrtnosti, čak dva i po puta u jednogodišnjem periodu. Povezanost između nižih vrednosti hemoglobina, pogoršanja ishemije miokarda i razvoja velikih neželjenih kardiovaskularnih događaja, u prvih 30 dana, kod pacijenata sa AKS-om, takođe je evidentirana u istraživanju koje su sprovedi Sabatin i saradnici [32].

Posmatrano prema klasifikaciji AKS-a, smrtni ishod je registrovan kod pacijenata sa infarktomiokarda sa ST elevacijom (STEMI) i infarktomiokarda bez ST elevacije (NSTEMI). Prospektivna studija, koja je analizirala mortalitet 1.188 pacijenata sa infarktomiokarda sa ST elevacijom, infarktomiokarda bez ST elevacije i nestabilnom anginom pectoris, hospitalizovanih u Univerzitetnoj bolnici Tampere u Finskoj, pokazala je da je bolnički mortalitet bio 9,6%, 13% i 2,6% ( $p < 0,001$ ) [33].

Još jedna determinanta, kod koje je zapažena povezanost sa lošim ishodom pacijenata sa AKS-om u našem istraživanju, jeste Killip klasa. Naime, sa povećanjem stepena Killip klasifikacije, rastao je i mortalitet pacijenata sa AKS-om, pa je udeo umrlih pacijenata sa Killip klasom III iznosio 23,1%, a onih sa Killip klasom IV iznosio je 100%. Studija koja je analizirala podatke 26.090 pacijenata sa AKS-om, kategorizovanih Killip klasifikacijom, potvrdila je povezanost višeg stepena Killip klase sa većim mortalitetom pacijenata, nakon mesec dana i nakon šest meseci. Iako su pacijenti sa Killip klasom II, III i IV činili 11% uzorka, učestvovali su sa čak 30% smrtnih ishoda u oba posmatrana perioda [34].

Čak 93,8% pacijenata sa AKS-om, kojima je bila neophodna primena manuelne kardiopulmonalne reanimacije, završilo je letalno. Reč je o inicijalno teškoj kliničkoj prezentaciji pacijenata sa AKS-om, pa ovakav rezultat nije neočekivan. Uvidom u rezultate desetogodišnjeg praćenja preživljavanja pacijenata u Koreji (njih 5.918), koji su u bolničkim uslovima zahtevali primenu kardiopulmonalne reanimacije zbog različitih uzroka, stopa preživljavanja je bila 11,7% do otpusta, a 8% u prvih šest meseci [35].

Evidentna je manja smrtnost pacijenata sa AKS-om, kojima su tokom bolničkog lečenja, od farmakoterapije, ordinirani: acetilsalicilna kiselina, beta blokatori, ACE inhibitori i statini. Prema smernicama za lečenje akutnog infarkta miokarda sa ST elevacijom Evropskog udruženja kardiologa [36], primena acetilsalicilne kiseline je indicirana, ne samo akutno, kod pacijenata sa akutnim infarktomiokarda, već i kao dugoročna prevencija sličnih neželjenih ishemijskih događaja. Kada je reč o beta blokatorima, njihova rana intravenska primena, kod pacijenata sa akutnim infarktomiokar-

was higher by 13.7% in patients with diabetes. A joint study of the American Heart Association and the Chinese Society of Cardiology [30], which included 63,450 patients with ACS, showed that in patients who had diabetes or suspected diabetes, the risk of death from any cause was twice higher, while the risk of death from major adverse cardiovascular and cerebrovascular events was one and a half times higher.

In our study, significantly lower levels of hemoglobin were registered in patients with ACS who belonged to the group with a death outcome. These results are in keeping with a prospective randomized control study, which included 7,781 patients with ACS [31]. In these patients, during in-hospital treatment, the decreased levels of hemoglobin ( $\geq 3$  g/dL) were independently associated with an increased risk of mortality, by as much as two and a half times, during a one-year period. The association between lower levels of hemoglobin, the exacerbation of myocardial ischemia, and the development of major adverse cardiovascular events, in the first 30 days, in patients with ACS, was also recorded in a study by Sabatine et al. [32].

In relation to ACS classification, the death outcome was registered in patients with myocardial infarction with ST elevation (STEMI) and in patients with myocardial infarction without ST elevation (NSTEMI). A prospective study, which analyzed mortality among 1,188 patients with myocardial infarction with ST elevation, myocardial infarction without ST elevation, and unstable angina pectoris, hospitalized at the Tampere University Hospital in Finland, showed that hospital mortality was 9.6%, 13%, and 2.6%, respectively ( $p < 0.001$ ) [33].

Another determinant which was observed to be associated with an adverse outcome in patients with ACS, in our study, is the Killip class. Namely, with the increase of the Killip class, mortality of patients with ACS also rose, whereby the percentage of deceased patients with Killip class III was 23.1%, while the percentage of deceased patients with Killip class IV was 100%. A study analyzing data pertaining to 26,090 patients with ACS, categorized according to the Killip class, confirmed the association of a higher Killip class with higher patient mortality, after one month and after six months. Although patients with Killip class II, III, and IV made up 11% of the sample, they accounted for as much as 30% of death outcomes in both observational periods [34].

As many as 93.8% of patients with ACS who required manual cardiopulmonary resuscitation died. This is an initially severe clinical presentation in patients with ACS, which is why this result was not surprising. Insight into the results of ten-year follow-up of patient survival in Korea (5,918 patients), regarding patients who required in-hospital cardiopulmonary resus-

da koji su podvrgnuti fibrinolizi, smanjuje incidenciju akutnih malignih ventrikularnih aritmija. Rana intravenaska primena metoprolola kod pacijenata sa AIM-om je povezana sa smanjenjem veličine zone infarkta, u periodu od 5 – 7 dana ( $p = 0,012$ ). Na osnovu trenutno dostupnih dokaza, kod pacijenata sa AIM-om, primenu statina treba započeti što ranije. Meta analiza Ibaneza i saradnika [36] je pokazala da intenzivnija terapija statinima dovodi do većeg smanjenja rizika od smrtnog ishoda zbog smanjenja vrednosti LDL holesterola (engl. *low density lipoprotein cholesterol*). Istraživanje je pokazalo da je primena ACE inhibitora u ranoj fazi, kod pacijenata sa akutnim infarktomiokarda sa ST elevacijom, povezana sa smanjenjem tridesetodnevog mortaliteta.

Svi pacijenti sa AKS-om, koji su primali inotrope tokom bolničkog lečenja (2,6% ukupnog uzorka), imali su smrtni ishod. Ovakav rezultat se može potkrepiti dobro poznatom činjenicom da su lekovi iz ove grupe indikovani kod najtežih pacijenata, koji u kliničkoj prezentaciji uglavnom već imaju znake kardiogenog šoka i srčanog popuštanja. Pregled retrospektivne kohortne studije [37], koja je analizirala podatke elektronske baze o mortalitetu 200.859 pacijenata sa kardiogenim šokom, hospitalizovanih u jedinicama intenzivne nege u SAD, koji su primali inotropne agense, pokazao je da su pacijenti kojima su ordinirani inotropi imali značajno veće stope bolničkog mortaliteta (24,03%), u odnosu na one koji nisu primali ove agense (12,40%).

## ZAKLJUČAK

U ovom radu je utvrđena statistički značajna povezanost između različitih determinanti: starosti, indeksa telesne mase, vrednosti arterijskog krvnog pritiska, pušenja, vrednosti glukoze i hemoglobina, Killip klase, primenjene manuelne kardiopulmonalne reanimacije, acetilsalicilne kiseline, beta blokatora, ACE inhibitora, statina, te inotropnih lekova, sa smrtnim ishodom pacijenata obolelih od akutnog koronarnog sindroma.

Veća smrtnost je zabeležena kod pacijenata starijeg životnog doba, manje telesne težine, nepušača, pacijenata sa izmerenim nižim vrednostima arterijskog krvnog pritiska prilikom prijema u bolnicu, pacijenata sa višim vrednostima glukoze i nižim vrednostima hemoglobina u krvi, pacijenata koji su imali STEMI i NSTEMI, pacijenata sa višim stepenom Killip klase i kod onih kod kojih je bila neophodna primena manuelne kardiopulmonalne reanimacije i inotropnih lekova. Sa druge strane, manja smrtnost je zabeležena među pacijentima sa AKS-om kojima su tokom hospitalizacije ordinirani acetilsalicilna kiselina, beta blokatori, ACE inhibitori i statini.

Poznavanje i praćenje zdravstvenog stanja stanovništva obolelog od AKS-a je važan element u daljem

citation, due to various causes, shows that the survival rate was 11.7% during hospital stay, and 8% in the first six months of follow-up [35].

It is evident that mortality was lower in patients with ACS who were treated with the following medications during their hospital stay: acetylsalicylic acid, beta blockers, ACE inhibitors, and statins. According to the guidelines for treating acute myocardial infarction with ST elevation of the European Society of Cardiology [36], the application of acetylsalicylic acid was indicated, not only acutely, in patients with acute myocardial infarction, but also as long-term prevention of similar adverse ischemic events. As far as beta blockers are concerned, their early intravenous application, in patients with acute myocardial infarction who underwent fibrinolysis, reduces the incidence of acute malignant ventricular arrhythmias. Early intravenous application of metoprolol in patients with AMI was connected with the reduction of the size of the infarction, within a period of 5 – 7 days ( $p = 0.012$ ). Based on evidence available so far, in patients with AMI, the administration of statins should be started as early as possible. A meta-analysis by Ibanez et al. [36] showed that more intensive therapy with statins led to a decreased risk of the death outcome due to the reduction in the level of LDL cholesterol (low density lipoprotein cholesterol). The study showed that the application of ACE inhibitors in the early stage, in patients with acute myocardial infarction with ST elevation, was associated with a reduction in thirty-day mortality.

All patients with ACS who received inotropes during their in-hospital treatment (2.6% of the overall sample) had a death outcome. Such a result can be substantiated with the well-known fact that drugs belonging to this group of medications are indicated in patients with the most severe presentation, who already display signs of cardiogenic shock and heart failure. A retrospective cohort study [37] analyzing data from an electronic data base on mortality in 200,859 patients with cardiogenic shock, hospitalized in intensive care units in USA, who received inotropic agents, showed that patients who were given inotropes had significantly higher in-hospital mortality rates (24.03%), as compared to patients who did not receive these medicaments (12.40%).

## CONCLUSION

In this study, a statistically significant association between different determinants, namely: age, body mass index, the value of arterial pressure, smoking status, levels of glucose and hemoglobin, the Killip class, applied manual cardiopulmonary resuscitation, acetylsalicylic acid, beta blockers, ACE inhibitors, statins, ino-



planiranju, organizaciji i sprovođenju zdravstvene zaštite populacije Kolubarskog okruga, radi očuvanja i unapređenja zdravlja. U cilju pravovremenog vođenja evidencije i poboljšanja kvaliteta podataka „Koronarnih listova“, neophodno je jačati kadrovske kapacitete u vidu povećanja broja lekara u Koronarnoj jedinici, produženja vremena potrebnog za uzimanje detaljne anamneze, obavljanje fizikalnog pregleda i popunjavanje „Koronarnih listova“, kao i u vidu dodatne obuke lekara o značaju preciznog i relevantnog vođenja medicinske dokumentacije.

Pored navedenog, potrebno je kreiranje takve javnozdravstvene politike koja podstiče unapređenje programa prevencije, sa ciljem smanjenja faktora rizika za nastanak akutnog koronarnog sindroma. Da bi se ova kva politika mogla valjano sprovoditi, neophodno je dodatno edukovati opštu i stručnu javnost o ovoj temi, kroz aktivniji zdravstveno-vaspitni rad, te nastaviti sa realizacijom sličnih istraživanja i obezbediti kontinuitet u sprovođenju pomenutih aktivnosti.

**Sukob interesa:** Nije prijavljen.

## LITERATURA / REFERENCES

1. WHO. Health Topics. Cardiovascular diseases. [Internet]. 2019. Dostupno na: [https://www.who.int/health-topics/cardiovascular-diseases#tab=tab\\_1](https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1)
2. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. *J Am Coll Cardiol*. 2017 Jul 4;70(1):1-25. doi: 10.1016/j.jacc.2017.04.052.
3. WHO. The top 10 causes of death. [Internet]. 2020. Dostupno na: <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death>
4. Institut za javno zdravlje Srbije „Dr Milan Jovanović Batut“. Zdravstveno-statistički godišnjak Republike Srbije 2020. [Internet]. 2021. Dostupno na: <https://www.batut.org.rs/download/publikacije/pub2020.pdf>
5. Institut za javno zdravlje Srbije „Dr Milan Jovanović Batut“. Incidencija i mortalitet od akutnog koronarnog sindroma u Srbiji 2020. [Internet]. 2021. Dostupno na: <https://www.batut.org.rs/download/publikacije/AKS2020.pdf>
6. Jankovic S, Vlajinac H, Bjegovic V, Marinkovic J, Sipetic-Grujicic S, Markovic-Denic L, et al. The burden of disease and injury in Serbia. *Eur J Public Health*. 2007 Feb;17(1):80-5. doi: 10.1093/eurpub/ckl072.
7. Ministarstvo zdravlja Republike Srbije. Republička stručna komisija za izradu i implementaciju vodiča dobre kliničke prakse. Nacionalni vodič dobre kliničke prakse za dijagnostikovanje i lečenje ishemijske bolesti srca 2/11. 2012. [Internet]. Dostupno na: [https://www.zdravlje.gov.rs/view\\_file.php?file\\_id=670&cache=sr](https://www.zdravlje.gov.rs/view_file.php?file_id=670&cache=sr)
8. Van Camp G. Cardiovascular disease prevention. *Acta Clin Belg*. 2014 Dec;69(6):407-11. doi: 10.1177/2295333714Y.0000000069.
9. Lapcević M, Vuković M. Faktori rizika za hronična nezarazna oboljenja: dvansestonediljna prospektivna studija [Risk factors for chronic noncontiguous diseases: twelve-week prospective study]. *Srp Arh Celok Lek*. 2004 Nov-Dec;132(11-12):414-20. Serbian. doi: 10.2298/sarh0412414I.
10. Babić Z, Zeljković I, Pintarić G, Vrsalović M, Jelavić MM, Mišigoj-Duraković M. The role of anthropometric parameters and physical activity level in patients with acute coronary syndrome admitted to the intensive cardiac care unit. *Acta Clin Croat*. 2021 Jun;60(2):201-8. doi: 10.20471/acc.2021.60.02.05.
11. Wan J, Zhou P, Wang D, Liu S, Yang Y, Hou J, et al. Impact of Normal Weight Central Obesity on Clinical Outcomes in Male Patients with Premature Acute Coronary Syndrome. *Angiology*. 2019 Nov;70(10):960-8. doi: 10.1177/0003319719835637.
12. Kringeland E, Tell GS, Midtbø H, Igland J, Haugsgjerd TR, Gerdtts E. Stage 1 hypertension, sex, and acute coronary syndromes during midlife: the Hordaland Health Study. *Eur J Prev Cardiol*. 2022 Feb 19;29(1):147-54. doi: 10.1093/eurjpc/zwab068.
13. Shehab A, Bhagavathula AS, Al-Rasadi K, Alshamsi F, Al Kaab J, Thani KB, et al. Diabetes and Mortality in Acute Coronary Syndrome: Findings from the Gulf COAST Registry. *Curr Vasc Pharmacol*. 2020;18(1):68-76. doi: 10.2174/157016116666181024094337.

tropes and the death outcome in patients with acute coronary syndrome, was determined.

Higher mortality was recorded in patients who were older, patients with a lower bodyweight, non-smokers, patients with lower values of arterial blood pressure measured at hospital admission, patients with higher levels of blood glucose and lower levels of hemoglobin, patients with STEMI and NSTEMI, patients with a higher Killip class, as well as patients in whom the application of manual cardiopulmonary resuscitation and inotropes was necessary. On the other hand, lower mortality was recorded amongst patients with ACS, who were given acetylsalicylic acid, beta blockers, ACE inhibitors, and statins.

Understanding and monitoring the health status of the population suffering from ACS is an important element in further planning, organizing, and implementing healthcare for the population of the Kolubara District, with the aim of preserving and improving health. In order to maintain timely recording and improve the quality of data in the *Coronary Sheets*, it is necessary to strengthen staff capacity by increasing the number of doctors working in the Coronary Unit, increasing the time available for documenting a detailed anamnesis, performing a physical examination, and filling out the *Coronary Sheets*, as well as by providing additional training for doctors regarding the importance of accurate and relevant medical record keeping.

Additionally, it is necessary to create such public health policies that promote the improvement of prevention programs, with the aim to reduce risk factors for the development of acute coronary syndrome. In order to properly implement such policies, it is necessary to educate both the public and the medical community on this issue, through more active educational work, to continue with similar research, as well as to ensure the continuity of the said activities.

**Conflict of interest:** None declared.

14. Ministarstvo zdravlja Republike Srbije. Republička stručna komisija za izradu i implementaciju vodiča u kliničkoj praksi, Odbor za lipide Endokrinološke sekcije Srpskog lekarskog društva, Udruženje za aterosklerozu Srbije, Agencija za akreditaciju zdravstvenih ustanova Srbije. Nacionalni vodič dobre kliničke prakse za dijagnostikovanje i lečenje lipidskih poremećaja 5/11. [Internet]. 2012. Dostupno na: [https://www.zdravlje.gov.rs/view\\_file.php?file\\_id=673&cache=sr](https://www.zdravlje.gov.rs/view_file.php?file_id=673&cache=sr)
15. Snaters M, Scholte Op Reimer WJ, Dobber J, Minneboo M, Ter Riet G, Jorstad HT, et al. Smoking cessation after an acute coronary syndrome: immediate quitters are successful quitters. *Neth Heart J*. 2015 Dec;23(12):600-7. doi: 10.1007/s12471-015-0755-9.
16. Steptoe A, Kivimäki M. Stress and cardiovascular disease. *Nat Rev Cardiol*. 2012 Apr 3;9(6):360-70. doi: 10.1038/nrcardio.2012.45.
17. Hbejan K. Smoking effect on ischemic heart disease in young patients. *Heart Views*. 2011 Jan;12(1):1-6. doi: 10.4103/1995-705X.81547.
18. Stajčić D, Đonović N. Kardiovaskularne bolesti – faktori rizika. *Med Čas (Krag)*. 2016;50(2):43-8.
19. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation*. 2001 Nov 27;104(22):2746-53. doi: 10.1161/hc4601.099487.
20. Ministarstvo zdravlja Republike Srbije. Nacionalni komitet za izradu Vodiča kliničke prakse u Srbiji, Radna grupa za kardiovaskularne bolesti. Nacionalni vodič kliničke prakse. Preporuke za prevenciju ishemijske bolesti srca. [Internet]. 2002. Dostupno na: [https://www.zdravlje.gov.rs/view\\_file.php?file\\_id=678&cache=sr](https://www.zdravlje.gov.rs/view_file.php?file_id=678&cache=sr)
21. Roberts R. Genetics of coronary artery disease. *Circ Res*. 2014 Jun 6;114(12):1890-903. doi: 10.1161/CIRCRESAHA.114.302692.
22. Graham G. Acute Coronary Syndromes in Women: Recent Treatment Trends and Outcomes. *Clin Med Insights Cardiol*. 2016 Feb 8;10:1-10. doi: 10.4137/CMC.S37145.
23. Službeni glasnik RS, br. 42/06, 119 /07, 84/08, 71/09, 85/09, 24/10, 6/12, 37/12, 8/14, 92/15, 111/17, 114/17 – ispr, 13/18, 15/18 – ispr, 68/19, 5/20, 11/20, 52/20, 88/20, 62/21, 69/21, 74/21, 95/21. Uredba o Planu mreže zdravstvenih ustanova. [Internet]. Dostupno na: [https://www.paragraf.rs/propsi/uredba\\_o\\_planu\\_mreze\\_zdravstvenih\\_ustanova.html](https://www.paragraf.rs/propsi/uredba_o_planu_mreze_zdravstvenih_ustanova.html)
24. Službeni glasnik RS, br. 123/2014-2, 106/2015-65, 105/2017-32, 25/2019-3 -dr. zakon. Zakon o zdravstvenoj dokumentaciji i evidencijama u oblasti zdravstva RS. [Internet]. Dostupno na: <https://www.paragraf.rs/propsi/zakon-o-zdravstvenoj-dokumentaciji-i-evidencijama-u-oblasti-zdravstva.html>
25. Simms AD, Batin PD, Kurian J, Durham N, Gale CP. Acute coronary syndromes: an old age problem. *J Geriatr Cardiol*. 2012 Jun;9(2):192-6. doi: 10.3724/SP.J.1263.2012.01312.
26. Rosengren A, Wallentin L, Simoons M, Gitt AK, Behar S, Battler A, et al. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. *Eur Heart J*. 2006 Apr;27(7):789-95. doi: 10.1093/eurheartj/ehi774.
27. Kong G, Chew NWS, Ng CH, Chin YH, Lim OZH, Ambhore A, et al. Prognostic Outcomes in Acute Myocardial Infarction Patients Without Standard Modifiable Risk Factors: A Multiethnic Study of 8,680 Asian Patients. *Front Cardiovasc Med*. 2022 Mar 29;9:869168. doi: 10.3389/fcvm.2022.869168.
28. Mouhat B, Putot A, Hanon O, Eicher JC, Chagué F, Beer JC, et al.; Observatoire des Infarctus de Côte d'Or Survey. Low Systolic Blood Pressure and Mortality in Elderly Patients After Acute Myocardial Infarction. *J Am Heart Assoc*. 2020 Mar 3;9(5):e013030. doi: 10.1161/JAHA.119.013030.
29. Liu Y, Han T, Gao M, Wang J, Liu F, Zhou S, et al. Clinical characteristics and prognosis of acute myocardial infarction in young smokers and non-smokers ( $\leq 45$  years): a systematic review and meta-analysis. *Oncotarget*. 2017 Sep 20;8(46):81195-81203. doi: 10.18632/oncotarget.21092.
30. Zhou M, Liu J, Hao Y, Liu J, Huo Y, Smith SC Jr, et al.; CCC-ACS Investigators. Prevalence and in-hospital outcomes of diabetes among patients with acute coronary syndrome in China: findings from the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome Project. *Cardiovasc Diabetol*. 2018 Nov 27;17(1):147. doi: 10.1186/s12933-018-0793-x.
31. Leonardi S, Gragnano F, Carrara G, Gargiulo G, Frigoli E, Vranckx P, et al. Prognostic Implications of Declining Hemoglobin Content in Patients Hospitalized With Acute Coronary Syndromes. *J Am Coll Cardiol*. 2021 Feb 2;77(4):375-88. doi: 10.1016/j.jacc.2020.11.046.
32. Sabatine MS, Morrow DA, Giugliano RP, Burton PB, Murphy SA, McCabe CH, et al. Association of hemoglobin levels with clinical outcomes in acute coronary syndromes. *Circulation*. 2005 Apr 26;111(16):2042-9. doi: 10.1161/01.CIR.0000162477.70955.5F.
33. Nikus KC, Eskola MJ, Virtanen VK, Harju J, Huhtala H, Mikkelsen J, et al. Mortality of patients with acute coronary syndromes still remains high: a follow-up study of 1188 consecutive patients admitted to a university hospital. *Ann Med*. 2007;39(1):63-71. doi: 10.1080/08037060600997534.
34. Khot UN, Jia G, Moliterno DJ, Lincoff AM, Khot MB, Harrington RA, et al. Prognostic importance of physical examination for heart failure in non-ST-elevation acute coronary syndromes: the enduring value of Killip classification. *JAMA*. 2003 Oct 22;290(16):2174-81. doi: 10.1001/jama.290.16.2174.
35. Park IY, Ju YS, Lee SY, Cho HS, Hong JI, Kim HA. Survival after in-hospital cardiopulmonary resuscitation from 2003 to 2013: An observational study before legislation on the life-sustaining treatment decision-making act of Korean patients. *Medicine (Baltimore)*. 2020 Jul 24;99(30):e21274. doi: 10.1097/MD.00000000000021274.
36. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al.; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018 Jan 7;39(2):119-77. doi: 10.1093/eurheartj/ehx393.
37. Gao F, Zhang Y. Inotrope Use and Intensive Care Unit Mortality in Patients With Cardiogenic Shock: An Analysis of a Large Electronic Intensive Care Unit Database. *Front Cardiovasc Med*. 2021 Sep 21;8:696138. doi: 10.3389/fcvm.2021.696138.