

# The Impact of Pre-Hospital Emergency Care on Outcome in Patients with Acute Coronary Syndrome

---

Gashi, Musli

Doctoral thesis / Disertacija

2024

Degree Grantor / Ustanova koja je dodijelila akademski / stručni stupanj: **University of Zagreb, School of Medicine / Sveučilište u Zagrebu, Medicinski fakultet**

Permanent link / Trajna poveznica: <https://urn.nsk.hr/urn:nbn:hr:105:673798>

Rights / Prava: [In copyright](#) / [Zaštićeno autorskim pravom.](#)

Download date / Datum preuzimanja: **2024-11-29**



Repository / Repozitorij:

[Dr Med - University of Zagreb School of Medicine Digital Repository](#)



UNIVERSITY OF ZAGREB  
SCHOOL OF MEDICINE

**Musli Gashi**

**The Impact of Pre-Hospital Emergency  
Care on Outcome in Patients with Acute  
Coronary Syndrome**

**DISSERTATION**



Zagreb, 2024

UNIVERSITY OF ZAGREB  
SCHOOL OF MEDICINE

**Musli Gashi**

**The Impact of Pre-Hospital Emergency  
Care on Outcome in Patients with Acute  
Coronary Syndrome**

**DISSERTATION**

Zagreb, 2024

This dissertation was made at the University of Zagreb School of  
Medicine and University Clinical Center of Kosovo

Mentor: Professor Vesna Degoricija, MD, PhD  
Co-mentor: Professor Gani Bajraktari, MD, PhD

## **Acknowledgements**

I would like to express my thanks to my mentor Professor Vesna Degoricija, MD, PhD for her contribution to the realisation of this PhD.

Also I want to thanks my Co-mentor Professor Gani Bajraktari, MD, PhD for his contribution.

A special thanks to my wife Sanije and my son Jon.

## Table of contents

<b>1.</b>	<b>INTRODUCTION .....</b>	<b>1</b>
1.1.	Emergency Medical Service (EMS) systems .....	2
1.1.1.	Background .....	3
1.1.2.	Human resources, education .....	5
1.1.3.	Working Principle .....	5
1.1.4.	Utstein style .....	6
1.2.	Acute Coronary Syndrome (ACS) .....	8
1.2.1	Definition .....	8
1.2.2	The pathogenesis of acute myocardial infarction (AMI) .....	8
1.2.3	Risk factors of atherosclerotic disease .....	9
1.2.4.	Angina Pectoris .....	10
1.2.5.	Electrocardiography findings and biochemical markers in ACS .....	10
1.2.6.	Management of STEMI .....	12
1.3.	The strategy of treating patients with angina and unstable NON-STEMI (66) ....	20
1.4.	Identifying patients at high risk for ACS.....	21
1.5.	Delays in the treatment of AMI .....	23
<b>2.</b>	<b>HYPOTHESIS .....</b>	<b>24</b>
<b>3.</b>	<b>AIMS AND PURPOSE OF THE RESEARCH .....</b>	<b>25</b>
<b>4.</b>	<b>MATERIAL AND METHODOLOGY .....</b>	<b>26</b>
<b>5.</b>	<b>RESULTS .....</b>	<b>29</b>
5.1.	Socio demographic characteristics of patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period .....	29
5. 2.	Patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period by groups .....	36
5. 3.	Patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period by types of acute coronary syndrome .....	47
<b>6.</b>	<b>DISCUSSION .....</b>	<b>53</b>
6.1.	Socio demographic characteristics of patients with acute coronary syndrome .....	53
6.2.	Patients with acute coronary syndrome treated at the University Clinical Center of Kosovo for the analyzed period by groups .....	58
6. 3.	Patients with acute coronary syndrome treated at the University Clinical Center of Kosovo for the analyzed period by types of acute coronary syndrome .....	69
<b>7.</b>	<b>CONCLUSIONS .....</b>	<b>74</b>
<b>8.</b>	<b>ABSTRACT IN CROATIAN .....</b>	<b>78</b>
<b>9.</b>	<b>ABSTRACT IN ENGLISH .....</b>	<b>79</b>
<b>10.</b>	<b>LIST OF REFERENCES .....</b>	<b>80</b>
<b>11.</b>	<b>CURRICULLUM VITAE .....</b>	<b>106</b>

## **List of symbols and abbreviations**

ACS - Acute coronary syndrome

AMI – Acute myocardial infarction

APSAC – Anisoylated plasminogen streptokinase activator complex

ASA – Acetosalicylic acid

CHD – coronary heart disease

CI - Confidence interval

CPC – Cerebral performance category

CPR – Cardiopulmonary resuscitation

ECG – Electrocardiogram

EMS – Emergency medical service

EMT – Emergency medical technician

ED - Emergency department

ESC – European Society of Cardiology

HEMS – Helicopter emergency medical service

ICH – Intracerebral hematoma

IU – International unit

MI – Myocardial infarction

MACE - Major adverse cardiac events

NSTEMI - Non-ST-elevation myocardial infarction

NS – Not significant

OR – Odds-ratio

PCI – Percutaneous coronary intervention

SD – Standard deviation

STEMI – ST – elevation myocardial infarction

# 1. INTRODUCTION

Acute coronary syndrome is the leading cause of cardiovascular morbidity and mortality, resulting in substantial health care utilization and costs (1). The increase in cardiovascular diseases burden is largely the result of both an increase in the prevalence of the risk factors and a relative lack of access to well-recognized interventions that prolong survival once CVD is manifest. Extremely limited data are available about the mortality rates of acute CVD in Central and Eastern European countries (2-4) although the available data suggest higher proportion of in-hospital mortality deaths attributed to CVD in these countries when compared with the European member states (2).

The mortality rate of ACS in the first 30 days after the onset of disease ranges from 30-50%, with about half of deaths occurring within the first 2 hours (5,6). Yet, despite parallel reductions in 30 day case fatality rates, the British Heart Foundation reports that acute coronary syndromes remain one of the major causes of premature death in men and women in the UK (7).

The main objective of treating patients with ACS is to re-establish myocardial perfusion within a few hours from the onset of pain, in order to save the ischemic myocardium and increase the chance of survival (8-10). The emergency physician's role in the stabilization, evaluation, and treatment of the patient who has ACS is critical (11). ACS is one of the main causes of death in Kosova (12) and it is among the medical emergencies that benefit most from an efficient system of pre-hospital care (13). Most deaths from ACS occur in the first few hours after the onset of symptoms, mainly from fatal arrhythmias which could be prevented by rapid access to specialized care (5). Recent studies (14-20) have demonstrated the effectiveness of Pre-Hospital Emergency in reducing the time between onset of symptoms, diagnosis and beginning of treatment, as well as in reducing mortality in ACS patients (14,15). Global data on the management and therapies of patients with ACS are needed to improve the outcomes of these patients, especially in countries with low-to-middle income economies (16).



## **1.1. Emergency Medical Service (EMS) systems**

According to the European Society for Emergency Medicine: “Emergency Medicine is a specialty based on the knowledge and skills required for the prevention, diagnosis and management of urgent and emergency aspects of illness and injury affecting patients of all age groups with a full spectrum of undifferentiated physical and behavioral disorders. It is a specialty in which time is critical. The practice of Emergency Medicine encompasses the pre-hospital and in-hospital triage, resuscitation, initial assessment and management of undifferentiated urgent and emergency cases until discharge or transfer to the care of another physician or health care professional. It also includes involvement in the development of pre-hospital and in-hospital emergency medical systems” (17).

Emergency medical service is a link between primary health care and secondary health care. This service addresses to people who have disorders of vital functions, or disruption of these functions. An Emergency Medical Service (EMS) can be defined as "a comprehensive system which provides the arrangements of personnel, facilities and equipment for the effective, coordinated and timely delivery of health and safety services to victims of sudden illness or injury." (18, 19)

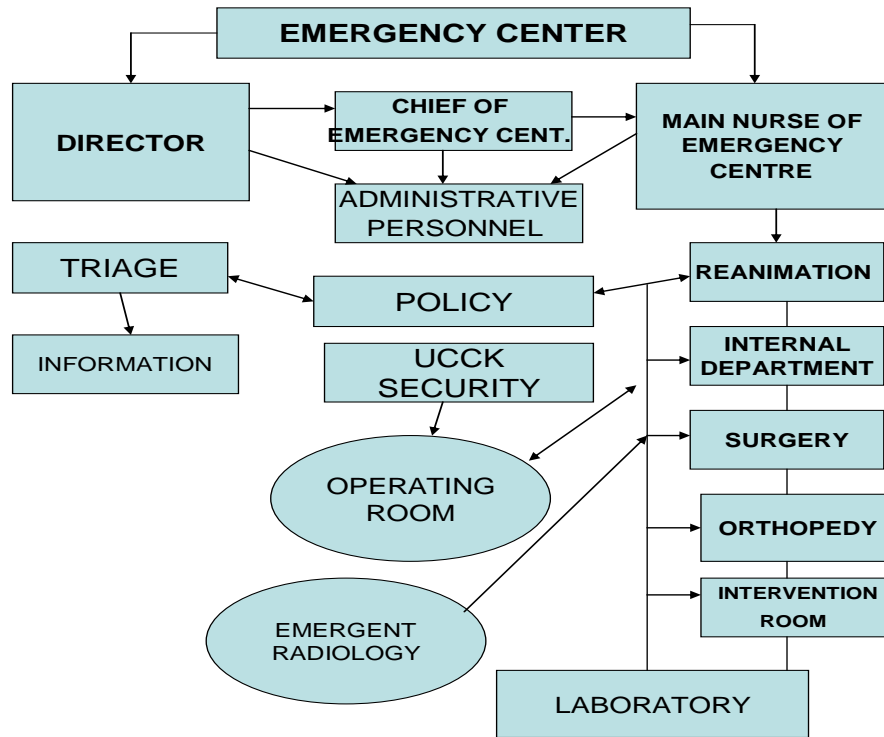
For patients with ACS, early symptom recognition, early activation of emergency medical service (EMS), early transportation to the hospital and early administration of definitive treatment are associated with improved clinical outcomes (20) Guidelines from European Society of Cardiology,(21) American College of Cardiology (ACC) and American Heart Association (AHA)(20,22) strongly recommend activation of the EMS, a rapid and effective means of obtaining medical care, for patients who have symptoms consistent with ACS. EMS is critical to provide an opportunity for earlier initiation of evidence-based therapies, faster receipt of initial reperfusion therapies and also earlier coordination with capable centers for efficient delivery of care (23,24).

### 1.1.1. Background

Advanced emergency medical service for the first time has been displayed in early '60ties of XX century in Europe and USA. The first ambulance was used in 1906 (USA). Since 1970s, the mode of emergency health care delivery in pre-hospital environment evolved around two main models of EMS with distinct features. These are the Anglo-American and the Franco-German model. These categorical distinctions were obvious during the 1970s until the end of the 20th century. Today, most EMS systems around the world have varied compositions from each model (25).

In Kosovo, before 1999 EMS has been similar to the system which has been applied in the former Yugoslavia. The development of an Anglo-American model of emergency medicine came post conflict, with the involvement of international governmental and non governmental organizations. These organizations built or renovated hospital emergency departments, donated ambulances and equipment, and trained healthcare professionals. At first the emergency centers were established near the regional hospitals. In October 1999, the emergency center it was established in Kosovo University Clinical Center (UCCCK). The organogram of Emergency Center in UCCCK is presented in Fig. 1. These centers are equipped with new modern equipment for monitoring, diagnosis and treatment of seriously ill and injured patients. At the same time it has been worked on establishing primary cells in emergency medicine health houses which were being transformed in family medicine bases in all municipalities of Kosovo. These cells were equipped with the necessary equipment and vehicles for transporting patients. The British Department for International Development supported the construction of a new emergency department at the Kosovo University Clinical Center, Pristina, Kosova. The Johns Hopkins University in cooperation with Samaritan's Purse developed an emergency medicine residency program. Various other non governmental organizations such as Die Johan niter, International Medical Corps and the Spanish Red Cross provided training to emergency medical service providers (26). The World Health Organization (WHO) assessed Kosovo's emergency medical services in 2000 and made recommendations to the Joint Interim Administrative Structure—the United Nations/Kosovar government (27).

**ORGANOGRAM OF EMERGENCY CENTER IN UCC OF KOSOVA**



12/30/2016

1

**Fig. 1. Organogram of Emergency Center in UCC of Kosova**

### **1.1.2. Human resources, education**

For the new system, the existing resources of “acceptance service” from the old establishment were not enough. Therefore, for this purpose a considerable number of new personnel were educated. Today this system counts about 1000 employees distributed in primary and secondary medicine. This system takes care of treating about 200,000 patients per year. Nearly two thirds of the patients are treated at primary health care level and more than one third in regional emergency centers, at the secondary level. UCC Emergency Centre just within a year treats 30,000 emergency patients.

In the fall of 2000, the first generation began its specialization in Emergency Medicine, a step that was made possible by the international staff of the Emergency Medicine John Hopkins University (26). Lecturers and trainers, 21 prominent experts from the US were for two consecutive years. In this plan, Kosovo doctors benefited in different aspects such as: medical logistics, efficient organization and modern medicine.

### **1.1.3. Working Principle**

The working principle is based on the emergency chain: 1) telephone call , 2 ) recognition of the patient's condition , 3) medical assistance at the scene , 4) medical assistance during transport , 5) further diagnostics in the intensive care unit , 6) if needed transportation and treatment within hospital premises and further in intensive care unit ( ICU ) , or the surgery room .

Emergency medical assistance is based on three basic principles:1) Actual patient, 2) Emergency medical assistance at the right time, 3) Transport and placement of the patient in the correct hospital. The overall work during first hour, which in medicine is called "golden hour", determines the outcome between life and death. The actions which determine patient's life are: a) arriving at the spot as fast as possible, b) early cardiopulmonary reanimation (CPR - cardiopulmonary resuscitation). The employees of pre-hospital emergency medical unit

(medical technicians and emergency medicine specialists) are in service 24 hours non-stop. They are trained to make endotracheal intubation and defibrillate patients, find intravenous line (intravenous open access), fluid resuscitation with crystalloids, injecting adrenaline or epinephrine, dopamine, amiodarone, pain killers intravenous analgesics and are able making ECG with 12 derivations also known as (12 lead electrocardiography – ECG).

#### **1.1.4. Utstein style**

Thirty years ago, a conference was held at Utstein Abbey in 1990 which resulted in the publication of guidelines for uniform reporting of data from out-of-hospital cardiac arrest (OHCA). The term ‘Utstein Style’ is now synonymous with resuscitation reporting and registries. Clear definitions and performance indicators enable a collective approach to measuring and improving patient outcomes. A template for reporting these agreed measures with standardized definitions is now known as the Utstein style or just Utstein. The Utstein Style has had greatest influence in resuscitation, registries, pre-hospital and disaster medicine (28-30).

The Utstein Formula for Survival (31) is now a widely recognized model which includes three elements in hypothesizing potential survival rates from cardiac arrest: medical science, educational efficiency and local implementation (Fig. 2).

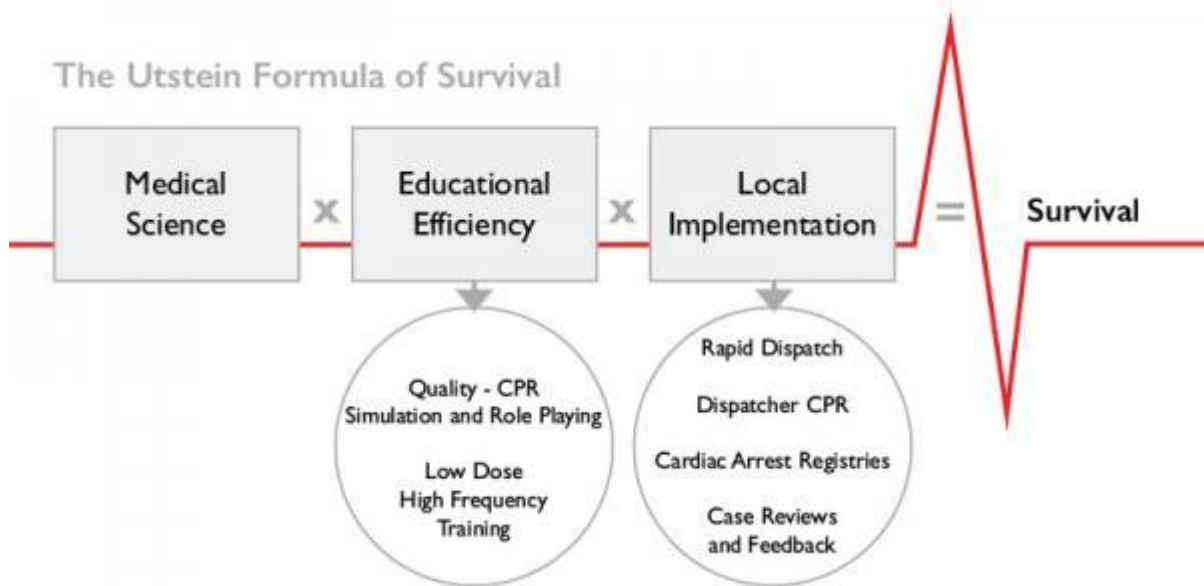


Fig. 2 The Utstein Formula of Survival

## **1.2. Acute Coronary Syndrome (ACS)**

### **1.2.1 Definition**

Acute Coronary Syndrome is the clinical condition in which patient is suffering from signs of myocardial ischemia. So, ACS has to do with overall reduction or complete cessation of blood flow in the coronary arteries and consequently it ends up with heart muscle necrosis. Updated classification of ACS introduced the following conditions: 1) Unstable angina; 2) ST-elevation myocardial infarction (STEMI), 3) non-ST- elevation myocardial infarction (NSTEMI), (32).

### **1.2.2 The pathogenesis of acute myocardial infarction (AMI)**

Acute thrombosis in coronary arteries is caused by detachment of atherosclerotic plaque. Atherosclerotic plaques begin to form very early in a human's life. Atherosclerosis is the pathology in which dominates the extracellular accumulation of lipids and where small lipoprotein particles are deposited within intimate part of arterial. Atherosclerotic plaque extends in advance because the white blood cells migrate into them and also cells of smooth musculature. Even the plate can also develop blood microcirculation, which helps the continued growth of plaque (atheroma). Detachment or (cracks) of atherosclerotic plaque promotes a cascade process of substance action which would put into motion thrombolytic aggregation and the generation of trombones, inside areas (field) of ruptured, forming up clotting and in the worst case causing the sudden thrombotic closure (occlusion ) of coronary artery, and as a result acute myocardial infarction. AMI can also be caused by coronary spasm in patients who have normal coronary arteries (33).

### **1.2.3 Risk factors of atherosclerotic disease**

#### **- Dyslipoproteinemia**

Many studies have shown that high cholesterol values in serum have an important role in the development of coronary heart diseases. Also increased levels of lipoprotein in the blood speed up atherosclerotic plaque formation. Treating in time the hyperlipidemia prevents coronary heart disease (34, 35)

#### **- Smoking**

Smoking increases the risk of coronary heart disease. Smoking increases platelet aggregation and also causes coronary spasm (34, 36)

#### **- Diabetes mellitus**

Diabetes increases the risk for cardiovascular disease. Hyperglycemia increases the production of lipoprotein with very low density (VLDL) in the liver, the final products of which increase the risk for vascular damage (34, 37).

.

#### **- Arterial Hypertension**

Arterial hypertension increases the risk of coronary heart disease. The main mechanism is the pulsative pressure causing endothelial cell dysfunction and cell hypertrophy of the smooth muscles (34, 38).



#### **1.2.4. Angina Pectoris**

Generally, chest pain can be divided into two major groups: cardiac pain and non cardiac chest pain. Chest pain can be categorized as cardiac ischemic pain, pericardial or atypical. Retrosternal pain of unexpected character "tightening" and "the collapse" that lasts a few minutes is pathognomonic sign for angina pectoris. Angina pectoris usually occurs during physical strain or emotional strengths that is associated with a significant fear for existence and this pain then stops and disappears slowly. If for any reason such a pain appears suddenly even during the rest time accompanied by sweating, and not reacting in nitroglycerine, then all chances are that it comes to an acute myocardial infarction. When coronary artery closes the pain is more severe and high intensity and lasts more than 20 minutes. There are times when patients feel no pain (silent myocardial infarction), especially in patients with diabetes mellitus and hypertension. About 2/3 of patients with AMI have prodromal signs first days or weeks characterized by increasing angina, fatigue and difficult breathing. The first symptoms of AMI is usually a deep pain, substernal, visceral, which often spreads to the back, jaw or left arm. In severe episodes the patients are afraid of dying, anxiety, and gloomy thoughts in general; here dominates symptomatic left ventricular failure, pulmonary edema, shock or have cardiac arrhythmia (39).

#### **1.2.5. Electrocardiography findings and biochemical markers in ACS**

The two primary approaches for optimizing ACS patient outcomes are to reduce treatment delay and to minimize total ischemic time, defined as time of symptom onset to reperfusion of culprit arteries (20,40). To minimize total ischemic burden time, the American Heart Association and European Society of Cardiology (AHA/ESC) recommend that individuals with chest pain seek medical attention immediately and receive a 12-lead electrocardiogram (ECG) within 10 min of hospital arrival, based on evidence that longer delays are associated with adverse prognoses (20). ECG results should be analyzed in conjunction with patient history and clinical presentation to assess the likelihood of an ACS diagnosis (20).

The most important laboratory procedure that is done in patients suspected of having ACS is the analysis of ECG. STEMI patients are presented with ischemic symptoms and ST elevation of the segment in ECG also develops AMI and "Q" wave. Most of these patients have increased typical biomarkers of necrosis. ECG findings could be relative, but biochemical markers are strong indicators that myocardial cells are suffering from ischemia, or are dead, and known intracellular macromolecules as cardiac marker end up in the bloodstream. These markers known as creatine kinase (CK), cardiac specific isoenzymes (CK. MB) and troponin TnT and TNI. Cardiac troponins are the most sensitive and specific biomarkers for NSTEMI-ACS. They rise within a few hours of symptom onset and typically remain elevated for several days (but may remain elevated for up to 2 weeks with a large infarction). A negative cardiac troponin obtained with more sensitive cardiac troponin assays on admission confers a >95% negative predictive value for MI compared with high-sensitivity assays that confer a negative predictive value  $\geq 99\%$  (41-43).

Patients with NSTEMI in their ECG don't have elevation of ST segment neither Q wave, but they have increased level of biomarkers known as cardiac markers. Non stable angina represents third expression spectrum of acute coronary syndrome and it is pathological substrate, similar to NSTEMI, because at unstable angina we do not have the presence of biomarkers (cardiac markers) in the blood (44, 32). Of all patients with acute coronary syndrome, 42% had STEMI, 51% have NSTEMI and 7% have unstable angina.

ACS is divided into "two branches" according to ECG; STEMI and NSTEMI together with AJS. NSTEMI is differentiated from AJS with biomarkers. Differential diagnosis of STEMI should be made with: angina pectoris, dissection aortic aneurysm, pericarditis, pneumothorax, pulmonary embolism etc.

### **1.2.6. Management of STEMI**

A "diagnostic test" can be understood as a laboratory or imaging test: however, the concepts related to "test" also apply to clinical information from other findings, such as physical examination and patient history. The sensitivity of a test is understood as the capacity of the test to detect individuals who present with a particular condition, or the proportion of individuals with a particular condition who have been tested positive for this condition (true positive). Highly sensitive tests can be used at the beginning of the diagnostic process, when a great number of possibilities are being considered, with the intention of excluding as many options as possible. The specificity of a test is defined as the capacity of the test to identify individuals who do not have a particular medical condition, or the proportion of individuals without the condition who have a negative test (true negative). A triage system that presents a good sensitivity can minimize the occurrence of under triage, the same way, systems with suitable specificity can avoid the occurrence of over triage. The assessment of patients with ACS suspected using the MTS, can occur through different flow charts, since the patient does not always have typical symptoms and concerns such as chest pain as the main complaint. For this reason, in addition to the flowchart "chest pain", other flowcharts, including "shortness of breath in adults", "unwell adult", "collapsed adult", and "palpitations", enable distinguishing chest pain and other urgent conditions from non-urgent conditions, and can assist the appraiser to establish the highest priority level to treat patients with these urgent conditions. According to the algorithm from the American Heart Association, every patient who presents symptoms of chest discomfort suggestive of ischemia must receive medical attention within 10 minutes. Therefore, in order to recognize patients in those conditions, the health care professional applying MTS must establish priority levels of "red" or "orange", thereby setting a safe waiting time for these patients. Although there are well-established criteria for the prioritization of patients with suspected ACS, several studies have reported the difficulties of evaluating patients with these conditions. Various factors can interfere with the outcome of this process, such as atypical presentation of symptoms, AMI classification, patient age, and professional skill. Primary studies have addressed the issue from different perspectives. Studies have been conducted to evaluate the ability of nurses using MTS to detect high-risk

patients with chest pain, the impact of MTS on short-term mortality in AMI, and the sensitivity and specificity of MTS for patients with ACS, and to assess whether the MTS was used effectively in patients admitted to the hospital with a diagnosis of acute coronary syndrome. These studies concluded that use of the MTS by nurses is a sensitive method for identifying high risk cardiac chest pain, but further studies are required to assess whether additional training can improve the sensitivity of MTS. The MTS safeguards patients with typical AMI presentation and ST elevation during myocardial infarction, and who are under 70 years of age. The MTS has a high sensitivity in prioritization (immediate/very urgent) of patients with ACS. Additionally, most patients admitted for ACS are initially triaged as "orange" or "yellow", an indication for prompt assessment in the emergency department. This has a positive effect on time to first medical assessment, but has no effect on time to hospital admission (45).

The Global Registry of Acute Coronary Events (GRACE) risk score, which is used as a predictor of the risk for death in ACS, is determined based on age, vital signs, creatinine and Killip class (46). However, when trying to determine the mortality in these patients, other laboratory data are not usually included in this score. Furthermore, with the exception of elevated creatinine kinase MB or troponin T, the Thrombolysis in Myocardial Infarction (TIMI) risk score, which is a risk score for patients with non-ST elevated ACS, does not include any other biomarkers used in the calculation of the risk (47).

The GRACE (46) score, which is a well-known and classical predictor of in-hospital mortality, involves checking several items related to a patient's baseline physical data that can be analyzed within the emergency department. However, only one laboratory value (serum creatinine level) is required for this classical risk score. Of note, during the enrollment period for the GRACE registry, the efficacy of aggressive lipid lowering therapy for ACS patients (48, 49) and the utility of highly sensitive cardiac biomarkers in improving the accuracy of the ACS diagnosis (50, 41) had yet to be definitively established and applied to ACS patients. Several studies comparing the classical risk score with the risk assessment based on the results of biomarkers have suggested that C-reactive protein (51) or troponin T (52) levels can

provide a better prognostic accuracy than the GRACE risk score. However, several verification studies that examined the GRACE risk score have reported finding similar accuracies despite differences in the study period, the countries involved and the risk assessments used (52-57).

In-hospital mortality of ACS in North America has decreased from 25-30% to 7-10% in the past 30 years. This decrease can be attributed to the introduction of CCUs (1960s), administration of beta blockers (1970s), introduction of fibrinolytic therapy (1980s) and percutaneous coronary intervention (PCI) (1990s), (5,58). The proportion of ACS with STEMI—when a blood clot completely blocks a coronary artery—is declining (59), possibly due to reductions in smoking, aging of the population (STEMI is more common in middle age, while NSTEMI occurs more in the elderly), and greater use of statin therapy. Similar trends have been seen for sudden cardiac arrest. NSTEMI—usually when a clot partially blocks a coronary artery—is now the dominant type of ACS, and outcomes after the acute phase are significantly worse than for STEMI.

There has been a consistent decline in mortality rates for hospitalized acute MI, thanks in part to better in-hospital management of patients with ACS. There has also been an increasing emphasis on prevention and awareness, as well as advances in diagnostics and treatment, all taking place alongside societal and socio-economic changes and population migration (60). As the evidence base in acute coronary syndromes (ACS) has expanded dramatically over decades, longitudinal data demonstrate improvements in risk factor modification, organization of healthcare systems, and disease management that have substantially attenuated the adverse prognosis of both ST-segment elevation myocardial infarction (STEMI) and non-ST segment elevation ACS (NSTEMI-ACS). Nevertheless, discrepancies remain between genders, and women with ACS often sustain worse outcomes than men (61).

Triage, or risk classification, is a clinical management tool used in emergency services to guide patient flow when the need for medical attention exceeds that available. The Manchester Triage Group was developed in 1994 in the United Kingdom. The aim was to establish a consensus among physicians and nurses in the emergency room by creating a triage pattern

focused on the development of the following: Thus, the Manchester Triage System (MTS) was created. The MTS simplifies the clinical management of each patient, and consequently, the whole service, by utilizing a system that defines the clinical priority for adults and children (62). Despite advances in the treatment of ACS and the dissemination of formal recommendations on approaches to managing NSTEMI ACS, pharmacologic and reperfusion therapy remain underused and often delayed. This results in an increase in adverse cardiac events for patients and rising health care costs for the public. The key to NSTEMI ACS management is rigorous adherence and application of evidence-based recommendations. The American Heart Association (AHA) and the American College of Cardiology (ACC) have released comprehensive clinical practice guidelines to manage NSTEMI ACS. These include a process of risk stratification of patients presenting with NSTEMI ACS or possible NSTEMI ACS. Risk stratification can be performed using a number of scoring models, including the Thrombolysis in Myocardial Infarction (TIMI), the Global Registry of Acute Coronary Events (GRACE), and the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) scoring models (63).

Patients with ACSs are a heterogeneous population with varying risks of death and recurrent cardiac events, in long-term as well as short-term follow-up. In these patients, early risk stratification plays a central role, as the benefit of newer and more aggressive and a costly treatment strategy seems to be proportional to the risk of adverse clinical events. The TIMI score was developed with the database from a large clinical trial of NSTEMI-ACS.[44] The Global Registry of Acute Coronary Events score was developed from the registry, with a population of patients across the entire spectrum of ACS.[47] Even though the prognostic impact of both scores have been confirmed after longer follow-up periods both these scores were initially developed for short-term assessment of risk and to define risk oriented therapies in emergency departments and chest pain units (64, 65).

For the treatment of patients with STEMI guidelines have been prepared by European Society of Cardiology – ESC, American College of Cardiology –ACC and American Heart Association – AHA. Their goal is to improve clinical practice and quality of care for patients

in Europe and the USA. The Guide is a book "law to doctors" how to deal with patients in every instance of this life-threatening condition. Guidelines derived from the so-called – Evidence Based Medicine – EBM, which is not experience or opinion of some experts, but large collection of studies of important clinical records, comparisons, analysis, meta-analysis, special clinical studies, and studies of epidemiological things etc.

Treatment of patients with AMI, and especially with STEMI can be organized in three phases (21).

### **1.2.6.1. The first medical contact with a STEMI patient**

Initial diagnosis

- Patient history in chest pain, typical or equivalent, lasting or resistant to therapy.
- Elevation of ST segment or block of the left branch (LBBB) in ECG.
- Increase in blood of biomarkers of myocardial necrosis (CK MB and Troponin).

Reperfusion therapy might be:

- Mechanical, primary PCI, which means swelling of the balloon under pressure and stent implantation to keep the coronary artery open, and
- Pharmacological, thrombolytic therapy (TT) which is intended the merge of thrombus that has clogged coronary artery.

Possibility of the patient with AMI and reperfusion TT will die is 7-8% in the first month, and 3-4% of patients who undergo reperfusion with primary PCI. Medicine based on evidence (Evidence Based Medicine) emphasizes two important things in the treatment of patients with STEMI; Reperfusion and function of time, the probability of survival will be greater the shorter the time of start of reperfusion therapy. Of course, there are other actions that should be undertaken by the doctor who fights AMI.

### **1.2.6.2. Early Care Hospital**

PCI primary should be performed in patients with STEMI, including AMI in the back wall of the left ventricle, or new LBBB, if done within 12 hours of onset of symptoms, especially if done at the right time, which means two hours after the first medical presentation, or within 90 minutes if a large mass of myocardium is at risk. Primary PCI must be performed in patients with expressed heart weakness or pulmonary oedema within 12 hours of onset symptom. Primary PCI must be performed in patients in shock and those with contraindication to thrombolytic therapy regardless of the time of onset of symptoms, or delay time. Rescue PCI is undertaken when thrombolytic therapy fails. Sometimes it happens that the patient is not sent directly to the hospital with possible PCI, then the family doctor or cardiologist should give therapy.

Evidence based medicine (EBM) shows that primary PCI is superior to thrombolysis. PCI provides greater opportunity for the patient with AMI to survive. At some conditions and some forms of AMI, such as cardiogenic shock or severe weakness of the heart, is the only chance to survive. Such patients are known as a "high risk" patient and these are with: Hypotension, congestive heart weakness, sinus tachycardia, age, female gender, diabetes mellitus, uninterrupted pain regardless of drugs, the presence of elevation of the ST segment, anemia, higher number of WBC leukocyte (leukocytosis) and chronic kidney disease. Patients with these findings should be transferred as soon as possible to the PCI center. Sometimes PCI center is too far away and primary PCI can not be done within two hours of first medical contact. Physicians should inform the patient and his family that primary PCI is the best treatment and most favored for AMI.

In this context, in Kosovo the most remote primary PCI is not away more than two hours' drive. In the US there is broad national register of AMI (National Registry of Myocardial Infarction 2 and 3, NRMI 2 AND 3) involving more than 300,000 patients with AMI and primary PCI. The technical success rate of stents in AMI is high with minor procedural complications, even if patients with high-risk are involved. Primary PCI results are excellent when conducted by the operator with experience in interventional center with large volume. In



an interventional center with a small volume mortality rate is the same as the TT (thrombolytic therapy). In the US only 20% of hospitals have heart catheterization laboratory, and very few are available for hospitals with primary PCI. Thus, most patients with AMI are transferred, but 87% of these are more than two hours late. The low rate of mortality after primary PCI connects with short time door to balloon, shorter than 90 minutes, which laboratories with 24/7 services are equipped.

## **Coronarography**

Coronarography is a diagnostic method. It is considered the gold standard for diagnosis of coronary disease. When there are, or where other diagnostic elements suggest advanced coronary disease, coronarography is indicated. Through arteries in the legs (rarely hand arteries) a tube is placed (catheter) that is placed at the entrance of the coronary arteries, through this catheter the contrast is injected into the coronary arteries, which enables visualization of the lumen of these arteries, it is obvious whether they are tight how much are tightened and where are the bottlenecks. On the basis of this outcome can decide what the patient should do further- thrombolytic drug therapy or mechanical revascularization with stent (Angioplasty).

Coronarography is an invasive method (with various means we enter into the human body), so there exists the possibility of complications. Complications are infrequent. Only 2% of coronarography have complications. World statistics show the possibility of death in 0.1% of coronarography. In principle (if no new clinical moments occur), the result of coronarography can serve about 6 months. After coronarography doctor may propose the continuation of the procedure (angioplasty). The decision for angioplasty is taken from the patient itself after getting the adequate information.

## **Percutaneous coronary intervention (PCI)**

PCI is an invasive procedure by which a metal stent is placed in the closed coronary artery by atherosclerotic plaques, in order to improve blood flow and prevent restenosis. The first percutaneous transluminal coronary angioplasty was performed in 1977 (Gruentzig, 1979).

Less than 50% of patients receiving thrombolytic therapy have good recovery flow through arteries that caused heart attack (infarct-related artery IRA). To these patients TIMI flow is at 3-rd grade (Thrombolysis in myocardial infarction). This leakage is crucial for reducing the mortality of AMI from 16% to 7%. But a third of these reopened arteries areas with a high degree of obstructive lesions, favorable to be enclosed (most often without symptoms). The reason is that fibrinolytic agents are effective in the destruction of the fibrin network in the occlusive thrombus, without having to remove the core rich in platelets. They have no effect on thrombin, which is the most powerful activator of platelets. Their lytic effect is blocked by inhibitors of platelet activator I I (PAI I- platelets -I inhibitor activator), which is the inhibitor of fibrinolysis. The accuracy of the identification of patients who fail thrombolysis is limited. Also, clinical markers reperfusion (removal of pain, partial elevation resolution of ST - segment and reperfusion arrhythmias have limited predictive value).

### **1.2.6.3. Preventive secondary period**

Evidence based medicine (EBM) recommends interventions that can improve prognosis after STEMI. Coronary artery disease is chronic and progressive. Basic disease and risk factors should be treated by the patient, the family and the family doctor or cardiologist. This treatment is called secondary prevention and it is initiated in hospital after PCI. This is a lifelong process and should be controlled by the family doctor. Secondary prevention improves health and prolongs the life of patient who has experienced myocardial infarction (AMI). The patient must take responsibility for their own health. The family should help the patient to change lifestyle and nutrition, as well as controlling diabetes mellitus and arterial tension.

### **1.3. The strategy of treating patients with angina and unstable NON-STEMI (66).**

The first step that must be done in ACS (Acute coronary syndrome) is to identify patients by risk profile.

- Exact treatment by EBM (Evidence Based Medicine).
- Patient to be send for invasive and PCI treatment study
- To be initiated the program of modification of risk factors, early in the hospital, and to be educated the patient and family.
- To be assigned monitoring for coronary artery disease (CAD) and the control of risk factors

## 1.4. Identifying patients at high risk for ACS.

High-risk patients should be considered for early invasive strategy. It should be risk stratification in three groups according to the **TIMI RISK SCORE** calculation:

- Age > 65 years
- Previous coronary stenosis > 50%
- Three or more risk factors for coronary artery disease (CAD); Hypertension, Hypercholesterolemia, active smoker, diabetes, family history of CAD
- Taking aspirin 7 days ago
- Depression of ST-segment
- Increase of biomarkers of heart
- Two or more episodes of angina in the last 24 hours (de novo angina).

Some of these findings are sufficient to align the patient in the group with "high risk": depression of ST segment, increase of heart biomarkers (troponin or CK-MB) with angina pectoris in peace. In the group with "high risk" are also more than 4 risk factors. The group of "average risk" has the result of 3-4 risk factors. The group of "low risk" has one or two risk factors mentioned above.

Characteristics that favor early invasive strategy in ACS:

- Repeated angina pectoris (recurrent) ischemia at rest or with small load, despite intensive anti-ischemic therapy.
- Increased levels of troponin
- New depression or depression of ST segment
- Angina / recurrent ischemia with symptoms of heart weakness S3 gallop, pulmonary edema, crackle deterioration, or worsen mitral regurgitation.
- High Risk found in stress test
- Systolic dysfunction of the left ventricle with EF <40%

- Hemodynamic instability
- Stable ventricular tachycardia
- PCI within 6 months
- CABG (coronary artery bypass - graft) Previous

So, these are the situations that should make the doctor to take the decision for early PCI strategy. All other patients who are not considered high-risk, the decision for early PCI should be based on technical feasibility, the experience of the operator and patient's preference. But, the surveillance is recommended, risk stratification and selective invasive strategy. Sometimes it is difficult for cardiologist to convince the referral physician or patient and his family that the best treatment is coronary angiography with possible PCI.

## 1.5. Delays in the treatment of AMI

The total delay in the treatment of AMI with thrombolytic therapy includes the patient, the EMS and the hospital delays (Figure 3). It has been shown that nearly half of the AMI patients suitable for thrombolytic therapy are waiting up to three to four hours before calling for help (67,68). Female and elderly (>65 years old) patients have been reported to wait longer before calling for help than others (69). Media campaigns have been shown to have only marginal impact on the help-seeking delay (70,71). Improvement of prehospital management of AMI is expected to cut the delay in the call-to-therapy time (72). Short prehospital EMS door-to-therapy time may save time for the patient, but the time benefit also comes from rapid transportation to the hospital.

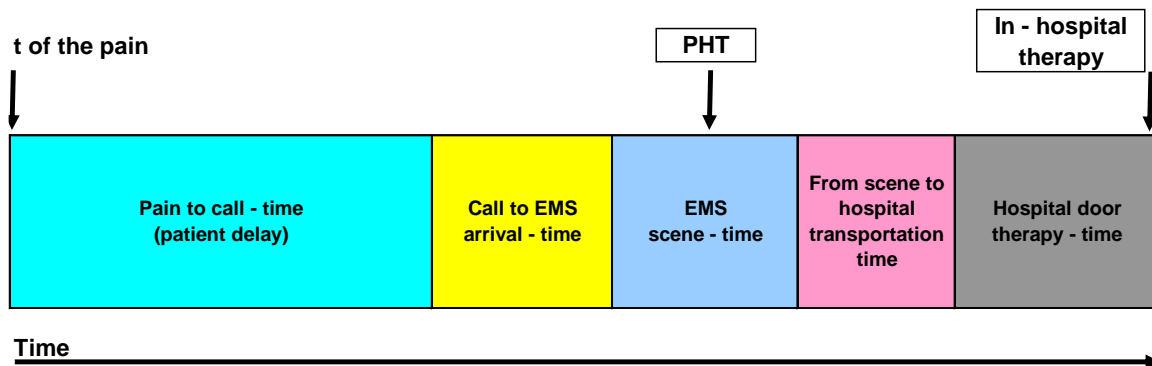


Figure 3. Delays in the treatment of AMI

A study performed at the Vancouver General Hospital (73) showed an average reduction in 67 minutes in the door-to-needle time in patients seen by cardiologists. Patient care performed by a specialized physician is fundamental to reduce the time used to determine the therapy and starts thrombolysis.

The performance of the Kosova emergency system for the acute treatment of ACS patients has not been thoroughly studied. Emergency medicine, a field relatively new to even the most developed societies (74), is in its infancy in Kosova. There has been little formal training, the EMS system lacks organization, equipment, and a reliable communication system, and centralized emergency centers, other than the center at Prishtina Hospital, are inadequate (75)

## **2. HYPOTHESIS**

Pre-hospital and hospital emergency care will improve prognosis of patients admitted to hospital with acute myocardial infarction.

### **3. AIMS AND PURPOSE OF THE RESEARCH**

The general aim of the study was to analyze the most recent trends in acute coronary syndrome care, to evaluate the impact of pre-hospital and hospital emergency care in the management and prognosis of patients admitted to the hospital with ACS.

#### **SPECIFIC AIMS:**

1. To analyze the outcome of ACS pts admitted to emergency department through pre-hospital emergency care.
2. To analyze the outcome of ACS patient admitted to emergency department who self-transported to the ED and those who were sent there by a health center or family physician, whatever the type of transport used (including ambulances operated by the fire services).
3. To illustrate the importance of pre-hospital emergency care on outcome of ACS pts.
4. To illustrate the importance of time in minutes between the onset of symptoms as reported by the patient and admission to the hospital, between the onset of symptoms and the first ECG and between entering the ED and the beginning of the therapy.



## **4. MATERIAL AND METHODOLOGY**

Observational prospective clinical study has included all cases of ACS patients (defined in accordance with the criteria of the 2000 consensus document “Myocardial Infarction redefined” of the ESC/ACC Joint Committee) admitted to emergency department of University Clinical Center of Kosova between January 1, 2011 and December 31, 2012. Inclusion criteria were clinical signs and symptoms of acute coronary syndrome, ECG changes and enzyme values in blood analysis. Location of myocardial infarction was determined according to ECG changes. ST elevation more than 1 mm and growing troponin were denoted as STEMI, ST denivelation more than 1 mm and T wave inversion with growing value of troponin were denoted as NSTEMI infarction.

The patients are divided into two groups, depending on whether pre-hospital emergency care was used; and in the three groups of different clinical presentations of ACS: unstable angina, NSTEMI and STEMI. For the purposes of the study, we defined the Pre-hospital emergency (PHE) group as those who were referred to the emergency department (ED) via PHE, and the control group as all other patients. In the control group, we include those who were self-transported to the ED and those who were sent there by a health center or family physician, whatever the type of transport used (including ambulances operated by the fire services).

Self-transport was defined as any mode of transportation that did not involve ambulance, including taking taxis or any public transportation, driving by themselves, driven by others and walking to the hospital.

The final ED diagnosis was defined as the discharge diagnosis for patients discharged home or the admitting diagnosis for patients admitted to an inpatient setting.

### **Electrocardiographic presentation**

The patients' electrocardiographic presentations are divided into two groups, depending on the alterations recorded on the first ECG performed at hospital arrival: with ST elevation or *de novo* LBBB, and without ST elevation or *de novo* LBBB. ST elevation is considered to exist when ECG showed the ST segment > 1 mm above the baseline in the limb leads or > 2 mm in the pre-cordial leads in two or more consecutive leads. *De novo* LBBB is defined as this pattern being previously unknown but found on the admission ECG. All other forms of initial ECG presentation, including ST depression, T wave abnormalities, normal ECG, or previously documented LBBB, were classified as non-ST elevation.

### **Symptoms-to-ED time**

This was taken as the time in minutes/hours between the onset of symptoms as reported by the patient and admission to hospital's emergency department.

### **Symptoms-to-ECG time**

This is the time in minutes/hours between the onset of symptoms and the first ECG in the hospital.

### **Door-to-needle/balloon time**

This is the time between entering the ED and beginning reperfusion therapy (injection of thrombolytic) in patients with ST elevation or *de novo* LBBB.

### **Ejection fraction**

In patients with ACS elevation/*de novo* LBBB on admission, ejection fraction was assessed by 2D transthoracic echocardiography in four-chamber view on the day of discharge.

### **Follow-up**

All the patients were followed in the hospital and for at least six months after discharge. During this time, mortality rates was monitored and readmissions for all causes were recorded directly or by telephone contact.

## **Statistical analysis**

Data are expressed as median and inter quartile ranges (IQR) for continuous variables with non-normal distribution and as percentages for categorical ones. Pearson's chi-square test or Fisher's exact test are used for categorical variables. Mann Whitney U test and Kruskal Wallis test are used for testing the difference between quantitative variables when distribution was not normal and Student t-test or ANOVA test when distribution is normal. The odds ratio (OR) and the corresponding 95% confidence intervals (CI) were calculated. Differences in survival were analyzed with the Kaplan-Meier method, data on surviving patients were censored at the date of hospital discharge, and data for non-surviving patients were censored at the date of hospital death, the results were compared with the use of log-rank test.  $P < 0.05$  was considered statistically significant. Data analysis was performed with the Statistical Package for Social Sciences 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

## 5. RESULTS

For the sake of easier elaboration, the research results are divided into three parts. In three parts the patients were analyzed according to clinical characteristics, risk factors and survival.

1. Socio demographic characteristics of patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period
2. Patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period by groups
3. Patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period by types of acute coronary syndrome

### **5.1. Socio demographic characteristics of patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period**

For the period January 1, 2011 and December 31, 2012, 1498 patients diagnosed as ACS were admitted to emergency department of the University Clinical Center of Kosovo. In 2011 were received much higher numbers compared to 2012 (61.7% versus 38.3%). With the distribution of cases by gender and years we did not earn significant difference ( $P = 0.636$ ). For the two genders we have had more cases in 2011 compared to 2012 (Table 1).

**Table 1. Patients with acute coronary syndrome by socio demographic characteristics**

	F	M	Total	OR (95% CI) P-value
Total	546	952	1498	
<b>Year N (%)</b>				
2011	332 (60.8)	592 (62.2)	924 (61.7)	P=0.619
2012	203 (39.2)	360 (37.8)	574 (38.3)	
<b>Age (years)</b>				
< 70	343 (62.8)	696 (73.1)	1039 (69.4)	0.746 (0.652 - 0.853)
≥ 70	203 (37.2)	256 (26.9)	459 (30.6)	P=0.000
Median (IQR)	65.5 (20-92)	63 (18-99)	64 (18-99)	P=0.0001
<b>Residence N (%)</b>				
Village	185 (33.9)	309 (32.5)	494 (33.0)	1.06 (0.853 - 1.333)
Town	361 (66.1)	643 (67.5)	1004 (67.0)	P=0.612
<b>Acute coronary syndrome N (%)</b>				
UA	123 (22.5)	215 (22.6)	338 (22.6)	0.820* (0.643 - 1.046) P=0.279
STEMI	169 (31.0)	330 (34.7)	499 (33.3)	
NSTEMI	254 (46.5)	407 (42.8)	661 (44.1)	
<b>Group N (%)</b>				
PHE group	73 (13.4)	97 (10.2)	170 (11.3)	1.36 (0.984 - 1.881)
Control group	473 (86.6)	855 (89.8)	1328 (88.7)	P=0.063
<b>Status on discharge N (%)</b>				
Survived	478 (87.5)	866 (91.0)	1344 (89.7)	1.242 (1.025 - 1.504)
Deceased	68 (12.5)	86 (9.0)	154 (10.3)	P=0.041
<b>LVEF N (%)</b>				
< 40%	195 (35.7)	339 (35.6)	534 (35.6)	1.005 (0.806 - 1.251)
≥ 40%	351 (64.3)	613 (64.4)	964 (64.4)	P=0.988

\* OR for STEMI/NSTEMI by gender

By age, 1039 or 69.4% were younger than 70 years. In a higher percentage, females were 70 and older compared to males (37.2% versus 26.9%), the difference being statistically significant ( $P < 0.001$ ). Patients with acute coronary syndrome were less likely to be women aged  $\geq 70$  years OR 0.746 (95% CI 0.652-0.853). The mean age of patients with acute coronary syndrome was 63.2 years (SD  $\pm$  11.2 years), ranging from 18 to 99 years. The mean age of

female patients with acute coronary syndrome was 64.6 years (SD  $\pm$  11.4 years), the range 20-92 years. The average age of male patients with acute coronary syndrome was 62.4 years (SD  $\pm$  11.0 years), ranging from 18 to 99 years. With T-test, we gained significant statistical difference in the average age of patients with acute coronary syndrome by gender (P <0.001). About two-thirds of patients with acute coronary syndrome (67.0%) were living in the city. Patients of both genders were more commonly in the city without any significant difference (OR 1.06, 95% 0.853-1.333), (P = 0.612). For the two-year analysis of 1498 patients in the Emergency Center of the University Clinical Center of Kosovo with acute coronary syndrome, 338 or 22.6% were diagnosed as unstable angina, 499 or 33.3% as STEMI and 661 or 44.1% as NSTEMI. The Odds of STEM is lower in females (OR 0.820, 95% CI 0.643-1.046) but without significant difference (P = 0.279). For the purposes of the study, we defined the Pre-hospital emergency (PHE) group as those who were referred to the emergency department (ED) via PHE, and the control group as all other patients. In the control group, we include those who were self-transported to the ED and those who were sent there by a health center or family physician, whatever the type of transport used (including ambulances operated by the fire services). In PHE group were 170 or 11.3% of patients. Women (13.4%) often used PHE services compared to males (10.2%) OR 1.36 (95% CI 0.984-1.881) but without significant difference (P = 0.063). In hospital mortality rate for ACS was 10.3% more for female 12.5% vs. male patients (9.0%) with significant difference (P=0.041). Female were in higher risk than man OR 1.242 (95% CI 1.025 - 1.504). By LVEF, 534 or 35.6% has LVEF <40%, similar by gender (Females 35.7% versus Males 35.6%), OR 1.005 (95% CI 0.806 - 1.251), (Table 1).

**Table 2. Patients with acute coronary syndrome by risk factors**

Total	F 546	M 952	Total 1498	OR (95% CI) P-value
<b>Hypertension N (%)</b>				
Yes	385 (70.5)	461 (48.4)	846 (56.5)	2.547 (2.037 - 3.185) P=0.000
No	161 (29.5)	491 (51.6)	652 (43.5)	
<b>SAP (mmHG)</b>				
Mean ± SD	139.7 ± 24.9	134.6 ± 26.2	136.4 ± 25.9	P=0.0001
<b>DAP (mmHG)</b>				
Mean ± SD	83.7 ± 14.1	82.6 ± 15.1	83.0 ± 14.7	P=0.205
<b>Heart rate</b>				
Mean ± SD	83.2 ± 20.7	81.2 ± 24.0	82.0 ± 22.9	P=0.205
<b>Diabet N (%)</b>				
Yes	218 (39.9)	240 (25.2)	458 (30.6)	1.972 (1.574 - 2.470) P=0.000
No	328 (60.1)	712 (74.8)	1040 (69.4)	
<b>Hiperlipidemia N (%)</b>				
Yes	285 (52.2)	516 (54.2)	697 (46.5)	0.922 (0.747 - 1.139) P=0.487
No	261 (47.8)	436 (45.8)	801 (53.5)	
<b>Obesity N (%)</b>				
Yes	83 (15.2)	70 (7.4)	153 (10.2)	2.259 (1.612 - 3.165) P=0.000
No	463 (84.8)	882 (92.6)	1345 (89.8)	
<b>Smoking N (%)</b>				
Current smoker	80 (14.7)	463 (48.6)	543 (36.2)	0.155 (0.121 - 0.199) P=0.000
No smoker	441 (80.8)	376 (39.5)	817 (54.5)	
Ex smoker	25 (4.6)	113 (11.9)	138 (9.2)	
<b>Alcohol N (%)</b>				
Yes	1 (0.2)	18 (1.9)	19 (1.3)	0.142* (0.021 - 0.963) P=0.003
No	219 (40.1)	837 (87.9)	1056 (70.5)	
No data	326 (59.7)	97 (10.2)	423 (28.2)	
<b>Comorbidity N (%)</b>				
Yes	310 (56.8)	346 (36.3)	656 (43.8)	2.301 (1.856 - 2.852) P=0.000
No	236 (43.2)	606 (63.7)	842 (56.2)	
<b>Cardiac event history N (%)</b>				
Yes	210 (38.5)	300 (31.5)	510 (34.0)	1.358 (1.090 - 1.693) P=0.007
No	336 (61.5)	652 (68.5)	988 (66.0)	
<b>Family history for cardiac event N (%)</b>				
Yes	187 (34.2)	331 (34.8)	518 (34.6)	0.977 (0.783 - 1.220) P=0.883
No	359 (65.8)	621 (65.2)	980 (65.4)	

Patients with ACS in 56.5% of cases had hypertension, females more often 70.5% vs. males 48.4% with significant difference ( $P=0.000$ ). Female were in higher risk for hypertension than man OR 2.547 (95% CI 2.037 - 3.185). The mean systolic arterial pressure of patients with acute coronary syndrome was 136.4 mmHg (SD  $\pm$  25.9 mmHg), ranging from 0 to 240 mmHg. The mean systolic arterial pressure of female patients with acute coronary syndrome was 139.7 mmHg (SD  $\pm$  24.9 mmHg), the range 70-230 mmHg. The average systolic arterial pressure of male patients with acute coronary syndrome was 134.6 mmHg (SD  $\pm$  26.2 mmHg), ranging from 0 to 240 mmHg. With Mann-Whitney test, we gained significant statistical difference in the average systolic arterial pressure of patients with acute coronary syndrome by gender ( $P=0.0001$ ).

The mean diastolic arterial pressure of patients with acute coronary syndrome was 83.0 mmHg (SD  $\pm$  14.7 mmHg), ranging from 0 to 160 mmHg. The mean diastolic arterial pressure of female patients with acute coronary syndrome was 83.7 mmHg (SD  $\pm$  14.1 mmHg), the range 30 - 160 mmHg. The average diastolic arterial pressure of male patients with acute coronary syndrome was 82.6 mmHg (SD  $\pm$  15.1 mmHg), ranging from 0 to 140 mmHg. With Mann-Whitney test, we didn't gained significant statistical difference in the average diastolic arterial pressure of patients with acute coronary syndrome by gender ( $P=0.205$ ).

The mean heart rate of patients with acute coronary syndrome was 82.0 (SD  $\pm$  22.9), ranging from 0 to 244. The mean heart rate of female patients with acute coronary syndrome was 83.2 (SD  $\pm$  20.7), the range 30-200 mmHg. The mean heart rate of male patients with acute coronary syndrome was 81.2 (SD  $\pm$  24.0), ranging from 0 to 244. With Mann-Whitney test, we gained significant statistical difference in the average heart rate of patients with acute coronary syndrome by gender ( $P=0.0018$ ).

Patients with ACS in 30.6% of cases had diabetes, females more often 39.9% vs. males 25.2% with significant difference ( $P=0.000$ ). Female were in higher risk for diabetes than man OR 1.972 (95% CI 1.574 - 2.470). Patients with ACS in 10.2% of cases were Obese, females more often 15.2% vs. males 7.4% with significant difference ( $P=0.000$ ). Female were in higher risk for obesity than man OR 2.259 (95% CI 1.612 – 3.165). Patients with ACS in 36.2% of cases



were Current smoker, males more often 48.6% vs. females 14.7% with significant difference (P=0.000). Female were in lower risk for smoking than man OR 0.155 (95% CI 0.121 – 0.199).

Male patients were more often alcohol users (1.9%) compared to female patients (0.2%) with significant difference (P=0.003). Generally speaking, the rate of reporting alcohol use is low.

Patients with ACS in 46.5% of cases had hyperlipidemia, females less often 52.2% vs. males 54.2% with no significant difference (P=0.487). Female were in lower risk for hyperlipidemia than man OR 0.922 (95% CI 0.747 - 1.139). Patients with ACS in 43.8% of cases had Comorbidity, females more often 56.8% vs. males 36.6% with significant difference (P=0.000). Female were in higher risk for comorbidity than man OR 2.301 (95% CI 1.856 - 2.852). Patients with ACS in 34.0% of cases had Cardiac event history, females more often 38.5% vs. males 31.5% with significant difference (P=0.007). Female were in higher risk for Cardiac event history than man OR 1.358 (95% CI 1.090 - 1.693). Patients with ACS in 34.6% of cases had Family history for cardiac event, with similar percent according to gender females 34.2% vs. males 34.8% with no significant difference (P=0.883, OR 0.977 (95% CI 0.783 - 1.220), (Table 2).

**Table 3. Patients with acute coronary syndrome by gender and duration of symptoms**

<b>Total</b>	<b>F 546</b>	<b>M 952</b>	<b>Total 1498</b>	<b>OR (95% CI) P-value</b>
<b>Duration of symptoms N (%)</b>				
< 6 hours	174 (31.9)	343 (36.0)	517 (34.5)	1.271* (1.005-1.607) P=0.051
6-12 hours	4 (0.7)	14 (1.5)	18 (1.2)	
> 12 hours	277 (50.7)	437 (45.9)	714 (47.7)	
Unknown	91 (16.7)	158 (16.6)	249 (16.6)	
<b>Onset of symptoms as reported by the patient and admission to the hospital (hours)</b>				
Median (IQR)	8 (1-16)	8 (1-14)	8 (1-16)	P=0.278
<b>Time between the onset of symptoms as reported by the patient and first ECG (hours)</b>				
Median (IQR)	8.5 (1-17)	8.5 (1-17)	8.5 (1-17)	P=0.798
<b>Time between entering the ED and the beginning of the therapy (minutes)</b>				
Median (IQR)	50 (15-60)	40 (15-65)	40 (15-65)	P=0.923

\* OR for 12 hours and less/ >12 hours by gender

For the two-year analysis of 1498 patients in the Emergency Center of the University Clinical Center of Kosovo with acute coronary syndrome, at 517 or 34.5% duration of symptoms from the onset of symptoms as reported by the patient and admission to the hospital were < 6 hours, 18 or 1.2% from 6 to 12 hours, 714 or 47.7% more than 12 hours and 249 or 16.6% was unknown. The Odds of > 12 hours is higher in females (OR 1.271, 95% CI 1.005- 1.607) but without significant difference (P = 0.051), (Table 3).

## **5. 2. Patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period by groups**

In 2012, twice more patients with ACS requested PHE assistance compared to 2011, this difference was with statistical significance ( $P=0.000$ ). According to the gender females have frequently sought PHE service assistance compared to men OR 1.312 (95% CI 0.986 to 1.745) but without significant difference ( $P=0.063$ ). Patients older than 70 years of age have more often requested PHE assistance than those <70 years OR 0.625 (95% CI 0.450 - 0.869) with significant difference ( $P=0.006$ ). Patients who used PHE services to be admitted to the Emergency Center were older than the control group. The average age of patients in the PHE group was 66.2 years ( $SD \pm 11.2$  years) ranging from 37 to 92 years. The average age of patients in the control group was 62.8 years ( $SD \pm 11.1$  years) ranging from 18 to 99 years. This difference with significant statistical significance ( $P = 0.0001$ ).

Frequently, PHE assistance has required STEMI patients (47.1%) or 1.780 (95% CI 1.343 - 2.358), while with less AI (10.6%) OR 0.406 (95% CI 0.253 - 0.652), with significant difference by groups.

Rarely PHE services have been used by patients living in the village (19.4% vs. 80.6%) and compared to the control group (34.7% vs. 65.3%) this difference was significant statistical significance ( $P < 0.0001$ ), OR 0.489 (95% CI 0.340 - 0.705).

The mortality rate was higher in PHE patients 28.8% compared to that of the control group 7.9% OR 3.534 (95% CI 2.652 - 4.709), with significant statistical difference ( $P = 0.000$ ).

This high mortality rate of patients who have been using pre-emergency services can be explained by the fact that they were more often STEMI patients, older than patients of control group, 40.0% who were 70 years or older.

Patients of PHE group on 45.9% of cases had LVEF < 40% compared to Control group 34.3% with significant difference ( $P=0.004$ ), PHE group were in higher risk for LVEF < 40% than Control group OR 1.621 (95% CI 1.175 – 2.238), (Table 4).

**Table 4. Patients with acute coronary syndrome by groups and year of treatment**

	<b>PHE group</b>	<b>Control group</b>	<b>OR (95% CI)</b>
<b>Total</b>	<b>170</b>	<b>1328</b>	<b>P-value</b>
<b>Year N (%)</b>			
<b>2011</b>	48 (28.2)	876 (66.0)	0.203 (0.142 - 0.288)
<b>2012</b>	122 (71.8)	452 (34.0)	P=0.000
<b>Gender N (%)</b>			
<b>F</b>	73 (42.9)	473 (35.6)	1.312 (0.986 - 1.745)
<b>M</b>	97 (57.1)	855 (64.4)	P=0.063
<b>Age (years)</b>			
< 70	102 (60.0)	937 (70.6)	0.662 (0.497 - 0.883)
≥ 70	68 (40.0)	391 (29.4)	P=0.006
Mean ± SD	66.2 ± 11.2	62.8 ± 11.1	P=0.0001
Runk	37 - 92	18 - 99	
<b>Residence N (%)</b>			
Village	33 (19.4)	461 (34.7)	0.489 (0.340 - 0.705)
Town	137 (80.6)	867 (65.3)	P=0.000
<b>Acute coronary syndrome N (%)</b>			
UA	18 (10.6)	320 (24.1)	0.406 (0.253 - 0.652)
STEMI	80 (47.1)	419 (31.6)	1.780 (1.343 - 2.358)
NSTEMI	72 (42.4)	589 (44.4)	0.930 (0.698 - 1.239)
			P=0.681
<b>Status on discharge N (%)</b>			
Survived	121 (71.2)	1223 (92.1)	4.717 (3.202 - 6.947)
Deceased	49 (28.8)	105 (7.9)	P=0.000
<b>LVEF N (%)</b>			
< 40%	78 (45.9)	456 (34.3)	1.621 (1.175-2.238)
≥ 40%	92 (54.1)	872 (65.7)	P=0.004

**Table 5. Patients with acute coronary syndrome by groups and hypertension**

	<b>PHE group</b>	<b>Control group</b>	<b>OR (95% CI)</b>
<b>Total</b>	<b>170</b>	<b>1328</b>	<b>P-value</b>
<b>Other diseases N (%)</b>			
Hypertension	89 (52.4)	735 (55.3)	0.898 (0.677 - 1.193) P=0.462
Diabet	72 (42.4)	386 (29.1)	1.668 (1.256 - 2.216) P=0.000
Obesity	11 (6.5)	142 (10.7)	0.608 (0.337 - 1.095) P=0.105
Hiperlipidemia	101 (59.4)	700 (52.7)	1.313 (0.949 - 1.817) P=0.117
<b>SAP (mmHG)</b>			
Mean ± SD	132.0 ± 29.1	136.9 ± 25.4	P=0.018
<b>DAP (mmHG)</b>			
Mean ± SD	79.1 ± 16.8	83.5 ± 14.4	P=0.690
<b>Heart rate</b>			
Mean ± SD	88.3 ± 20.5	81.2 ± 21.6	P=0.008
<b>Smoking N (%)</b>			
Current smoker	56 (32.9)	487 (36.7)	0.970* (0.703 - 1.339) P=0.000
Ex smoker	17 (10.0)	93 (7.0)	
No smoker	97 (57.1)	748 (56.3)	
<b>Alcool N (%)</b>			
Yes	2 (1.2)	17 (1.3)	0.926 (0.247 - 3.465) P=0.999
<b>Comorbidity N (%)</b>			
Yes	95 (55.9)	561 (42.2)	1.732 (1.255 - 2.389) P=0.045
<b>Cardiac event history N (%)</b>			
Yes	70 (41.2)	440 (33.1)	1.413 (1.020 - 1.958) P=0.045
<b>Family history for cardiac event N (%)</b>			
Yes	77 (45.3)	441 (33.2)	1.665 (1.206 - 2.300) P=0.002

\* OR for current+ex-smoker/ No smoker by groups

According to risk factors for ACS, hypertension was similar in structure to patients of both groups (PHE group 52.4% vs. Contr. Gr. 55.3%) without significant difference ( $p = 0.511$ ). The mean systolic arterial pressure of PHE group patients with acute coronary syndrome was 132.0 mmHg (SD  $\pm$  29.1 mmHg), the range 70-240 mmHg. The average systolic arterial pressure of Control group patients with acute coronary syndrome was 136.9 mmHg (SD  $\pm$  25.4 mmHg), ranging from 0 to 230 mmHg. With Mann-Whitney test, we gained significant statistical difference in the average systolic arterial pressure of patients with acute coronary syndrome by groups ( $P = 0.018$ ).

The mean diastolic arterial pressure of PHE group patients with acute coronary syndrome was 79.1 mmHg (SD  $\pm$  16.8 mmHg), the range 10-120 mmHg. The average diastolic arterial pressure of Control group patients with acute coronary syndrome was 83.5 mmHg (SD  $\pm$  14.4 mmHg), ranging from 0 to 160 mmHg. With Mann-Whitney test, we gained significant statistical difference in the average diastolic arterial pressure of patients with acute coronary syndrome by groups ( $P = 0.028$ ).

The mean heart rate of PHE group patients with acute coronary syndrome was 88.3 beats (SD  $\pm$  30.9), the range 30- 244. The average heart rate of Control group patients with acute coronary syndrome was 81.2 (SD  $\pm$  21.6), ranging from 0 to 231. With Mann-Whitney test, we gained significant statistical difference in the average heart rate of patients with acute coronary syndrome by groups ( $P = 0.008$ ).

As seen in Table 5, out of the 170 patients of PHE group with diabetes were 42.4% compared to 29.1% of patients with diabetes from the control group, with significant statistical significance ( $P = 0.001$ ). The Odds of using PHE services was greater in patients with diabetes OR 1.668 (95% CI 1.256-2.216). Obese patients were often patients of control group (PHE group 6.5% vs. Contr. Gr. 10.7%), but without significant difference ( $p = 0.115$ ). Patients of PHE groups were often Ex smoke compared to the control group (10.0% vs. 7.0%), with significant difference ( $P = 0.000$ ). Patients of PHE group on 1.2% of cases were alcohol users compared to control group 1.3% with no significant difference ( $P = 0.706$ ), OR 95%CI 0.926 (0.247-3.465). Patients of PHE group on 59.4% of cases had hiperlipidemia compared to

Control group 52.7% with no significant difference (P=0.706), PHE group were in higher risk for hyperlipidemia than Control group OR 1.313 (95% CI 0.949 - 1.817).

Patients of PHE group on 55.9% of cases had comorbidity compared to Control group 42.2% with significant difference (P=0.001), PHE group were in higher risk for comorbidity than Control group OR 1.732 (95% CI 1.255 - 2.389).

Patients of PHE group on 41.2% of cases had Cardiac event history compared to Control group 33.1% with significant difference (P=0.045), PHE group were in higher risk for Cardiac event history than Control group OR 1.413 (95% CI 1.020 - 1.958). Patients of PHE group on 45.3% of cases had Family history for cardiac event compared to Control group 33.2% with significant difference (P=0.002), PHE group were in higher risk for Family history for cardiac event than Control group OR 1.665 (95% CI 1.206 – 2.300), (Table 5).

**Table 6. Patients with acute coronary syndrome by groups and duration of symptoms**

	<b>PHE group</b>	<b>Control group</b>	<b>OR (95% CI)</b>
<b>Total</b>	<b>170</b>	<b>1328</b>	<b>P-value</b>
<b>Duration of symptoms N (%)</b>			
< 6 hours	81 (47.6)	436 (32.8)	1.630* (1.171-2.269) P=0.004
6-12 hours	6 (3.5)	12 (0.9)	
> 12 hours	76 (44.7)	638 (48.0)	
Unknown	7 (4.1)	242 (18.2)	
Onset of symptoms as reported by the patient and admission to the hospital (hours)			
Median (IQR)	7 (1-13)	11 (1-16)	P=0.008
Time between the onset of symptoms as reported by the patient and first ECG (hours)			
Median (IQR)	8 (1-14)	12 (1-17)	P=0.008

\* OR for 12 hours and less/ >12 hours by groups

Patients of PHE group on 47.6% of cases duration of symptoms from the onset of symptoms as reported by the patient and admission to the hospital were < 6 hours compared to Control group 32.8% with significant difference (P=0.004), PHE group were in higher risk for from the onset of symptoms as reported by the patient and admission to the hospital were < 6 hours than Control group OR 1.630 (95% CI 1.171 – 2.269).

Of the 499 patients with ST elevation/de novo LBBB, 331 underwent thrombolysis and the other 168 primary angioplasty, but only 65 has done angioplasty in UCCK other go to private institutions. Door-to-needle (67 vs. 135 min) and door-to-balloon (89 vs. 142 min) times were shorter in the PHE group, but not significantly (p = 0.08), (Table 6).



**Table 7. Univariate Cox regression analysis for the predictors of mortality**

	<b>HR</b>	<b>95% CI</b>	<b>P-value</b>
Age $\geq$ 70 yr	2.81	1.99 - 3.97	< 0.001
Female sex	1.39	1.00 - 1.93	0.041
UA	1.00	-	-
STEMI	8.51	5.88 - 12.31	< 0.001
NSTEMI	2.18	1.19 - 3.98	< 0.001
PHE group	3.92	2.35 - 6.54	< 0.001
Urban residence	1.02	0.73 - 1.43	0.928
Hypertension	0.36	0.26 - 0.49	< 0.001
Diabetes	2.39	1.69 - 3.37	< 0.001
Hiperlipidemia	1.68	1.22 - 2.31	0.032
Obesity	0.06	0.03 - 0.09	0.001
No smoker	1.00	-	-
Current smoker	0.76	0.53 - 1.08	0.130
Ex smoker	1.86	1.09 - 3.17	0.006
LVEF < 40%	15.95	9.11 - 27.91	< 0.001

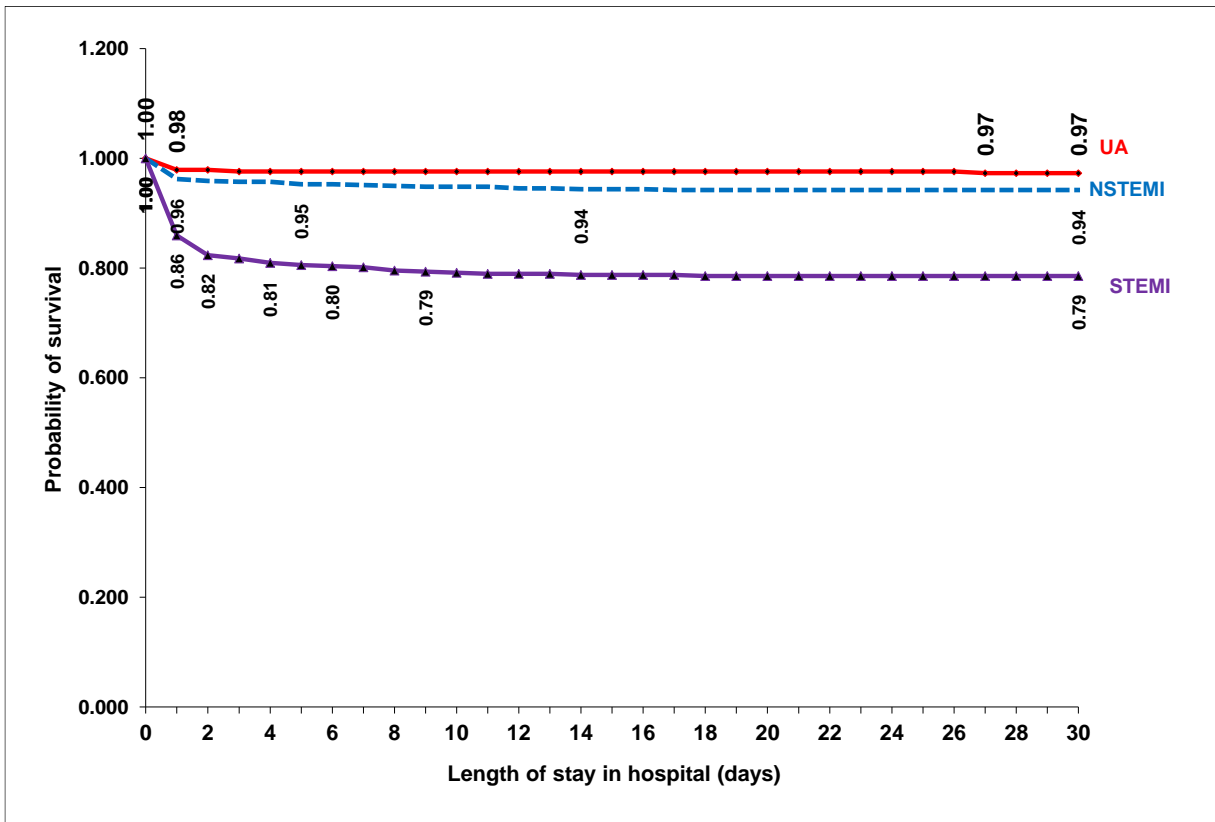
*Abbreviations: STEMI: ST-segment elevation myocardial infarction, NSTEMI: non-ST- elevation myocardial infarction; LVEF: left ventricular ejection fraction; PHE: pre-hospital emergency treatment*

Age, female sex, STEMI, NSTEMI, PHE treatment, diabetes, hiperlipidemia, smoking and low LVEF were significant risk factors for in-hospital mortality in patients admitted for ACS, in univariate Cox regression analysis (Table 7). However, only age, the presence of STEMI, the lack PHE treatment, diabetes mellitus, low LVEF and smoking remain independent predictors of mortality in patients admitted for ACS, in multivariate Cox regression analysis (Table 8).

**Table 8. Multivariate Cox regression analysis of in-hospital mortality**

	<b>HR</b>	<b>95% CI</b>	<b>P-value</b>
Age $\geq$ 70 yr	2.37	1.67 - 3.52	< 0.001
Female sex	1.01	0.87 - 1.23	0.067
STEMI	6.17	3.22 - 15.31	< 0.001
PHE group	3.92	2.35 - 6.54	< 0.001
Diabet	3.01	1.98 - 3.78	< 0.001
Hiperlipidemia	1.2	0.98 - 1.89	0.054
Ex smoker	2.34	1.57 - 3.85	0.01
LVEF < 40%	17.63	11.2 - 30.54	< 0.001

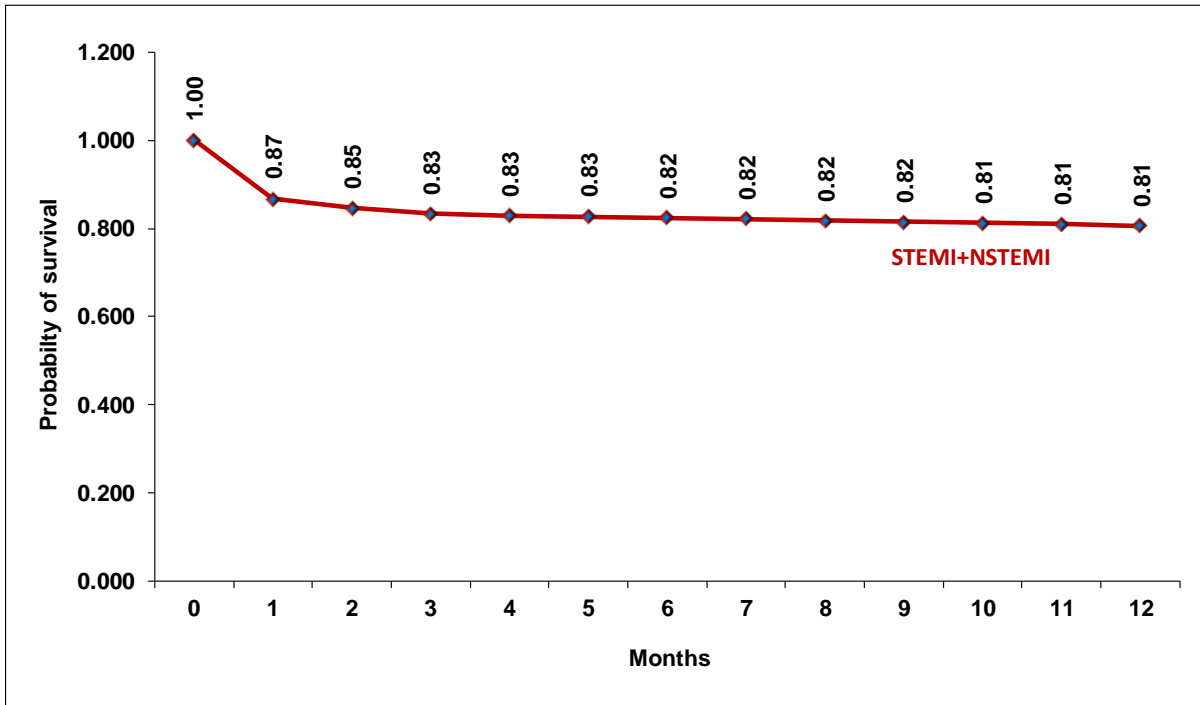
*Abbreviations: STEMI: ST-elevation myocardial infarction; LVEF: left ventricular ejection fraction; PHE: pre-hospital emergency treatment*



**Figure 1. The Kaplan Meier survival curve of patient with STEMI, NSTEMI**

The Kaplan-Meier survival curve revealed that STEMI patients had a higher in-hospital mortality rate and a lower survival rate when compared to patients admitted for ACS and having NSTEMI or UA (Figure 1).

Using the Log rank test, we discovered a significant difference on in- hospital mortality between STEMI and NSTEMI patients ( $P < 0.001$ ), STEMI and UA patients ( $P < 0.001$ ) and NSTEMI and UA patients ( $P < 0.001$ ).



**Figure 2. The Kaplan Meier survival curve of patient with STEMI, NSTEMI after 1 year follow up**

After one year, when the patients were contacted by phone, the probability of survival was 0.81, and the mortality rate from admission to 12 months was 19.4%. (Figure 2)

Patients over the age of 70 (18.3%), female patients (12.5%), STEMI patients (21.4%), PHE treated patients (28.8%), patients who did not have arterial hypertension prior to hospitalization (15.4%), diabetics (17.0%), non-obese patients (10.8%), and ex-smokers (18.8%) had a higher in-hospital mortality rate. The mortality rate did not differ between patients living in cities and those living in rural areas (Table 9).

**Table 9. Risk factor for in hospital mortality**

	<b>Deceased on discharge</b>	<b>X<sup>2</sup>-test</b>
<b>Total, n=1498</b>	154 (10.3)	
<b>Gender</b>		
F, n=546	68 (12.5)	0.041
M, 952	86 (9.0)	
<b>Clinical presentation</b>		
UA, n=338	9 (2.7)	0.000
STEMI, n=499	107 (21.4)	
NSTEMI, n=661	38 (5.7)	
<b>Group</b>		
PHE group, n=170	49 (28.8)	0.000
Control group, n=1328	105 (7.9)	
<b>Age group</b>		
<70, n=1039	70 (6.7)	0.000
≥70, n=459	84 (18.3)	
<b>Residence</b>		
Rural, n=494	50 (10.1)	0.928
Urban, n=1004	104 (10.4)	
<b>Hypertension</b>		
Yes, n=846	50 (6.1)	0.000
No, n=652	104 (15.4)	
<b>Diabet</b>		
Yes, n=458	78 (17.0)	0.000
No, n=1040	76 (7.3)	
<b>Obesity</b>		
Yes, n=153	1 (1.2)	0.001
No, n=1345	153 (10.8)	
<b>Smoking</b>		
No smoker, n=817	85 (10.4)	0.000
Current smoker, n=543	43 (7.9)	
Ex smoker, n=138	26 (18.8)	
<b>Duration of symptoms</b>		
< 6 hours, n=517	68 (44.2)	0.000
6-12 hours, n=18	10 (6.5)	
> 12 hours, n=714	73 (47.4)	
Unknown, n=249	3 (1.9)	

### **5. 3. Patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period by types of acute coronary syndrome**

In 2011 we had the largest number of admissions in general, especially patients with Unstable angina and NSTEMI. In 2012, we had less patients with ACS, especially we had a decrease in the number of patients with UA and NSTEMI, while the number of patients with STEMI was similar (240 vs 259), the difference with significant statistical significance ( $P = 0.000$ ).

According to the clinical presentation of ACS we had a similar structure at both genders without significant difference ( $P = 0.279$ ). In the two genders the most frequent cases were NSTEMI cases (F 46.5% versus M 42.8%), then STEMI (F 31.0% versus M 34.7%) and UA (F 22.5% vs. M 22.6%).

By clinical presentation of ACS and age group we have earned significant difference ( $P=0.000$ ). At age group  $\geq 70$  years 37.0% were patients with STEMI compared to those aged  $<70$  years 31.7% (Table 10). However, between the average age of the patients by clinical presentation of ACS we didn't earn significant difference. The mean age of patients with unstable angina was 62.7 years ( $SD \pm 10.7$  years), ranging from 33 to 88 years. The mean age of STEMI patients was 63.6 years ( $SD \pm 11.7$  years), the range 18-99 years. The mean age of NSTEMI patients was 63.0 years ( $SD \pm 11.1$  years), the range 20-92 years. With Kruskal – Wallis test, we didn't distinguish significant statistical difference in the average age of patients with acute coronary syndrome by clinical presentation of ACS ( $P=0.406$ ).

The number of patients by residence and clinical presentation of ACS is presented in table 10. The STEMI patients were more often from town (36.4%) compared to village (27.1%), with significant difference ( $P=0.000$ ).

The STEMI patients were more often from PHE group (16.0%) compared to NSTEMI (10.9%) and UA patients (5.3%) with significant difference ( $P=0.000$ ). The survival of ACS patients varied significantly according to the clinical presentation. STEMI patients had a lower

rate (78.6%) than UA patients (97.3%) and NSTEMI patients (94.3%), with a significant difference (P=0.000) (Table 10).

**Table 10. Patients with acute coronary syndrome by clinical presentation of ACS and year of treatment**

	<b>UA</b>	<b>STEMI</b>	<b>NSTEMI</b>	
<b>Total</b>	<b>338</b>	<b>499</b>	<b>661</b>	<b>P-value</b>
<b>Year N (%)</b>				
2011	250 (74.0)	240 (48.1)	434 (65.7)	P=0.000
2012	88 (26.0)	259 (51.9)	227 (34.3)	
<b>Gender N (%)</b>				
F	123 (36.4)	169 (33.9)	254 (38.4)	P=0.279
M	215 (63.6)	330 (66.1)	407 (61.6)	
<b>Age (years)</b>				
< 70	238 (22.9)	329 (31.7)	472 (45.4)	P=0.000
≥ 70	100 (21.8)	170 (37.0)	189 (41.2)	
Mean ± SD	62.7 ± 10.7	63.6 ± 11.7	63.0 ± 11.1	
Runk	33 - 88	18 - 99	20 - 92	
<b>Residence N (%)</b>				
Village	133 (39.3)	134 (26.9)	227 (34.3)	P=0.000
Town	205 (60.7)	365 (73.1)	434 (65.7)	
<b>Group N (%)</b>				
PHE group	18 (5.3)	80 (16.0)	72 (10.9)	P=0.000
Control group	320 (94.7)	419 (84.0)	589 (89.1)	
<b>Status on discharge N (%)</b>				
Survived	329 (97.3)	392 (78.6)	623 (94.3)	P=0.000
Deceased	9 (2.7)	107 (21.4)	38 (5.7)	
<b>LVEF N (%)</b>				
< 40%	5 (1.5)	255 (51.1)	274 (41.5)	P=0.000
≥ 40%	333 (98.5)	244 (48.9)	387 (58.5)	

**Table 11. Patients with acute coronary syndrome by clinical presentation of ACS and hypertension**

	<b>Total</b>	<b>UA 338</b>	<b>STEMI 499</b>	<b>NSTEMI 661</b>	<b>P-value</b>
<b>Other diseases N (%)</b>					
Hypertension	207 (61.2)	242 (48.5)	397 (60.1)		P=0.000
Diabetes	82 (24.3)	176 (35.3)	200 (30.3)		P=0.003
Obesity	40 (11.8)	29 (5.8)	84 (12.6)		P=0.000
Hiperlipidemia	161 (47.6)	319 (63.9)	321 (48.6)		P=0.000
<b>SAP (mmHG)</b>					
Mean ± SD	138.6 ± 25.2	134.5 ± 29.0	136.7 ± 23.6		P=0.021
<b>DAP (mmHG)</b>					
Mean ± SD	83.0 ± 13.1	82.7 ± 17.6	83.2 ± 13.2		P=0.690
<b>Heart rate</b>					
Mean ± SD	80.9 ± 20.5	83.8 ± 22.6	81.2 ± 24.1		P=0.002
<b>Smoking N (%)</b>					
Current smoker	106 (31.4)	222 (44.5)	199 (30.1)		
Ex smoker	28 (8.3)	28 (5.6)	58 (8.8)		P=0.000
No smoker	204 (60.4)	249 (49.9)	404 (61.1)		
<b>Alcohol N (%)</b>					
Yes	4 (1.2)	8 (1.6)	7 (1.1)		
No	212 (62.7)	425 (85.2)	419 (63.4)		P=0.706
No data	122 (36.1)	66 (13.2)	235 (35.6)		
<b>Comorbidity N (%)</b>					
Yes	148 (43.8)	179 (35.9)	329 (49.8)		P=0.000
No	190 (56.2)	320 (64.1)	332 (50.2)		
<b>Cardiac event history N (%)</b>					
Yes	133 (39.3)	98 (19.6)	279 (42.2)		P=0.000
No	205 (60.7)	401 (80.4)	382 (57.8)		
<b>Family history for cardiac event N (%)</b>					
Yes	120 (35.5)	286 (57.3)	112 (16.9)		P=0.000
No	218 (64.5)	213 (42.7)	549 (83.1)		



Patients with UA (61.2%) and NSTEMI (60.1%) were more often hypertensive compared to STEMI patients (48.5%) with significant difference ( $P=0.000$ ), (Table 11). STEMI patients had more often diabetes (35.3%) compared to NSTEMI patients (30.3%) and UA patients (24.3%) with significant difference ( $P=0.003$ ). Patients with UA (11.8%) and NSTEMI (12.7%) were more often obese compared to STEMI patients (5.8%) with significant difference ( $P=0.000$ ). Patients with STEMI in 63.9% of cases had hyperlipidemia, NSTEMI patients in 48.6% and rarely UA patients with 47.6% of cases had hyperlipidemia with significant difference ( $P=0.000$ ).

The mean systolic arterial pressure of patients with unstable angina was 138.6 mmHg ( $SD \pm 25.2$  mmHg), ranging from 0 to 210 mmHg. The mean systolic arterial pressure of STEMI patients was 134.5 mmHg ( $SD \pm 29.0$  mmHg), the range 0 - 240 mmHg. The mean systolic arterial pressure of NSTEMI patients was 136.7 mmHg ( $SD \pm 23.6$  mmHg), the range 25 - 230 mmHg. Using Kruskal – Wallis test, we gained significant statistical difference in the average systolic arterial pressure of patients with acute coronary syndrome by clinical presentation of ACS ( $P=0.0215$ ).

The mean diastolic arterial pressure of patients with unstable angina was 83.0 mmHg ( $SD \pm 13.1$  mmHg), ranging from 0 to 130 mmHg. The mean diastolic arterial pressure of STEMI patients was 82.7 mmHg ( $SD \pm 17.6$  mmHg), the range 0 - 150 mmHg. The mean diastolic arterial pressure of NSTEMI patients was 83.2 mmHg ( $SD \pm 13.2$  mmHg), the range 30-160 mmHg. Using Kruskal– Wallis test, we didn't distinguish significant statistical difference in the average diastolic arterial pressure of patients with acute coronary syndrome by clinical presentation of ACS ( $P=0.690$ ). The mean heart rate of patients with unstable angina was 80.9 beats ( $SD \pm 20.5$  beats), ranging from 0 to 219. The mean heart rate of STEMI patients was 83.8 ( $SD \pm 22.6$ ), the range 1 - 230 beats. The mean heart rate of NSTEMI patients was 81.2 ( $SD \pm 24.1$ ), the range 30-244. Using Kruskal – Wallis test, we gained significant statistical difference in the average heart rate of patients with acute coronary syndrome by clinical presentation of ACS ( $P=0.0024$ ).

At 1.5% of patients with unstable angina, at 51.1% of STEMI patients and at 41.5% of NSTEMI patients the LVEF were < 40%. With X<sup>2</sup>- test, we gained significant statistical difference on percent of LVEF by clinical presentation of ACS (P=0.0000).

STEMI patients were more often current smoker (44.5%) compared to UA patients (31.4%) and NSTEMI patients (30.1%) with significant difference (P=0.000). STEMI patients were more often alcohol users (1.6%) compared to UA patients (1.2%) and NSTEMI patients (1.1%) without significant difference (P=0.706). Generally speaking, the rate of reporting alcohol use is low.

Patients with NSTEMI in 49.8% of cases had Comorbidity, patients with UA more often 43.8% vs. STEMI patients 35.9% with significant difference (P=0.000). Patients with UA in 39.3% of cases had history for cardiac event, STEMI patients in 19.6% and NSTEMI patients on 42.2% of cases had history for cardiac event with significant difference (P=0.000).

Patients with UA in 35.5% of cases had Family history for cardiac event, STEMI patients in 57.3% and NSTEMI patients on 16.9% of cases had Family history for cardiac event with significant difference (P=0.000), (Table 11).

**Table 12. Patients with acute coronary syndrome by clinical presentation and duration of symptoms**

	UA	STEMI	NSTEMI	
Total	338	499	661	P-value
<b>Duration of symptoms N (%)</b>				
< 6 hours	88 (26.0)	246 (49.3)	183 (27.7)	P=0.000*
6-12 hours	-	10 (2.0)	8 (1.2)	
> 12 hours	154 (45.6)	223 (44.7)	337 (51.0)	
Unknown	96 (28.4)	20 (4.0)	133 (20.1)	
<b>Onset of symptoms as reported by the patient and admission to the hospital (hours)</b>				
Median (IQR)	8 (1-16)	7 (1-14)	8 (1-16)	P=0.002
<b>Time between the onset of symptoms as reported by the patient and first ECG (hours)</b>				
Median (IQR)	8.5 (1-17)	7 (1-17)	8 (1-17)	P=0.002
<b>Time between entering the ED and the beginning of the therapy (minutes)</b>				
Median (IQR)	50 (15-65)	30 (10-45)	40 (15-65)	P=0.0002

\* for 12 hours and less/ >12 hours by clinical presentation

The duration of symptoms from the onset of symptoms as reported by the patient to admission to the hospital was more than 12 hours in 61.2% of patients with unstable angina, 46.1% of STEMI patients, and 60.8% of NSTEMI patients. With X<sup>2</sup>- test, found a statistically significant difference in the duration of symptoms from the onset of symptoms as reported by the patient to admission to the hospital due to clinical presentation of ACS (P=0.0000), (Table 12).

## **6. DISCUSSION**

### **6.1. Socio demographic characteristics of patients with acute coronary syndrome**

The Republic of Kosovo has an area of 10 905.25 km<sup>2</sup>, located on the south-eastern Europe, bordering Albania in south-west, Montenegro in northwest, Serbia to the north-east and Macedonia to south. Currently there are 38 municipalities with 1,469 settlements organized by the laws of the country. According to the KAS estimates, the resident population in Kosovo is about 1.78 million people. 24% of the population is under 14 years old and 9% are over 65. Life expectancy at birth in 2011 was 76.7 years, 74.1 years for males and 79.4 for females (76).

The performance of the Kosovo emergency system in terms of acute care for ACS patients has not been thoroughly studied. Even in the most developed societies, emergency medicine is a relatively new field (75), whereas it is in its infancy in Kosovo. There has been little formal training, the EMS system lacks organization, equipment and a reliable communication system, and all of these were inadequate also for the UCCK emergency center (77 – 79) and it is expected to find specific in-hospital mortality rates of patients with ACS.

The use of EMS services for patients experiencing chest pain or who are suspected of having ACS is complicated (80) and major public health initiatives have encouraged the activation of emergency services as soon as possible in order to optimize timely diagnosis and treatment.

Two key findings from our study merit consideration. First, despite a publicly funded health system, only one-nine patients in this study were transported to the emergency department by pre-emergency services. Second, several factors such as older age, comorbidity, in higher risk for LVEF < 40 more often STEMI patients, Family history for cardiac event, cardiac event history were associated with higher PHE use, which may indicate that those who are most vulnerable are using PHE. The use of PHE for cardiac symptoms, the rate of ambulance use increased in this patient population from year 2011 to 2012. The increase in PHE use over

time that we observed in this study may not be a widespread global phenomenon and the pattern might be different in other jurisdictions (80).

In the study that include 50,881 patients with main ED diagnosis of acute coronary syndrome, stable angina or chest pain in the metropolitan areas of Edmonton and Calgary in the years of 2007–2013, 30.5% presented by emergency medical services. Same with our study use of emergency medical services was linked to an increased risk of 7-day and 30-day clinical events (80).

Triage, or risk classification, is a clinical management tool used in emergency services to guide patient flow when the need for medical attention exceeds that available. The Manchester Triage Group was developed in 1994 in the United Kingdom. The aim was to establish a consensus among physicians and nurses in the emergency room by creating a triage pattern focused on the development of the following: Thus, the Manchester Triage System (MTS) was created (45).

According to our findings, our patients have a higher percentage of in-hospital mortality. The in-hospital mortality rate for ACS was 10.3% higher in female patients (12.5% vs. 9.0%), with a significant difference ( $P=0.041$ ). Females were at a higher risk than men, with an OR of 1.242 (95% CI 1.025 - 1.504). According to Bajraktari et al. (81), the overall in-hospital mortality rate for AMI patients in a Cardiology Department without a primary PCI centre in 2008 was 10.3% (12.3% for women and 9.5% for men).

The average age of AMI patients increased between 1999 and 2012, but the mortality rate remained stable. The in-hospital mortality rate for unstable angina was 2.7%, STEMI patients 21.4%, and NSTEMI patients 5.7%. In the study of Ishida et al. (53), the overall in-hospital mortality from ACS was 5.9%. The European Society of Cardiology (ESC) recommends timely coronary artery reperfusion in patients with ST-elevation myocardial infarction (STEMI) and emphasizes that primary percutaneous coronary intervention (PPCI) is the preferred strategy if available (82). Despite its benefits, PPCI is not universally used, and thrombolysis is still used in many patients. Furthermore, a large number of STEMI patients do not receive reperfusion therapy (83-84). The reasons for these disparities in reperfusion

therapy use across ESC countries are unknown (85). And in other states the in-hospital mortality rate was higher before percutaneous coronary intervention (PCI), (2,3,4). In the study of Mirić et al. (86) in Split/Croatia the number of hospitalized patients with AMI, in ten years, were 5339 (67.5% males vs. 32.5% females). before percutaneous coronary intervention (PCI) mortality rate was 13,5% after PCI procedures 7.6%. The mortality in the first group was significantly higher in females (22.7 vs. 12%) and in males (9 vs. 5.5%) comparing with second group. In-hospital mortality in the patients with STEMI was significantly higher in the first group (16.6 vs. 9%). Among the patients with NSTEMI there were no significant differences in the in-hospital mortality (4 vs. 2.5%). The most frequent trigger of death in males were ventricular fibrillation in both groups such as heart failure in females. Cx occlusion is more often among the male patients treated with PCI. In-hospital mortality in patients with STEMI treated with PCI was 5.7%. A in-hospital mortality in the patients with AIM after PCI was almost halved. Females had two times higher in-hospital mortality before and after PCI introduction

The lack of percutaneous coronary intervention procedures in AMI patients may have contributed to the high in-hospital mortality in our population. Kosovo University Clinical Center - Cardiac Surgery Service with Invasive Cardiology is the only public institution in the country that offers invasive cardiology services. From February 2018 it was introduced primary PCI for STEMI in Kosovo University Clinical Center (88). In some hospitals in the private sector, PCI has been done since 2011.

In an effort to reduce disparities in a number of European countries, the Stent for Life Initiative, which supports timely PPCI implementation, was established in September 2008, as a coalition of the European Society of Cardiology, European Association for Percutaneous Cardiovascular Interventions and Eucomed. The goal is to raise awareness of the life-saving indications for percutaneous coronary interventions, particularly in all types of acute myocardial infarction. The participating countries have already reported significant increases in PPCI utilization, mortality reductions, and overall, more effective management/organization of the STEMI treatment system, which strongly calls for the continuation of an implementation strategy and support for countries with low activity (89- 91).

To improve the rate of timely PPCI for STEMI patients, quality improvement initiatives such as "Stent for Life" in Europe, the "D2B Alliance," and "Mission: Lifeline" in the United States were established. The SFL initiative established three main goals: (1) to treat 70% of STEMI patients by pPCI; (2) to perform 600 pPCI/year/million population; and (3) to ensure that centers with pPCI perform this procedure 24/7 (92-96).

The ACCA-EAPCI STEMI registry will document the current status of management and outcomes of patients admitted with an initial diagnosis of STEMI in a large number of ESC (European Society of Cardiology) member countries. This registry allows researchers to assess whether current ESC STEMI guidelines are being followed in clinical practice (97). Kosovo is member of this registry from 2017. In Kosovo is not yet implemented Utstein Style (98).

Over the last 30 years, the in-hospital mortality rate for ACS in North America has decreased from 25-30% to 7-10%. This reduction can be attributed to the introduction of the Coronary Care Unit (1960s), the administration of beta blockers (1970s), the introduction of fibrinolytic therapy (1980s), and percutaneous coronary intervention (PCI) (1990s) (6), as well as improvements in risk factor modification, healthcare system organization, and disease management, which have significantly reduced the adverse prognosis of both STEMI and NSTEMI (61). According to the British Heart Foundation, despite reductions in 30-day case fatality rates, acute coronary syndromes remain one of the leading causes of premature death in both men and women in the UK (7). In their systematic review, Sarkees et al. (99) discovered that older age groups, previous atheromatous cardiovascular disease, diabetes, smoking, hypertension, hypercholesterolemia, male sex, and a family history of premature ischemic heart disease are risk factors for ACS. Between 9% and 19% of patients with ACS die within the first 6 months of being diagnosed, with roughly half dying within 30 days. The mortality rate in different countries remains different as there are differences in the application of methods for diagnosis and treatment.

Prospective cohort (EURObservational Research Programme STEMI Registry) of hospitalized STEMI patients with symptom onset within 24 hours in 196 centers across 29 countries, enrolling 11 462 patients who received primary percutaneous coronary intervention (PCI)

(total cohort frequency: 72.2%, country frequency range 0-100%), fibrinolysis (18.8%; 0-100%), and no reperfusion therapy (9.0%; 0-75%). Reperfusion therapy was widely used for STEMI in ESC member and affiliated countries. Primary PCI was the most commonly used treatment, with an associated total in-hospital mortality rate of less than 5%. However, there was geographic variation in primary PCI use, which was linked to differences in in-hospital mortality (100).

In our study, female patients had a higher in-hospital mortality rate for ACS (12.5% vs. 9.0%). Females were more likely to die than men, with an OR of 1.242 (95% CI 1.025 - 1.504). A number of studies, including the effects of age, oestrogen, and different patterns of atherosclerosis, support a biological mechanism for sex-based differences in clinical presentation (82, 101-106). Furthermore, in the study of Novak et al. (107), women were significantly older than men (71,11 years vs. 64 .12 years, p 0.001) and had a higher in-hospital mortality rate and complications as a result of this age difference. When examining sex differences in mortality following acute ST-STEMI, there are numerous debates (108,109). Some studies indicate a disadvantage for women in the context of STEMI (110,111). Others show comparable outcome profiles for men and women (112). However, the majority of these studies focused solely on clinical covariates, which should be interpreted with caution given that therapeutic interventions have a large impact on outcomes (113,114). According to Bugiardini et al. (115), the gender disparity in mortality after STEMI persists and appears to be driven by prehospital delays in hospital presentation. Women appear to be more susceptible to untreated ischemia over longer time periods.



## **6.2. Patients with acute coronary syndrome treated at the University Clinical Center of Kosovo for the analyzed period by groups**

According to the American Heart Association, the best option in the event of a suspected ACS event is to call the mobile emergency medical service (EMS) (116). This recommendation is based on the possibility of safer transportation and shorter time-to-treatment intervals. Despite guidelines, the majority of patients with symptoms suggestive of an acute coronary syndrome do not use emergency medical services to reach the emergency department (ED), (75) In LMICs, ambulance and emergency medical services (EMS) are underdeveloped, particularly outside of large urban areas. Typically, patients experiencing ACS symptoms will use available public transportation and private cars to get around (117,118). In large urban cities where EMS is more fully developed and available, it has contributed to significant improvements in the timely management of patients with an ACS, but it is estimated that only 5% of patients use these services (119, 120). In our study, only 11.3% of patients received pre-hospital emergency care, with females receiving 13.4% and males receiving 10.2%. Emergency Medical Services were utilized by 53.4% of MI patients in developed countries such as the United States (24).

From 2010 to 2019, Valent et al. (121) examined EMS use by patients with AMI, factors associated with EMS use, and outcomes in 14,900 AMI patients in the Italian region of Friuli Venezia Giulia. Only half of the people used EMS, and there were no changes over time. Patients transported by EMS had a higher mortality rate, most likely due to residual confounding from AMI severity (121).

So et al. (122) compare patients who arrived via EMS to those who arrived via self-transport. Among the 401 patients, 59.9% arrived via EMS and 40.1% via self-transport. Patients who arrived by EMS were older (p 0.001) and had higher Killip's scores (p 0.001). Patients who arrived via EMS had shorter door-to-needle and door-to-balloon intervals (42 vs 57 minutes, p 0.001, and 124 vs 154 minutes, p 0.001, respectively). In-hospital mortality was higher in patients who used EMS (13.3% vs 5.0%, p 0.001). Patients who arrived by EMS also had a higher mortality rate within the first hour (4.2% vs 0%, p = 0.007). Only age and systolic

blood pressure were found to be predictors of mortality in a multivariate analysis. Despite the fact that patients who arrived by EMS received reperfusion therapy sooner, mortality was higher. Almost 33% of these deaths occurred during the early in-hospital period, owing to the tendency of older and sicker patients to arrive via EMS.

Boothroyd et al. (123) conducted a study that included 82 acute care hospitals in Quebec (Canada) that treated 1,956 patients, 1,222 (62.5%) of whom arrived by ambulance. Users of an ambulance were older, more often women, and more likely to have co-morbidities, low systolic pressure, an abnormal heart rate, and a higher Thrombolysis in Myocardial Infarction risk index at presentation when compared to non-users. Ambulance users were less likely than nonusers to receive fibrinolysis or be sent for primary angioplasty (78.5% vs 83.2%,  $p = 0.01$ ), but if they did, treatment delays were shorter ( $p 0.001$ ). The 1-year mortality rate for users was 18.7% compared to 7.1% for nonusers ( $p 0.001$ ). STEMI ambulance users were older and sicker than nonusers. After adjusting for clinical risk factors, user mortality was significantly higher, despite receiving faster reperfusion treatment overall.

Sepehrvand et al. (80) included all patients who presented to an ED in the metropolitan areas of Edmonton and Calgary between 2007-2013 with the primary ED diagnosis of acute coronary syndrome, stable angina, or chest pain. EMS used 30.5% of the 50,881 patients. Patients who were older, female, had an acute coronary syndrome diagnosis in the ED, had more comorbidities, and had a lower household income were more likely to use EMS to get to the hospital. Longer travel distance was associated with greater use of EMS, but it was not a predictor of clinical events.

Kodama et al. (124) analyzed 1,172 STEMI patients from the AMI Kyoto Registry who underwent PPCI between January 2009 and December 2013. The self-transport group ( $n=368$ ) was younger and had a significantly longer DBT (115 min vs. 90 min,  $P0.01$ ) than the EMS group ( $n=804$ ), with fewer patients having a Killip classification of 2 or higher. The self-transport group had a lower in-hospital mortality rate than the EMS group (3.3% vs. 7.1%,  $P0.01$ ). In EMS patients, a DBT of more than 90 minutes was an independent predictor of in-hospital mortality, but not in self-transport patients (118). The same findings were found in a

prospective observational study of all patients who presented to the ED of Basel University Hospital (125).

According to a study conducted by the Medical Center University of Alabama (126), in-hospital mortality was 8% in patients with a pre-hospital ECG and 12% in those without (p 0.001). In our study, the PHE group had a higher in-hospital mortality rate (28.8%) than the control group (7.9%). This can be explained by the fact that the usage of pre-emergency services was very scarce (11.3%) and they were only used for patients with a more severe health condition. The self-transport patients with STEMI have the prolonged treatment periods compared to the EMS-transported patients (127).

A substantial part of ACS mortality occurs during the first hours of symptoms (128). Furthermore, timely diagnosis and treatment have an impact on the occurrence of long-term fatal (129) and non-fatal (130) complications. In the emergency department, timely prescription may also be a sign of adequate monitoring and quick decision-making. Exploring bottlenecks in early medication use is important in this regard, as it may reveal alternative options in the ACS patient care system. The majority of evidence for factors influencing time to treatment is based on data on aspirin administration (131) and, in STEMI patients, thrombolytic treatment (9) or revascularization procedures (132).

Thuresson et al. (133) found that half of the patients went to the hospital by ambulance. Factors associated with ambulance use were knowledge of the importance of quickly seeking medical care and calling for an ambulance when having chest pain, abrupt onset of pain reaching maximum intensity within minutes, nausea or cold sweat, vertigo or near syncope, ST-elevation ACS, increasing age (per year), previous history of heart failure, and distance to the hospital of >5 km. Those who did not call for an ambulance thought self-transport would be faster or did not believe they were sick enough.

Ma et al. (134) found that only 21.6% patients with ACS chose taking ambulance to hospital. Factors associated with ambulance use were single, taking Suxiaojiuxin pills or nitrates before

going to hospital, diagnosed as STEMI, with persistent symptoms and symptoms accompanied with vomiting.

EMS transport to hospital is recommended in acute coronary syndrome (ACS) guidelines, but Cartledge et al. (135) found in the study with patients admitted to an Australian tertiary hospital with a diagnosis of ACS only 54% of them used EMS for transport to hospital. A large proportion of patients (43%) using other transport thought it would be faster. In this study, factors associated with EMS use for ACS were: age >65 years, ST-elevation myocardial infarction, a sudden onset of pain and experiencing vomiting.

Studies (136) suggest that patients who got to the hospital by ambulance present a shorter door-to-needle time. In the study of Muller et al (137), 28.1% of the patients got to the hospital by ambulance, but the total time taken to start the therapy was not reduced (P=0.81). Studies have shown a reduction in mortality after thrombolytic therapy in patients that received pre-hospital care (8% *versus* 13%) (P = 0.04), (14, 138)

According to studies conducted in various parts of the world (139-143), a significant proportion of patients with ACS do not use EMS, with the percentage ranging from 4.5% to 50.4% and the social demographics such as old age (22, 23, 142) and female sex (23) as well as a history of heart disease (23, 143, 144), hemodynamic complications (22) and living far from the hospital (22, 143) were associated with increased ambulance use. Several studies have documented that delays can occur from different sources, including patients and providers and the healthcare system itself (145,146).

Previous research has found that patients who arrived by ambulance with a STEMI had a two-fold higher in-hospital mortality rate than self-presenters, highlighting the fact that the sickest patients are more likely to use EMS. EMS use is supported by practice guidelines and consensus documents (147, 148), and it has been shown to reduce time to treatment and improve survival in STEMI patients (149–152) As a result, we do not believe that the medical community should change the value of the EMS in caring for patients with CP.

According to the standard guidelines, an ECG should be obtained within the first 10 minutes of arrival at the hospital in patients suspected of having acute coronary syndrome, and the

ideal door to needle time should be less than 30 minutes (153). The average door to needle time in our study was  $34 \pm 24$  minutes, and the average door to ECG time was 16 minutes, both of which were longer than the recommended guidelines. In a study by Mohannan et al. (154), less than one-third of STEMI patients who received thrombolysis had door-to-needle times longer than 30 minutes. Door-to-needle time of less than 30 minutes was associated with lower in-hospital mortality (154). Indoor admittance delays (time delays in OPD/IPD registration), indoor transport delays (lack of personnel, insufficient transportation carrier), and indoor ECG recording and interpretation delays are regarded to be the most likely reasons of these indoor delays. This indoor time delay can be shortened by commencing thrombolytic treatment in the emergency department or in pre-hospital cardiac ambulances. The widespread availability of cardiac ambulances outfitted with trained doctors and facilities for capturing and electronically transmitting ECGs to an experienced Cardiologist/physician, as is done routinely in numerous countries, can be a valuable strategy to achieve reduced ischemia periods. However, major management guidelines (117,155) emphasize the need of early detection and treatment as a helpful method for lowering the risk of mortality associated with an untreated ACS incident. Time to treatment may be a valuable measure of the quality of care provided during an ACS episode in this scenario.

The success of this treatment is contingent on providing thrombolysis as soon as symptoms occur, and the time it takes the patient to decide that their symptoms require medical attention is the main reason of delay in patients arriving at the hospital after MI. Although it is advised that the time from the onset of pain to hospitalization be shorter than 90 minutes, urban patients admitted for MI in Central Dalmatia required a median of 2 hours after the onset of pain to call the emergency, and the total pre-hospital delay was 4.3 hours (156).

The reperfusion time of STEMI patients in China is evidently delayed when compared to the time required by the guidelines. (157). Provincial and municipal hospitals had door-to-balloon times of  $172 \pm 13$  and  $251 \pm 14$  minutes, respectively, for patients undergoing primary percutaneous coronary intervention. In patients receiving thrombolysis treatment, the door-to-needle times of provincial hospitals, municipal hospitals and country hospitals were  $86 \pm 7$ ,  $91 \pm 7$  and  $123 \pm 11$  minutes, respectively.

In recent years, enormous progress has been made in treating acute coronary syndrome (ACS) and shortening the time between the onset of pain and intervention. However, the time between the onset of pain and the request for assistance is still far too long.

According to a study conducted by the Institute of Cardiology in Warszawa (158), the time between the onset of symptoms and the call for medical assistance ranged from 4 to 1140 minutes. Patients aged 56-70 years experienced the longest delay. Half of them requested assistance after 3 hours. Women waited longer than men. They also waited 20 minutes longer for an ambulance ( $p < 0.01$ ). The main reasons for the delay were: being confident that the symptoms would go away (201 patients - 57.6%) or believing that the symptoms were not related to heart disease (45 patients - 12.9%).

The only component of the pre-hospital delay that is entirely dependent on patients rather than the health-care system is the pain-to-call time. Dalmatia's median pain-to-call time was 2 hours in 2005, and it remained constant in 2010-2011 (156). This means that residents of Central Dalmatia wait far too long before calling for assistance, wasting valuable time required for optimal reperfusion. Improvements in the health-care system are not accompanied by increased patient awareness of AMI symptoms. According to a recent study, up to half of coronary patients are not taught how to respond to heart attack symptoms (159).

Most of the patients in this study were treated with conservative therapy due to a late arrival of patients into the hospital. Reperfusion treatment (whether PCI or fibrinolysis) is most successful when performed within the 1st hour from the onset of pain, but in the studied cohort only 5.7% of patients arrived at the hospital within 90 minutes from the onset of pain.

Coronary heart disease is the leading cause of morbidity and mortality in both men and women in the United States. Despite dramatic changes in the management of patients hospitalized with acute myocardial infarction over the last several decades, a significant proportion of AMI patients continue to delay seeking medical care. A systematic review of the literature from 1960 to 2008 was conducted, including publications that provided data on the duration of prehospital delay in AMI patients hospitalized. The current study included 44

articles (42 studies) in total (160). When compared to other groups, the elderly and women were more likely to delay seeking medical care after developing symptoms suggestive of AMI. More research is required to fully understand the causes of delay in these vulnerable groups.

In the Rucker et al (161) study, 32% of patients who completed the survey reported a delay in seeking ED care. 71% of patients who reported a delay believed their problem would go away or was not serious. Patients who were older, had higher acuity, or used the ED frequently reported less delay, whereas patients without a regular physician or who were African American reported more delay. Frequent ED users and those with lower baseline physical function reported an increased number of days ill prior to visiting the ED, whereas patients with higher acuity reported fewer days ill prior to visiting the ED.

Ting et al. (162) discovered that longer time to treatment, as measured by door-to-balloon or door-to-needle time, was linked to higher in-hospital mortality rates.

Primary PCI has emerged as an effective treatment strategy for acute STEMI; however, patient survival and outcome are dependent on the time to treatment. The international standard for all programs dealing with STEMI patients with acute coronary syndrome has been established as 90 minutes or less from the time the patient arrives at the hospital to the opening of the affected vessel in the cardiac catheterization laboratory, known as "door-to-balloon time" or D2B. During the year 2014, the STEMI, D2B time of 90 minutes was attained in 25% of patients at the King Faisal Cardiac Center (one of the key centers that conduct primary PCI as treatment for STEMI in Jeddah, Saudi Arabia). Several reasons have contributed to the delays in meeting the objective level of more than 90%, including late diagnosis of STEMI patients, delays in acquiring the ECG, activation of the catheterization laboratory, and patient transportation delays (163).

Wilson et al. (164) compared 101 STEMI patients transported in 2007 to 442 STEMI patients transferred after launching these STEMI initiatives from 2008 to 2011, with the median door-in-to-door-out time decreasing from 44 to 35 minutes, the median first D2B decreasing from 109.5 to 88.0 minutes, and the percentage under 90 minutes increasing from 22.8% to 55.9%. Overall, transport durations remained stable (median 36.5 vs. 36.0 min) from 2007 to 2011, whereas PCI hospital D2B fell from 20.0 to 16.0 min. The average length of stay was 3.0 days,

and the in-hospital death rate was less than 4%. Significant developments in STEMI workflow over the last decade have led in most hospitals reporting door-to-balloon (D2B) timings within the 90-minute norm (165). For STEMI, the In-House Interventional Team Program (IHIT) might achieve D2B times of less than 60 minutes. The availability of a 24-hour STEMI team in-house considerably reduced reperfusion time, resulting in improved clinical outcomes and a shorter duration of stay for PCI-treated STEMI patients. If performed promptly, primary percutaneous coronary intervention for STEMI is favorable. Individuals who self-transport with STEMI have longer treatment periods than patients who are transferred by Emergency Medical Services. Shavelle et al. (127) compared patients with D2B times greater than 90 minutes to those with D2B times less than 90 minutes. Using logistic generalized estimating equations, the factors associated with extended D2B (>90 minutes) were investigated. Off-hour presentation (weekends and 7 p.m. to 7 a.m. weekdays), failure to obtain an electrocardiogram within 10 minutes of hospital arrival, previous coronary artery bypass surgery, black race, older age, and female gender were the key characteristics related with longer treatment time. In conclusion, while delayed arrival to electrocardiographic acquisition is a modifiable factor contributing to prolonged D2B times among self-transport STEMI patients, other factors (age, race, and gender) indicate that historic disparities in cardiovascular care persist in terms of contemporary metrics for STEMI reperfusion.

Chen et al. (166) investigated the connection between delayed coronary care unit (CCU) admission and clinical outcomes in patients with ACS with non-ST-segment elevation (NSTEMI-ACS). Patients were separated into two groups based on their CCU wait duration (12h and >12h). There were no significant differences in in-hospital mortality, stroke incidence, or hospital stay duration across groups.

In their investigation, Bugiardini et al. (167) discovered that in patients with ACSs, earlier administration of oral blocker medication should be prioritized with a higher possibility of improving LV function and in-hospital survival rate. This early treatment regimen should be avoided in patients who present with acute pulmonary edema or cardiogenic shock.



In another study by Heitzler et al. (168), 1190 acute STEMI patients treated with primary PCI were studied prospectively in eight locations across Croatia (677 non-transferred, 513 transferred). All patients were divided according to door-to-balloon time in three subgroups (< 90, 90-180, and > 180 minutes) and according to symptom onset-to-balloon time in three subgroups (<180, 180-360, and > 360 minutes). Considering the symptom onset-to-balloon time subgroups, a statistically significant difference at multivariate level was highest for in-hospital mortality in the subgroup of patients with longest onset-to-balloon time (4.5 vs. 2.6 vs. 5.7%). Door-to-balloon time is one of the indicators of primary PCI network organization quality and targets for quality improvement, however it has little effect on early and six-month follow-up results of therapy for acute STEMI. The symptom onset-to-balloon time is more accurate for this purpose; however, reducing the latter is more complex than reducing the former.

Out of 1386 patients with STEMI, delayed presentation was seen in 1148 (> 2 hrs) and 805 (> 4 hrs) patients. The duration from onset of symptoms to the presentation in the emergency room (pre-hospital delay) was  $228 \pm 341$  minutes. The door to needle time was  $34 \pm 24$  minutes. The major factors for pre-hospital delay were misinterpretation of symptoms (45%) and transportation problems (27%), (169).

In a study of 6704 consecutive patients with ACS from Middle Eastern nations, 61% had NSTEMI and 39% had STEMI. Female gender, advanced age, diabetes, hypertension, dyslipidemia, and obesity were more common in NSTEMI patients. Prior to the index admission, STEMI patients were more likely to be smokers and less likely to be taking aspirin. CRF and diabetes were independent predictors of in-hospital cardiac failure in NSTEMI, whereas CRF and hypertension were predictors of STEMI. Female gender and CRF were both independent predictors of mortality in STEMI patients (170).

The rise in CVD burden is mostly due to an increase in the incidence of risk factors as well as a relative lack of access to well-recognized therapies that prolong survival once CVD has occurred. Risk factors (hypertension, diabetes, obesity) are more prevalent. Patients with AMI in Kosovo are younger than those in other developed countries. In our analysis, smoking was

related with a decreased risk of death in ACS, owing to smokers' younger age and less severe CAD. Similar data was discovered, as well as other authors (171-173).

Obesity at the time of ACS manifestation is related with a decreased in-hospital death rate. The "obesity paradox" may be due to younger age at presentation, earlier referral for angiography, and more aggressive care of ACS. The established CVD risk factors, such as high blood pressure, an abnormal blood lipid profile, diabetes mellitus, obesity, and smoking, have been addressed in recommendations and guidelines for at least a half-century. These well-known risk factors account for 80% of the ischemic heart disease burden (174).

Increased population aging and rising rates of several cardiovascular risk factors, such as obesity (175) and diabetes (176), have contributed to an increase in the number of people who have had an ACS event in recent decades.

The CroHort study published in 2012 highlighted trends in behavioral and biological CVD risk factors in Croatia, demonstrating that smoking and alcohol intake in men declined dramatically compared to 2008, whereas alcohol consumption, obesity, and hypertension in both sexes increased significantly (177). The study's negative findings indicate that more attention should be paid to CVD risk factors and CVD prevention.

According to the Euro Heart Survey, the majority of patients diagnosed with CAD, including ACS, have impaired glucose regulation (178), and two prior investigations that included previously healthy persons found that IGT increases the risk of CVD and death (179, 180).

AlHabib et al. (181) examined data from a cohort analysis of 7,930 post-ACS patients from six Middle Eastern nations and discovered that 50.1% had central obesity, 39.5% had diabetes, 47.2% had hypertension, 32.7% had hyperlipidemia, and 35.7% were current smokers.

There is currently no cardiac-specific serum marker that fits all of the criteria for a "ideal" AMI marker. No test is both highly sensitive and highly specific for acute infarction within 6 hours of the beginning of chest pain, which is the timeframe most emergency physicians consider when making diagnostic and therapeutic decisions. Patients presenting to the ED with

chest pain or other symptoms suggestive of acute cardiac ischemia cannot therefore rule out AMI based on a single cardiac marker value obtained within a few hours after symptom onset (136).

Tsai et al. (182) found that overall, ED concordance with guideline-recommended processes of care was low to moderate in their evaluation of quality of care for acute myocardial infarction in 58 U.S. emergency departments. Buclin et al. (183) and Tanzi et al. (184) discovered that the emergency medical team's diagnosis was adequate in 91% of cases, resulting in a 5% rate of unnecessary admissions to the critical care unit. Schewe et al. (185) assess the diagnostic accuracy of physician-staffed emergency medical teams (PEMTs) outside of the hospital. After matching the prehospital diagnosis with the appropriate hospital diagnosis, the overall diagnostic accuracy (correct or false) of PEMTs was assessed. PEMTs' overall diagnosis accuracy increased from 87.5% in 2004 to 92.6% in 2014. According to data from a Canadian study, 4.6% of patients with acute myocardial infarction and 6.4% of patients with unstable angina were misdiagnosed (186).

Gilutz et al. (187) investigated adherence to guidelines for NSTEMI in the ED and discovered a lack of timely detection and early medical treatment of NSTEMI in the ED. Better computerized medical history collection, attention to normal and atypical clinical presentation, and use of an appropriate cardiologic risk stratification tool may help to unblind treating teams at the point of treatment and enhance adherence to NSTEMI recommendations.

Percutaneous coronary intervention (PCI) within 120 minutes of commencement is indicated for patients with acute coronary syndrome (ACS). A helicopter emergency medical service (HEMS) can deliver ACS patients. Homma et al. (188) discovered that while HEMS reduced transport time when compared to ground emergency medical services, it did not contribute to PCI access within 120 minutes. The most critical component was direct transport to a PCI hospital (P.01).

### **6. 3. Patients with acute coronary syndrome treated at the University Clinical Center of Kosova for the analyzed period by types of acute coronary syndrome**

Several investigations (189-191) showed significant variations in the incidence of heart failure and mortality among STEMI, NSTEMI, and UA patients. Kaul et al. (189) discovered that the incidence of heart failure and mortality differs significantly across STEMI, NSTEMI, and UA patients. Piva e Mattos et al. (190) examined data from the Acute Coronary Care Evaluation of Practice Registry (ACCEPT study), a multicenter post-ACS Brazilian study with 2,485 patients between August 2010 and December 2011, and discovered 30-day mortality rates of 1.8% in patients with UA, 3.0% in NSTEMI patients, and 3.4% in STEMI patients. From 2,485 individuals, 31.6% had unstable angina, 34.9% had acute coronary syndrome without and 33.4% had acute coronary syndrome with ST-segment elevation. At 30 days, cardiac mortality was 1.0% vs. 2.3% in patients with UA ( $p = 0.268$ ), 1.9% vs. 4.2% ( $p = 0.070$ ) in patients with NSTEMI, and 2.0% vs. 8.1% ( $p = 0.001$ ) in patients with ST-segment elevation.

Santos et al. (191) found an overall one-year case-fatality rate of 12.0% for patients hospitalized to a community hospital with a diagnosis of ACS in their ERICO research. When the results were stratified by ACS type, there was a substantial difference in the death rate (5.4%, 9.6%, and 19.2% for patients with UA, STEMI, and NSTEMI diagnoses, respectively). A study of 1,027 patients with NSTEMI from a single tertiary cardiology clinic in So Paulo (191) discovered that 5.3% died or had a second infarction within 30 days.

According to a study conducted in the city of Zagreb in 2009 (192) that included patients with the diagnosis of ACS, intrahospital mortality was 14% and 22% died outside of the hospital. There were 56% of patients with STEMI, 34% with NSTEMI, and 10% with probable MI and MI with unclear ECG. The time from onset of symptoms to hospital attendance was less than 6 hours in 49.8% of patients, 6 to 12 hours in 13.8%, and more than 12 hours in 36.1%. In 19.0% of patients, the beginning of symptoms was uncertain. In 41% of patients, angiography and reperfusion therapy were performed; PCI/PCI + stent in 33% of males with ST or non-ST

segment elevation, and 25% of women with ST segment elevation and 19% of women with non-ST segment elevation. Fibrinolytic therapy was administered to 86 patients, 53 (7%) of whom were men and 30 (5%) of whom were women. Aspirin was taken by 85% of ACS patients (N=966), beta-blockers by 70%, angiotensin-converting enzyme inhibitors by 69%, and statins by 63%.

In the study of Novak et al. (107) women were significantly older compared to men ( $71 \pm 11$  years vs.  $64 \pm 12$  years,  $p < 0.001$ ) and had higher in-hospital mortality and complications due to this age difference. In women, regardless of age, smoking was less common, whereas hypertension and a history of angina pectoris were more common. PTCA with or without stenting, as well as coronary catheterization, significantly reduced in-hospital mortality and sequelae, but thrombolytic treatment was linked with a 3.3 times greater mortality odds ratio (OR,  $p = 0.01$ ). Other significant predictors of in-hospital mortality were in-hospital complications (OR 25,  $p < 0.001$ ) and ST segment elevation myocardial infarction (STEMI, OR 4.5,  $p < 0.001$ ).

Bugiardini et al. (2) examine the results of coronary reperfusion treatments and ST-segment elevation myocardial infarction (STEMI) in patients from Eastern nations with transitional economies. From January 1st to December 31st, 2009, there were 23,486 consecutive patients admitted to hospitals. In Western countries, in-hospital mortality was between 4% and 5%. Mortality rates were much higher in Serbia (10.8%) and Bosnia and Herzegovina (11.2%), intermediate in the Russian Federation (7.2%), and similar in Hungary (5.0%). Primary percutaneous coronary intervention (primary PCI) rates in Bosnia and Herzegovina were very low (18.3%), low in the Russian Federation (20.6%) and Serbia (22%), and high in Hungary (70%).

Aune et al. (193) reported a 16% one-year mortality rate in 307 post-MI patients treated in a non-tertiary hospital in Norway following the establishment of a reference system for invasive cardiac treatments in a cardiology referral center.

Data from the Australian and New Zealand SNAPSHOT ACS research (194) demonstrate that STEMI (16.2%) and non-STEMI (16.3%) patients had the highest all-cause mortality after 18 months, while those with unstable angina (6.8%) and non-cardiac chest pain (4.8%; P 0.0001 for trend).

Other researchers looked into post-ACS mortality as well. The Swedish Register of Cardiac Intensive Care was prospective observational research conducted in 58 Swedish hospitals' coronary care units from 1995 to 1998. Stenestrand et al. (195) discovered a one-year post-MI mortality rate of 7.8% in a cohort study with 19,599 participants. The usage of statins affected death rates. The unadjusted mortality rate in the no-statin group was 9.3%, while it was 4.0% in the statin treatment group.

Other researchers investigated post-ACS mortality as well. The Swedish Register of Cardiac Intensive Care was prospective observational research conducted in coronary care units at 58 Swedish hospitals from 1995 to 1998. Stenestrand et al. (195) discovered a 7.8% one-year post-MI mortality rate in their cohort analysis of 19,599 patients. The usage of statins had an effect on mortality rates. Unadjusted mortality was 9.3% in the no-statin group and 4.0% in the statin treatment group.

Skelding et al. (196) discovered a one-year mortality rate of 8% in 2,066 patients who received invasive examination after reviewing observational data from a single tertiary institution in Pennsylvania.

Similarly, Kleopatra et al. (197) examined data from 1,986 women with NSTEMI in 155 hospitals from the German Acute Coronary Syndromes registry between June 2000 and November 2002 and divided them into two groups: 1215 (61.2%) received coronary angiography, while 771 (38.8%) received conservative treatment. One-year death rates were 8.1% in those who underwent invasive stratification and 24.0% in those who did not, with in-hospital mortality rates of 3.2% vs. 10.5%.

Ruano-Ravina et al. (198) recently discovered a one-year mortality rate of 9.3% and a 30-day mortality rate of 6.8% in a sample of 1,461 people presenting with STEMI who received primary angioplasty in two hospitals in Spain.

Potočnjak et al. (199) discovered that the most common cause of acute heart failure was worsening of chronic heart failure in their prospective observational analysis at the University Hospital Center Emergency department in 2010. Females were more likely to suffer from hypertensive acute heart failure, while males were more likely to suffer from acute heart failure associated with acute coronary syndrome. Females were older, had a higher BMI, atrial fibrillation, urinary tract infections, a history of hypertension, hypertension upon admission, and a SAPS II score at admission. Males had a greater rate of ST-elevation myocardial infarction and dilated cardiomyopathy, as evidenced by lower ejection fraction and left ventricular dilatation with reduced ejection fraction on ultrasonography. Male smokers with a history of chronic obstructive pulmonary disease were more common.

Older age, past atheromatous cardiovascular disease, diabetes, smoking, hypertension, hypercholesterolemia, male sex, and a family history of early ischemic heart disease are all risk factors for ACS. ACS can occur in the presence of valvular disease, arrhythmias, and cardiomyopathies. Between 9% and 19% of people with ACS die within the first 6 months of being diagnosed, with around half dying within 30 days (99).

CVD was the top cause of death in Croatia in 2017, accounting for 44.0% of all deaths in both men and women (200).

In the study of Pocock et al. (201) within two years of discharge 5.5% of patients died. The 17 independent mortality predictors were: age, low ejection fraction, no coronary revascularization/thrombolysis, elevated serum creatinine, poor EQ-5D score, low hemoglobin, previous cardiac or chronic obstructive pulmonary disease, elevated blood glucose, on diuretics or an aldosterone inhibitor at discharge, male sex, low educational level, in-hospital cardiac complications, low body mass index, ST-segment elevation myocardial infarction diagnosis, and Killip class.

In the study of McNamara et al. (202) the in-hospital mortality rate was 4.6%. Age, heart rate, systolic blood pressure, presentation after cardiac arrest, presentation in cardiogenic shock, presentation in heart failure, presentation with ST-segment elevation myocardial infarction, creatinine clearance, and troponin ratio were all independently associated with in-hospital mortality. Observed mortality rates varied substantially across risk groups, ranging from 0.4% in the lowest risk group (score <30) to 49.5% in the highest risk group (score >59).



## 7. CONCLUSIONS

The results of our research do not confirm our hypothesis that the use of pre-hospital emergency care will improve prognosis of patients admitted to hospital with acute myocardial infarction. The mortality rate was higher in PHE patients 28.8% compared to that of the control group 7.9% OR 3.534 (95% CI 2.652 - 4.709), with significant statistical difference ( $P = 0.000$ ). This high mortality rate of patients who have been using pre-emergency services can be explained by the fact that:

1. They were more often STEMI patients, older than patients of control group, 40.0% who were 70 years or older, were in higher risk for LVEF < 40% than Control group with significant difference.
2. Significant difference on Family history for cardiac event (PHE group 45.3% vs. Control group 33.2%), Cardiac event history (PHE group 41.2% vs. Control group 33.1%), comorbidity (PHE group 55.9% vs. Control group 42.2%), diabetes (PHE group 42.4% vs. Control group 29.1%), Ex-smoker ((PHE group 10.0% vs. Control group 7.0%).
3. Door-to-needle (67 vs. 135 min) and door-to-balloon (89 vs. 142 min) times were shorter in the PHE group.
4. Patients of PHE group on 47.6% of cases duration of symptoms from the onset of symptoms as reported by the patient and admission to the hospital were < 6 hours compared to Control group 32.8% with significant difference ( $P=0.004$ ), PHE group were in higher risk for from the onset of symptoms as reported by the patient and admission to the hospital were < 6 hours than Control group OR 1.630 (95% CI 1.171 – 2.269).
5. Age, female sex, STEMI, NSTEMI, PHE treatment, diabetes, hyperlipidemia, smoking and low LVEF were significant risk factors for in-hospital mortality in patients admitted for ACS, in univariate Cox regression analysis.
6. Age, the presence of STEMI, the lack PHE treatment, diabetes mellitus, low LVEF and smoking remain independent predictors of mortality in patients admitted for ACS, in multivariate Cox regression analysis.

7. The Kaplan-Meier survival curve showed that STEMI patients had higher in-hospital mortality rate compared with patients that were admitted for ACS and had NSTEMI or UA.
8. With Log rank test was found significant difference on in- hospital mortality between STEMI and NSTEMI patient ( $P < 0.001$ ), STEMI and UA patients ( $P < 0.001$ ) and NSTEMI and UA patients ( $P < 0.001$ ).
9. After one year patient are called by phone mortality rate from admission to 12 month was 19.4 %.
10. Of the 499 patients with ST elevation/de novo LBBB, 331 underwent thrombolysis and the other 168 primary angioplasty, but only 65 has done angioplasty in UCKK other go to private institutions.
11. In-hospital mortality of patients admitted with ACS in Kosovo remains high, compared with developed countries.
12. The lack of pre-hospital emergency treatment, in addition to the old age, diabetes, STEMI type and compromised LV systolic function, was shown independent predictor of in-hospital mortality in ACS patients.
13. Major risk factors for death appear to be lack of reperfusion therapy, longer time delay from symptoms onset to hospital presentation as well as the higher percentage of patients with clinical presentation STEMI.
14. The usage of ambulance in patients with ACS presenting to the ED was low in Kosova.

### **Proposed measures**

We believe that the findings of this survey will help the policymakers in developing policy and programs on reducing the mortality rates of patients with ACS, especially by developing a better strategy for the pre-hospital emergency in Kosovo.

The following initiatives need to address: established hospital referral system, goal-oriented performance protocols, expedited transport by ground or air, first hospital activation of the

PCI hospital catheterization laboratory and outreach coordinator and patient-level web-based feedback to the referring hospital; institutional measures should be taken to reduce door-to-needle time and improve patients' life expectancy, such as implementing health care protocols for patients with chest pain and administering thrombolytics in the emergency department.

- Future education programs should focus on these factors and increase people's knowledge on ACS and the benefits of ambulance use. The fact that knowledge increases ambulance use and the need for behavioral change pose a challenge for health-care professionals. Public and targeted campaigns on primary prevention are urgently needed and could potentially lower morbidity and mortality rates due to ACS. Regular training of EMS personnel and public campaigns should be implemented to improve the diagnostic accuracy in the future.
- There is a urgent need to establish both an emergency medical system infrastructure and health coverage for life-saving treatments in order to improve the morbidity and mortality associated with ACS
- Training of multi-disciplinary emergency medical personnel in community hospitals and primary care settings on diagnostic procedures is a vital step.
- Emergency physicians should continue to work with other stakeholders in AMI care, such as emergency medical services (EMS) and cardiologists, to develop strategies to improve care processes.
- Lack of an organized health care system often delays transfer of ACS patients to cardiac intervention facilities. A country-wide or regional referral plan is urgently needed to insure timely transfer of patients from non-cardiac centers to interventional facilities.
- Public campaigns and screenings to increase awareness of hypertension, diabetes and other cardiovascular risk factors may potentially improve morbidity and mortality rates
- A major challenge for improvement of the care and outcome of STEMI patients in Europe is the lack of accurate and comprehensive data. The availability of complete reperfusion data and patient outcome is a prerequisite to address the full diversity of access to treatment in order to improve treatment availability and outcomes for STEMI

patients in the future. Systematic use of large data-based registries on STEMI treatment is highly needed. Also, the establishment of key indicators underpinned by key items of data with data definitions and clear analytical steps as used in other organizations might be helpful.

- Increasing national educational campaigns to improve knowledge about typical and atypical ACS symptoms and the importance of seeking early treatment is central for reducing the high morbidity and mortality in LMICs.
- Improving Red Crescent infrastructure, establishing integrated STEMI networks, and launching educational public campaigns are top health care system priorities.

## 8. ABSTRACT IN CROATIAN

### Utjecaj izvanbolničke skrbi na ishod bolesti u bolesnika s akutnim koronarnim sindromom

Hitna medicina, djelatnost medicine koja je relativno nova čak i u najrazvijenijim društvima, u povojima je na Kosovu. Opći cilj ove studije bio je procijeniti utjecaj pred-bolničke i bolničke hitne skrbi na ishod bolesti u bolesnika koji su primljeni u bolnicu radi ACS. Ova opservacijska, prospektivna, klinička studija uključila je sve slučajeve bolesnika s ACS-om koji su primljeni u hitnu službu UCCK-a između 1. siječnja 2011. i 31. prosinca 2012. godine. U tom razdoblju bolnički je liječeno 1498 bolesnika s dijagnozom ACS, od čega su žene činile 36,4%, a 69,4 % bolesnika bilo je mlađe od 70 godina. Žene su bile 70 i više godina starosti u odnosu na muškarce (37,2% prema 26,9%;  $p=0,000$ ). Klinička prezentacija nestabilnom anginom bila je u 22,6%, 33,3% STEMI i 44,1% NSTEMI bolesnika. U skupini PHE bilo je 170 ili 11,3% bolesnika. Žene su češće koristile PHE usluge u odnosu na muškarce (13,4% naprama 10,2%;  $p=0,063$ ). Ukupna bolnička smrtnost za ACS bila je 10,3% sa statistički značajnom razlikom prema spolu (žene 12,5%, muškarci 9,0%;  $p=0,941$ ). Bolesnici s ACS-om u 56,5% slučajeva bolovali su od arterijske hipertenzije, u 30,6% od šećerne bolesti, 10,2% bili su pretili i 36,2% bili su aktivni pušači. Stopa smrtnosti bila je veća u bolesnika s PHE 28,8% u odnosu na kontrolnu skupinu 7,9%;  $p=0,000$ . Ova visoka stopa smrtnosti bolesnika koji su koristili PHE uslugu može se objasniti činjenicom da su ti bolesnici češće imali STEMI i da su bili stariji od 70 godina.

**Ključne riječi:** ishod biolesti, akutni koronarni sindrom, pre-bolnička hitna skrb

## 9. ABSTRACT IN ENGLISH

### **The Impact of Pre-Hospital Emergency Care on Outcome in Patients with Acute Coronary Syndrome, Musli Gashi, 2023**

Emergency medicine, a field relatively new to even the most developed societies, is in its infancy in Kosova. The general aim of the study was to evaluate the impact of pre-hospital and hospital emergency care in the prognosis of patients admitted to the hospital with ACS. This observational prospective clinical study has included all cases of ACS patients admitted to emergency department of UCCK between January 1, 2011 and December 31, 2012. During this period 1498 patients diagnosed as ACS, from which 36.4% were females. By age, 69.4% were younger than 70 years. In a higher percentage, females were 70 and older compared to males (37.2% vs 26.9%;  $p=0,000$ ). 22.6% were diagnosed as UA, 33.3% as STEMI and 44.1% as NSTEMI. In PHE group were 170 or 11.3% of patients. Women often used PHE services compared to males (13.4% vs.10.2%;  $p=0,063$ ). In hospital mortality rate for ACS was 10.3% with significant difference by gender (F 12.5% vs. M 9.0%;  $p=0,941$ ). Patients with ACS in 56.5% of cases had hypertension, 30.6% diabetes, 10.2% Obese; 36.2% Current smokers. The mortality rate was higher in PHE patients 28.8% vs. control group 7.9%, with significant statistical difference ( $p=0,000$ ). This high mortality rate of patients who have been using PHE services can be explained by the fact that they were more often STEMI patients, older than patients of control group, 40.0% who were 70 years or older.

**Key words:** outcome, acute coronary syndrome, pre-hospital emergency care

## 10. LIST OF REFERENCES

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 2013;380 (9859):2095-128.
2. Bugiardini R, Manfrini O, Majstorovic Stakic M, Cenko E, Boytsov S, Merkely B, et al. Exploring in-hospital death from myocardial infarction in Eastern Europe: from the international registry of acute coronary syndromes in transitional countries (ISACS-TC); on the behalf of the working group on coronary pathophysiology & microcirculation of the european society of cardiology. *Curr Vasc Pharmacol*. 2014;12(6):903-9.
3. Pajak A, Kozela M. Cardiovascular disease in central and east europe. *Public Health Rev*. 2012; 33:416–435. doi: 10.1007/BF03391644
4. Tatu-Chitoiu G, Cinteza M, Dorobantu M, Udeanu M, Manfrini O, Pizzi C, et al. In-hospital case fatality rates for acute myocardial infarction in Romania. *CMAJ* 2009; 180:1207–13. doi: 10.1503/cmaj.081227
5. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). *JAm Coll Cardiol*. 2004;44: E1-211.
6. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB III, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). *JAm Coll Cardiol*. 2006;47: e1-121.
7. Timmis A. Acute coronary syndromes. *BMJ*. 2015 Oct 20;351:h5153.

8. Gusto investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med*. 1993;329(10):673-82.
9. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *The Lancet*. 1996;348(9030):771-5.
10. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-STsegment elevation myocardial infarction—summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients with Unstable Angina). *J Am Coll Cardiol*. 2002; 40:1366-74.
11. National Heart Attack Alert Program Coordinating Committee, 60 Minutes to Treatment Working Group. Emergency department: rapid identification and treatment of patients with acute myocardial infarction. *Ann Emerg Med*. 1994;23(2):311-29.
12. Kosovo Agency of Statistics. Causes of death in Kosovo 2012 and 2013. Prishtina, Kosovo; 2015. [accessed 26.10.2018]. Available on: [https://ask.rks-gov.net/media/1797/causes\\_of\\_death\\_in\\_kosovo2012-2013.pdf](https://ask.rks-gov.net/media/1797/causes_of_death_in_kosovo2012-2013.pdf)
13. National Institute of Public Health of Kosova. Morbidity report in primary health care for the period January December 2015. *Health Statistics Yearbook*, Prishtine, 2016.
14. Mathew TP, Menown IB, McCarty D, Gracey H, Hill L, Adgey AA. Impact of pre-hospital care in patients with acute myocardial infarction compared with those first managed inhospital. *Eur Heart J* 2003; 24(2):161-71.
15. Koefoed-Nielsen J, Christensen EF, Melchiorsen H, Foldspang A. Acute myocardial infarction: does pre-hospital treatment increase survival? *Eur J Emerg Med* 2002;9 (3):210-6.
16. Moran AE, Forouzanfar MH, Roth GA, Mensah GA, Ezzati M, Murray CJ, et al. Temporal trends in ischemic heart disease mortality in 21 world regions, 1980 to 2010: the Global Burden of Disease 2010 study. *Circulation*. 2014;129(14):1483–1492



17. European Society for Emergency Medicine EUSEM. Policy statements. [accessed 30.08.2017]. Available on: [http://www.eusem.org/Pages/About\\_EuSEM/Policy\\_Statements/Policy\\_Statements.html](http://www.eusem.org/Pages/About_EuSEM/Policy_Statements/Policy_Statements.html),
18. Moore L. Measuring quality and effectiveness of prehospital EMS. *Prehosp Emerg Care*. 1999;3(4):325-331.
19. Razzak JA, Kellermann AL. Emergency medical care in developing countries: is it worthwhile? *Bull World Health Organ*. 2002;80(11):900-905
20. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, De Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;61(4):e78-140.
21. Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. *European heart journal*. 2008 Dec 1;29(23):2909-45.
22. Mathews R, Peterson ED, Li S, Roe MT, Glickman SW, Wiviott SD, et al. Use of emergency medical service transport among patients with st-segment–elevation myocardial infarction: findings from the national cardiovascular data registry acute coronary treatment intervention outcomes network registry—get with the guidelines. *Circulation*. 2011 Jul 12;124(2):154-63.
23. Canto JG, Zalenski RJ, Ornato JP, Rogers WJ, Kiefe CI, Magid D. et al. National Registry of Myocardial Infarction 2 Investigators. Use of emergency medical services in acute myocardial infarction and subsequent quality of care: observations from the National Registry of Myocardial Infarction 2. *Circulation*. 2002;106(24):3018-23.
24. Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: the 'chain of survival' concept. A statement for health professionals from the

Advanced Cardiac Life Support Subcommittee and the Emergency Cardiac Care Committee, American Heart Association. *Circulation*. 1991 May;83(5):1832–47

25. Al-Shaqsi S. Models of international emergency medical service systems. *Oman medical journal*. 2010 Oct;25(4):320.
26. O'Hanlon KP, Lerner EB. Post-war development of emergency medicine in Kosovo. *Emergency medicine journal*. 2007 Jan 1;24(1):18-21.
27. O'Hanlon K. Kosovo Emergency Medical Services WHO Assessment March 2000, Local publication. Pristina, Kosovo: WHO, 2000.
28. Degoricija V. *Emergency Medicine Book*. page 113.
29. Cummins RO, Chamberlain DA, Abramson NS, Allen M, Baskett P, Becker L, et al. Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein Style. Task Force of the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the Australian Resuscitation Council. *Annals of emergency medicine*. 1991 Aug;20(8):861-74.
30. Cummins RO, Chamberlain DA, Abramson NS, Allen M, Baskett PJ, Becker L, et al. Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein Style. A statement for health professionals from a task force of the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the Australian Resuscitation Council. *Circulation*. 1991 Aug;84(2):960-75.
31. Chamberlain D, Cummins RO, Abramson N, Allen M, Baskett P, Becker L, et al. Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the 'Utstein style': prepared by a task force of representatives from the European Resuscitation Council, American Heart Association, Heart and Stroke Foundation of Canada, Australian Resuscitation Council. *Resuscitation*. 1991 Aug 1;22(1):1-26.
32. Søreide E, Morrison L, Hillman K, Monsieurs K, Sunde K, Zideman D, et al. The formula for survival in resuscitation. *Resuscitation*. 2013; 84(11):1487-93.

33. Kawai C. Pathogenesis of acute myocardial infarction. Novel regulatory systems of bioactive substances in the vessel wall. *Circulation*. 1994 Aug 1;90(2):1033-43.
34. Gyárfás I, Keltai M, Salim Y. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries in a case-control study based on the INTERHEART study. *Orv Hetil*. 2006 Apr 16;147(15):675-86.
35. Bush TL, Fried LP, Barrett-Connor E. Cholesterol, lipoproteins, and coronary heart disease in women. *Clin Chem*. 1988;34(8B): B60-70.
36. Eriksen M, Mackay J, Ross H. *The Tobacco Atlas, Fourth Edition*. Atlanta, GA: American Cancer Society, and New York, NY: World Lung Foundation; 2012.
37. Mo F, Pogany LM, Li FC, Morrison H. Prevalence of diabetes and cardiovascular comorbidity in the Canadian Community Health Survey 2002 2003. *The Scientific World Journal*. 2006; 6:96-105. doi:10.1100/tsw.2006.13
38. World Health Organization. *Global status report on noncommunicable diseases 2014*. Geneva: World Health Organization; 2015. [accessed 26.10.2018]. Available on: [https://apps.who.int/iris/bitstream/handle/10665/148114/9789241564854\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/148114/9789241564854_eng.pdf)
39. Ueda Y, Ogasawara N, Matsuo K, Hirotani S, Kashiwase K, Hirata A, et al. Acute coronary syndrome: insight from angioscopy. *Circ J*. 2010;74(3):411-7.
40. Hicks KA, Tchong JE, Bozkurt B, Chaitman BR, Cutlip DE, Farb A, et al. 2014 ACC/AHA key data elements and definitions for cardiovascular endpoint events in clinical trials: A report of the American College of Cardiology/American Heart association task force on clinical data standards (Writing Committee to Develop Cardiovascular Endpoints Data Standards). *J Am Coll Cardiol*. 2015 Jul 28;66(4):403-69.
41. Reichlin T, Hochholzer W, Bassetti S, et al. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. *N Engl J Med*. 2009 Aug 27;361(9):858-67.

42. Keller T, Zeller T, Ojeda F, Steuer S, Stelzig C, Hartwiger S, et al. Serial changes in highly sensitive troponin I assay and early diagnosis of myocardial infarction. *JAMA*. 2011;306(24):2684-93.
43. Than M, Cullen L, Aldous S, Parsonage WA, Reid CM, Greenslade J, et al. 2-Hour accelerated diagnostic protocol to assess patients with chest pain symptoms using contemporary troponins as the only biomarker: the ADAPT trial. *J Am Coll Cardiol*. 2012 Jun 5;59(23):2091-8.
44. Landesberg G, Shatz V, Akopnik I, Wolf YG, Mayer M, Berlatzky Y, et al. Association of cardiac troponin, CK-MB, and postoperative myocardial ischemia with long-term survival after major vascular surgery. *J Am Coll Cardiol*. 2003 Nov 5;42(9):1547-54.
45. Nishi FA, de Motta Maia FO. Assessing sensitivity and specificity of the Manchester Triage System in the evaluation of acute coronary syndrome in adult patients in emergency care: a systematic review protocol. *JBIC Database System Rev Implement Rep*. 2015 Nov;13(11):64-73.
46. Granger CB, Goldberg RJ, Dabbous O, Pieper KS, Eagle KA, Cannon CP, et al. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med*. 2003 Oct 27;163(19):2345-53.
47. Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. *JAMA*. 2000 Aug 16;284(7):835-42.
48. Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. *JAMA*. 2001 Apr 4;285(13):1711-8.
49. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med*. 2004 Apr 8;350(15):1495-504.

50. Reiter M, Twerenbold R, Reichlin T, Haaf P, Peter F, Meissner J, et al. Early diagnosis of acute myocardial infarction in the elderly using more sensitive cardiac troponin assays. *Eur Heart J*. 2011 Feb 28;32(11):1379-89.
51. Schiele F, Meneveau N, Seronde MF, Chopard R, Descotes-Genon V, Dutheil J, et al. C-reactive protein improves risk prediction in patients with acute coronary syndromes. *Eur Heart J*. 2009 Jul 4;31(3):290-7.
52. Carlton EW, Khattab A, Greaves K. Identifying patients suitable for discharge after a single-presentation high-sensitivity troponin result: a comparison of five established risk scores and two high sensitivity assays. *Ann Emerg Med*. 2015 Dec 1;66(6):635-45.
53. Zubaid M, Rashed WA, Al-Khaja N, Almahmeed W, Al-Lawati J, Sulaiman K, et al. Clinical presentation and outcomes of acute coronary syndromes in the gulf registry of acute coronary events (Gulf RACE). *Saudi Med J*. 2008 Feb;29(2):251-5.
54. Lev EI, Kornowski R, Vaknin-Assa H, Porter A, Teplitsky I, Ben-Dor I, et al. Comparison of the predictive value of four different risk scores for outcomes of patients with ST-elevation acute myocardial infarction undergoing primary percutaneous coronary intervention. *Am J Cardiol*. 2008 Jul 1;102(1):6-11.
55. Elbarouni B, Goodman SG, Yan RT, Welsh RC, Kornder JM, DeYoung JP, et al. Validation of the global registry of acute coronary event (GRACE) risk score for in hospital mortality in patients with acute coronary syndrome in Canada. *Am Heart J*. 2009 Sep 1;158(3):392-9.
56. Pieper KS, Gore JM, FitzGerald G, Granger CB, Goldberg RJ, Steg G, et al. Validity of a risk prediction tool for hospital mortality: the Global Registry of Acute Coronary Events. *Am Heart J*. 2009 Jun 1;157(6):1097-105.
57. Ishida M, Itoh T, Nakajima S, Ishikawa Y, Shimoda Y, Kimura T, et al. A low early high-density lipoprotein cholesterol level is an independent predictor of in-hospital death in patients with acute coronary syndrome. *Internal Medicine*. 2019 Feb 1;58(3):337-43.

58. Barcan A, Kovacs I, Blendea C, Orzan M, Chitu M. Factors associated with in-hospital mortality in patients with acute coronary syndrome. *Journal of Cardiovascular Emergencies*. 2015 Dec 1;1(2):68-74.
59. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB III, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). *JAm Coll Cardiol*. 2006;47:e1-121.
60. Meier P, Lansky AJ, Baumbach A. Almanac 2013: acute coronary syndromes. *Cardiologia Croatica*. 2013 Dec 17;8(12):424-34.
61. Iqbal J, Fox KA. Epidemiological trends in acute coronary syndromes: understanding the past to predict and improve the future. *Arch Med Sci*. 2010;6, 1A:S3-S14.
62. Tan NS, Yan AT. From mars to venus: gender differences in the management and outcomes of acute coronary syndromes. *Curr Pharm Des*. 2016;22:3790-801. doi : 10.2174/1381612822666160328113831.
63. Zachariasse JM, Seiger N, Rood PP, Alves CF, Freitas P, Smit FJ, et al. Validity of the Manchester Triage System in emergency care: A prospective observational study. *PLoS One*. 2017 Feb 2;12(2):e0170811.
64. Lefebvre CW, Hoekstra J. Approach to non-ST-segment elevation acute coronary syndrome in the emergency department: risk stratification and treatment strategies. *Hosp Pract (1995)*. 2010 Apr;38(2):40-9
65. Tang EW, Wong CK, Herbison P. Global Registry of Acute Coronary Events (GRACE) hospital discharge risk score accurately predicts long term mortality post-acute coronary syndrome. *Am Heart J*. 2007;153: 29–35.
66. Brezinov OP, Klempfner R, Zekry SB, Goldenberg I, Kuperstein R. Prognostic value of ejection fraction in patients admitted with acute coronary syndrome: A real world study. *Medicine*. 2017 Mar;96(9).

67. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32(23):2999-3054.
68. Bredmose PP, Hoybjor S, Sjoborg KA, Wisborg T. Prehospital thrombolysis in acute myocardial infarction in a very sparsely inhabited area in northern Norway. *Eur J Emerg Med*. 2003; 10:176-9.
69. Weaver WD, Cerqueira M, Hallstrom AP, Litwin PE, Martin JS, Kudenchuk PJ, et al. Prehospital-initiated vs hospital-initiated thrombolytic therapy. The Myocardial Infarction Triage and Intervention Trial. *JAMA*. 1993; 270:1211-6.
70. Leizorovicz A, Haugh MC, Mercier C, Boissel JP. Pre-hospital and hospital time delays in thrombolytic treatment in patients with suspected acute myocardial infarction. Analysis of data from the EMIP study. European Myocardial Infarction Project. *Eur Heart J*. 1997; 18:248-53.
71. Caldwell MA, Miaskowski C. Mass media interventions to reduce help-seeking delay in people with symptoms of acute myocardial infarction: time for a new approach? *Patient Educ Couns*. 2002 Jan 1;46(1):1-9.
72. Kildemoes HW, Kristiansen IS. Cost-effectiveness of interventions to reduce the thrombolytic delay for acute myocardial infarction. *Int J Technol Assess Health Care*. 2004; 20:368-74.
73. Goldstein P, Wiel E. Management of prehospital thrombolytic therapy in ST-segment elevation acute coronary syndrome (<12 hours). *Minerva Anestesiol* 2005; 71:297-302.
74. Zed PJ, Abu-Laban RB, Cadieu TM, Pursell RA, Filiatrault L. Fibrinolytic administration for acute myocardial infarction in a tertiary ED: factors associated with an increased door-to-needle time. *Am J Emerg Med*. 2004 May; 22(3):192-6.

75. Thomas TL. Developing and implementing emergency medicine programs globally. *Emerg Med Clin North Am.* 2005 Feb;23(1):177-97.
76. Kosovo Agency of Statistics. Kosovo in Figures 2021. Prishtina 2022. <https://ask.rks.gov.net/media/6975/kosovo-in-figures-2021.pdf> checked 06.10.2022
77. Eliades MJ, Lis J, Barbosa J, VanRooyen MJ. Post-war Kosovo: Part 2. Assessment of emergency medicine leadership development strategy. *Prehosp Disaster Med.* 2001 Oct-Dec;16(4):268-74.
78. Lis J, Eliades MJ, Benishi D, Koci B, Gettle D, VanRooyen MJ. Post-war Kosovo: Part 3. Development and rehabilitation of emergency services. *Prehosp Disaster Med.* 2001 Oct-Dec;16(4):275-80.
79. Vanier VK, VanRooyen MJ, Lis J, Eliades MJ. Post-war Kosovo: Part 1. Assessment of prehospital emergency services. *Prehosp Disaster Med.* 2001; 16:263-7.
80. Sephehrvand N, Alemayehu W, Kaul P, Pelletier R, Bello AK, Welsh RC, et al. Ambulance use, distance and outcomes in patients with suspected cardiovascular disease: a registry-based geographic information system study. *European Heart Journal: Acute Cardiovascular Care.* 2020 Mar 1;9(1\_suppl):45-58.
81. Bajraktari G, Thaqi K, Pacolli S, Gjoka S, Rexhepaj N, Daullxhiu I, et al. In-hospital mortality following acute myocardial infarction in Kosovo: a single center study. *Ann Saudi Med.* 2008 Nov-Dec;28(6):430-4.
82. Steg PG, James SK, Atar D, Badano LP, Lundqvist CB, Borger MA, et al. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). *Eur Heart J* 2012; 33:2569–2619.
83. Goodman SG, Huang W, Yan AT, Budaj A, Kennelly BM, Gore JM, et al. The expanded Global Registry of Acute Coronary Events: baseline characteristics, management



practices, and hospital outcomes of patients with acute coronary syndromes. *Am Heart J* 2009; 158:193–201, e1–5.

84. Puymirat E, Simon T, Steg PG, Schiele F, Gueret P, Blanchard D, et al. Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction. *Jama*. 2012 Sep 12;308(10):998-1006.
85. Widimsky P, Wijns W, Fajadet J, de Belder M, Knot J, Aaberge L, et al. Reperfusion therapy for ST elevation acute myocardial infarction in Europe: description of the current situation in 30 countries. *Eur Heart J* 2010; 31:943–957.
86. Mirić D, Novak K, Kovacević LM, Zanchi J. In-hospital mortality of patients with acute myocardial infarction before and after introduction of PCI in Split university hospital center, Croatia. *Coll Antropol*. 2013 Mar;37(1):207-12.
87. Kristensen SD, Laut KG, Fajadet J, Kaifoszova Z, Kala P, Di Mario C, et al. Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: current status in 37 ESC countries. *European heart journal*. 2014 Aug 1;35(29):1957-70. <https://doi.org/10.1093/eurheartj/eh529>
88. The Health Care Blog [Internet]. Prishtinë: Evropa e lirë. 1 March 2018 - [accessed on 20.02.2022.]. Available on: <https://www.evropaelire.org/a/29071031.html>
89. Widimsky P, Wijns W, Kaifoszova Z. Stent for Life: how this initiative began?. *Eurointervention: Journal of Europe in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology*. 2012 Aug 1;8:P8-10.
90. Jorgova J, Kanakakis J, Ostojic M, Pereira H, Sabate M, Sobhy M, et al. Implementation of primary angioplasty in Europe: stent for life initiative progress report, *EuroIntervention*, 2012;8 (1): 35-42
91. Kristensen SD, Laut KG, Fajadet J, Kaifoszova Z, Kala P, Di Mario C, et al. Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: current status in 37 ESC countries. *European heart journal*. 2014 Aug 1;35(29):1957-70.

92. Widimsky P, Wijns W, Fajadet J, de Belder M, Knot J, Aaberge L, et al. Reperfusion therapy for ST elevation acute myocardial infarction in Europe: description of the current situation in 30 countries. *Eur Heart J*. 2010 Apr 1;31(8):943-57.
93. Kristensen SD, Laut KG, Fajadet J, Kaifoszova Z, Kala P, Di Mario C, et al; European Association for Percutaneous Cardiovascular Interventions. Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: current status in 37 ESC countries. *Eur Heart J*. 2014; 35:1957–70. pmid:24419804 *Eur Heart J*. 2014 Aug 1;35(29):1957-70. doi: 10.1093/eurheartj/eh529.
94. Jacobs AK, Antman EM, Ellrodt G, Faxon DP, Gregory T, Mensah GA, et al. Recommendation to develop strategies to increase the number of ST-segment-elevation myocardial infarction patients with timely access to primary percutaneous coronary intervention. *Circulation*. 2006 May 2;113(17):2152-63. doi: 10.1161/CIRCULATIONAHA.106.174477.
95. Nallamothu BK, Krumholz HM, Peterson ED, Pan W, Bradley E, Stern AF, et al. Door-to-balloon times in hospitals within the get-with-the-guidelines registry after initiation of the door-to-balloon (D2B) Alliance. *Am J Cardiol*. 2009 Apr 15;103(8):1051-5.
96. Krumholz HM, Bradley EH, Nallamothu BK, Ting HH, Batchelor WB, Kline-Rogers E, et al. A campaign to improve the timeliness of primary percutaneous coronary intervention—Door-to-Balloon: An Alliance for Quality. *JACC Cardiovasc Interv*. 2008 Feb;1(1):97-104.
97. Zeymer U, Ludman P, Danchin N, Kala P, Maggioni AP, Weidinger F. Background and design of the ACCA–EAPCI registry on ST-segment elevation myocardial infarction of the European Society of Cardiology. *Eur Heart J: Acute Cardiovascular Care*. 2019 Feb 1;8(1):63-7.
98. Otto Q, Nolan JP, Chamberlain DA, Cummins RO, Soar J. Utstein Style for emergency care—the first 30 years. *Resuscitation*. 2021 Jun 1;163:16-25.

99. Sarkees ML, Bavry AA. Acute coronary syndrome (unstable angina and non-ST elevation MI). *BMJ Clin Evid* (Online). 2009 Jan 13;2009.
100. Zeymer U, Ludman P, Danchin N, Kala P, Laroche C, Sadeghi M, et al. Reperfusion therapies and in-hospital outcomes for ST-elevation myocardial infarction in Europe: the ACVC-EAPCI EORP STEMI Registry of the European Society of Cardiology. *Eur Heart J*. 2021 Nov 21;42(44):4536-4549. doi: 10.1093/eurheartj/ehab342.
101. Zanchi J, Mirić D, Giunio L, Vuković I, Marković B, Duplancić D, et al. Gender differences in in-hospital mortality and angiographic findings of patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI). *Coll Antropol*. 2009 Dec;33(4):1359-62.
102. Dittrich H, Gilpin E, Nicod P, Cali G, Henning H, Ross J. Acute myocardial infarction in women: influence of gender on mortality and prognostic variables. *Am J Cardiol*. 1988 Jul 1;62(1):1-7.
103. Mega JL, Hochman JS, Scirica BM, Murphy SA, Sloan S, McCabe CH et al. Clinical features and outcomes of women with unstable ischemic heart disease: observations from metabolic efficiency with ranolazine for less ischemia in non-ST-elevation acute coronary syndromes-thrombolysis in myocardial infarction 36 (MERLIN-TIMI 36). *Circulation*. 2010 Apr 27;121(16):1809-17.
104. Canto JG, Rogers WJ, Goldberg RJ, Peterson ED, Wenger NK, Vaccarino V, et al. NRMIs Investigators. Association of age and sex with myocardial infarction symptom presentation and in-hospital mortality. *JAMA*. 2012;307(8):813–822.
105. Tofler GH, Stone PH, Muller JE, Willich SN, Davis VG, Poole WK, et al. Effects of gender and race on prognosis after myocardial infarction: adverse prognosis for women, particularly black women. *J Am Coll Cardiol*. 1987;9(3):473–482.
106. Bell DM, Nappi J. Myocardial infarction in women: a critical appraisal of gender differences in outcomes. *Pharmacotherapy*. 2000;20(9):1034–1044.

107. Novak K, Vrdoljak D, Jelaska I, Borovac JA. Sex-specific differences in risk factors for in-hospital mortality and complications in patients with acute coronary syndromes. *Wiener klinische Wochenschrift*. 2017 Apr 1;129(7-8):233-42.
108. Vaccarino V, Badimon L, Corti R, de Wit C, Dorobantu M, Manfrini O, et al. Presentation, management, and outcomes of ischaemic heart disease in women. *Nat Rev Cardiol*. 2013 Sep;10(9):508-18. doi: 10.1038/nrcardio.2013.93.
109. Buchholz EM, Butala NM, Rathore SS, Dreyer RP, Lansky AJ, Krumholz HM. Sex differences in long-term mortality after myocardial infarction: a systematic review. *Circulation*. 2014 Aug 26;130(9):757-67.
110. Mehta LS, Beckie TM, DeVon HA, Grines CL, Krumholz HM, Johnson MN, et al. Acute myocardial infarction in women: a scientific statement from the American Heart Association. *Circulation*. 2016 Mar 1;133(9):916-47.
111. Berger JS, Elliott L, Gallup D, Roe M, Granger CB, Armstrong PW, et al. Sex differences in mortality following acute coronary syndromes. *JAMA*. 2009 Aug 26;302(8):874-82.
112. Gottlieb S, Harpaz D, Shotan A, Boyko V, Leor J, Cohen M, et al. Sex differences in management and outcome after acute myocardial infarction in the 1990s: a prospective observational community-based study. *Circulation*. 2000 Nov 14;102(20):2484-90.
113. Bugiardini R, Yan AT, Yan RT, Fitchett D, Langer A, Manfrini O, et al. Canadian Acute Coronary Syndrome Registry I and II Investigators. Factors influencing underutilization of evidence-based therapies in women. *Eur Heart J*. 2011 Jun 1;32(11):1337-44.
114. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al; ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J*. 2020 Jan 7;41(2):255–323. doi: 10.1093/eurheartj/ehz486. Erratum. In: *Eur Heart J*. 2020;41(45):4317.

115. Bugiardini R, Ricci B, Cenko E, Vasiljevic Z, Kedev S, Davidovic G, et al. Delayed care and mortality among women and men with myocardial infarction. *Journal of the American Heart Association*. 2017 Aug 21;6(8): e005968.
116. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, et al; ACC/AHA Task Force Members. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130(25): e344-426. Erratum in: *Circulation*. 2014;130(25): e433-4.
117. D.Y. Kim, Z. Wala, S. Islam, R. Islam, M. Ahn Clinical characteristics and outcomes of ST-segment elevation myocardial infarction in a low income setting in rural Bangladesh *Int J Cardiol Heart Vasc.*, 17 (23) (2019 May), doi: 10.1016/j.ijcha.2019.100376.
118. Doddipalli SR, Rajasekhar D, Vanajakshamma V, Naik KS. Determinants of total ischemic time in primary percutaneous coronary interventions: A prospective analysis. *Indian Heart J* 2018 Dec 1;70:S275-9.
119. Mohan B, Bansal R, Dogra N, Sharma S, Chopra A, Varma S, Bansal N, Tandon R, Goyal A, Singh B, Chhabra ST. Factors influencing prehospital delay in patients presenting with ST-elevation myocardial infarction and the impact of prehospital electrocardiogram. *Indian Heart J* 2018 Dec 1;70:S194-8.
120. Medagama, R. Bandara, C. De Silva, M.P. Galgomuwa. Management of acute coronary syndromes in a developing country; time for a paradigm shift? An observational study. *BMC Cardiovasc Disord.*, 15 (2015), p. 133 doi: 10.1186/s12872-015-0125-y.
121. Valent F, Di Chiara A. Use of emergency medical service in acute myocardial infarction in an Italian Northeastern region. *Journal of Public Health*. 2021 Jan 6:1-9.
122. So DY, Ha AC, Turek MA, Maloney JP, Higginson LA, Davies RF, et al. Comparison of mortality patterns in patients with ST-elevation myocardial infarction arriving by emergency medical services versus self-transport (from the prospective Ottawa Hospital STEMI Registry). *The American journal of cardiology*. 2006 Feb 15;97(4):458-61.

123. Boothroyd LJ, Lambert LJ, Segal E, Ross D, Kouz S, Maire S, et al. Comparison of outcomes of ambulance users and nonusers in ST elevation myocardial infarction. *The American journal of cardiology*. 2014 Nov 1;114(9):1289-94.
124. Kodama N, Nakamura T, Yanishi K, Nakanishi N, Zen K, Yamano T, et al. Impact of Door-to-Balloon Time in Patients With ST-Elevation Myocardial Infarction Who Arrived by Self-Transport—Acute Myocardial Infarction-Kyoto Multi-Center Risk Study Group—. *Circulation Journal*. 2017 Oct 25;81(11):1693-8.
125. Bosia T, Malinowska A, Weigel K, Schmid F, Nickel CH, Bingisser R. Risk of adverse outcome in patients referred by emergency medical services in Switzerland. *Swiss medical weekly*. 2017 Nov 23;147(4748).
126. Canto JG, Rogers WJ, Bowlby LJ, French WJ, Pearce DJ, Weaver WD. The prehospital electrocardiogram in acute myocardial infarction: is its full potential being realized?. *Journal of the American College of Cardiology*. 1997 Mar 1;29(3):498-505.
127. Shavelle DM, Chen AY, Matthews RV, Roe MT, de Lemos JA, Jollis J, et al. ACTION-GWTG Investigators. Predictors of reperfusion delay in patients with ST elevation myocardial infarction self-transported to the hospital (from the American Heart Association's Mission: Lifeline Program). *Am J Cardiol*. 2014 Mar 1;113(5):798-802
128. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. *Circulation*. 2015 Jan 27;131(4):e29-322.
129. de Labriolle A, Pacouret G, Giraudeau B, Fremont B, Desveaux B, Quilliet L, et al. Effect of time to treatment and age on one year mortality in acute STEMI: difference between thrombolysis and primary percutaneous coronary intervention. *Arch Cardiovasc Dis*. 2008;101(1):48-54.
130. Schömig A, Ndrepepa G, Mehilli J, Schwaiger M, Schühlen H, Nekolla S, et al. Therapy-dependent influence of time-to-treatment interval on myocardial salvage in patients with acute myocardial infarction treated with coronary artery stenting or thrombolysis. *Circulation*. 2003;108(9):1084-8.

131. Tataris KL, Mercer MP, Govindarajan P. Prehospital aspirin administration for acute coronary syndrome (ACS) in the USA: an EMS quality assessment using the NEMSIS 2011 database. *Emerg Med J.* 2015;32(11):876-81.
132. Sullivan AL, Beshansky JR, Ruthazer R, Murman DH, Mader TJ, Selker HP. Factors associated with longer time to treatment for patients with suspected acute coronary syndromes: a cohort study. *Circ Cardiovasc Qual Outcomes.* 2014;7(1):86-94.
133. Thuresson M, Jarlöv MB, Lindahl B, Svensson L, Zedigh C, Herlitz J. Factors that influence the use of ambulance in acute coronary syndrome. *Am Heart J.* 2008 Jul;156(1):170-6.
134. Ma J, Wang J, Zheng W, Zheng J, Wang H, Wang G, et al. Usage of ambulance transport and influencing factors in acute coronary syndrome: a cross-sectional study at a tertiary centre in China. *BMJ Open.* 2017 Aug 21;7(8): e015809.
135. Cartledge S, Finn J, Straney L, Ngu P, Stub D, Patsamanis H, et al. The barriers associated with emergency medical service use for acute coronary syndrome: the awareness and influence of an Australian public mass media campaign. *Emerg Med J.* 2017 Jul;34(7): 466-471.
136. McLean S, O'Reilly M, Doyle M, Rathaille M. Improving Door-to-Drug time and ST segment resolution in AMI by moving thrombolysis administration to the Emergency Department. *Accid Emerg Nurs.* 2004 January; 12(1):2-9.
137. Muller LA, Rabelo ER, Moraes MA, Azzolin K. Delay factors on the administration of thrombolytic therapy in patients diagnosed with acute myocardial infarction in a general hospital. *Rev Lat Am Enfermagem.* 2008 Jan-Feb;16(1):52-6.
138. Goodacre S, Kelly AM, Kerr D. Potential impact of interventions to reduce times to thrombolysis. *Emerg Med J.* 2004 September; 21(5):625-9.
139. Chew KS, Wan WM, Nik NH, Mohd FH, Shaik AF, Tuan TH, et al. A survey on the choice of transportation to come to emergency department among patients with acute coronary syndrome of a community in Malaysia. *Med J Malaysia.* 2015 Feb;70(1):6-11.

140. McKee G, Mooney M, O'Donnell S, O'Brien F, Biddle MJ, Moser DK. Multivariate analysis of predictors of pre-hospital delay in acute coronary syndrome. *Int J Cardiol.* 2013 Oct 3;168(3):2706-13.
141. Fares S, Zubaid M, Al-Mahmeed W, Ciottone G, Sayah A, Al Suwaidi J, et al. Utilization of emergency medical services by patients with acute coronary syndromes in the Arab Gulf States. *J Emerg Med.* 2011 Sep 1;41(3):310-6.
142. Brown AL, Mann NC, Daya M, Goldberg R, Meischke H, Taylor J, et al. Demographic, belief, and situational factors influencing the decision to utilize emergency medical services among chest pain patients. *Circulation.* 2000 Jul 11;102(2):173-8.
143. Thuresson M, Jarlöv MB, Lindahl B, Svensson L, Zedigh C, Herlitz J. Factors that influence the use of ambulance in acute coronary syndrome. *Am Heart J.* 2008 Jul 1;156(1):170-6.
144. Meischke H, Eisenberg MS, Schaeffer SM, Damon SK, Larsen MP, Henwood DK. Utilization of emergency medical services for symptoms of acute myocardial infarction. *Heart Lung.* 1995;24 (1):11–18.
145. Miedema MD, Newell MC, Duval S, Garberich RF, Handran CB, Larson DM, et al. Causes of delay and associated mortality in patients transferred with ST-segment–elevation myocardial infarction. *Circulation.* 2011 Oct 11;124(15):1636-44.
146. Perkins-Porras L, Whitehead DL, Strike PC, Steptoe A. Pre-hospital delay in patients with acute coronary syndrome: factors associated with patient decision time and home-to-hospital delay. *Eur J Cardiovasc Nurs.* 2009 Mar 1;8(1):26-33.
147. Goodacre SW, Bradburn M, Cross E, Collinson P, Gray A, Hall AS. The Randomised Assessment of Treatment using Panel Assay of Cardiac Markers (RATPAC) trial: a randomised controlled trial of point-of-care cardiac markers in the emergency department. *Heart.* 2011 Feb 1;97(3):190-6.
148. Nallamothu BK, Bradley EH and Krumholz HM. Time to treatment in primary percutaneous coronary intervention. *N Engl J Med* 2007; 357: 1631–1638.



149. Brunetti, N.D., Di Pietro, G., Aquilino, A., Bruno, A.I., Dellegrottaglie, G., Di Giuseppe, G., et al. Pre-hospital electrocardiogram triage with tele-cardiology support is associated with shorter time-to-balloon and higher rates of timely reperfusion even in rural areas: data from the Bari–Barletta/Andria/ Trani public emergency medical service 118 registries on primary angioplasty in ST-elevation myocardial infarction. *Eur Heart J Acute Cardiovasc Care*. 2014 Sep 1;3(3):204-13.
150. Callachan EL, Alsheikh-Ali AA, Nair SC, Bruijns S, Wallis LA. Outcomes by mode of transport of ST elevation MI patients in the United Arab Emirates. *West J Emerg Med* 2017 Apr;18(3):349-355.
151. Farshid A, Allada C, Chandrasekhar J, Marley P, McGill D, O'Connor S, et al. Shorter ischaemic time and improved survival with pre-hospital STEMI diagnosis and direct transfer for primary PCI. *Heart Lung Circ* 2015 Mar 1;24(3):234-40.
152. Kahlon TS, Barn K, Akram MM, Blankenship JC, Bower-Stout C, Carey DJ, et al. Impact of pre-hospital electrocardiograms on time to treatment and one year outcome in a rural regional ST-segment elevation myocardial infarction network. *Catheter Cardiovasc Interv* 2017 Feb 1;89(2):245-51.
153. O'Connor RE, Brady W, Brooks SC, Diercks D, Egan J, Ghaemmaghami C, Menon V, O'Neil BJ, Travers AH, Yannopoulos D. Part 10: acute coronary syndromes: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010 Nov 2;122(18\_suppl\_3):S787-817.
154. Mohanan PP, Mathew R, Harikrishnan S, Krishnan MN, Zachariah G, Joseph J, et al. Presentation, management, and outcomes of 25 748 acute coronary syndrome admissions in Kerala, India: results from the Kerala ACS Registry. *Eur Heart J* 2013 Jan 7;34(2):121-9.
155. Krumholz HM, Anderson JL, Bachelder BL, Fesmire FM, Fihn SD, Foody JM, et al; American College of Cardiology/American Heart Association Task Force on Performance Measures; American Academy of Family Physicians; American College of Emergency Physicians; American Association of Cardiovascular and Pulmonary Rehabilitation; Society for Cardiovascular Angiography and Interventions; Society of Hospital Medicine. ACC/AHA

2008 performance measures for adults with ST-elevation and non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures (Writing Committee to develop performance measures for ST-elevation and non-ST-elevation myocardial infarction): developed in collaboration with the American Academy of Family Physicians and the American College of Emergency Physicians: endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, Society for Cardiovascular Angiography and Interventions, and Society of Hospital Medicine. *Circulation*. 2008;118(24):2596-648.

156. Novak K, Aljinović J, Kostić S, Čapkun V, Novak Ribičić K, Batinić T, et al. Pain to hospital times after myocardial infarction in patients from Dalmatian mainland and islands, southern Croatia. *Croat Med J*. 2010;51(5):423–431.
157. Dong S, Chu Y, Zhang H, Wang Y, Yang X, Yang L, et al. Reperfusion times of ST-Segment elevation myocardial infarction in hospitals. *Pak J Med Sci*. 2014 Nov-Dec;30(6):1367-71.
158. Walkiewicz M, Krówczyńska D, Kuchta U, Kmiećicka M, Kurjata P, Stepieńska J. Acute coronary syndrome--how to reduce the time from the onset of chest pain to treatment? *Kardiol Pol*. 2008 Nov; 66(11):1163-70; discussion 1171-2.
159. Jankowski P, Bednarek A, Surowiec S, Loster M, Pająk A, Kawecka-Jaszcz K. Half of coronary patients are not instructed how to respond to symptoms of a heart attack. *Cardiol J*. 2011;18(6):668–674.
160. Nguyen HL, Saczynski JS, Gore JM, Goldberg RJ. Age and sex differences in duration of prehospital delay in patients with acute myocardial infarction: a systematic review. *Circ Cardiovasc Qual Outcomes*. 2010 Jan;3(1):82-92.
161. Rucker D, Brennan T, Burstin H. Delay in seeking emergency care. *Acad Emerg Med*. 2001 Feb;8(2):163-9.

162. Ting HH, Rihal CS, Gersh BJ, Haro LH, Bjerke CM, Lennon RJ, et al. Regional systems of care to optimize timeliness of reperfusion therapy for ST-elevation myocardial infarction: the Mayo Clinic STEMI Protocol. *Circulation*. 2007 Aug 14;116(7):729-36.
163. Al Bugami S, Alrahihi J, Almalki A, Alamger F, Krimly A, Al Kashkari W. ST-Segment Elevation Myocardial Infarction: Door to Balloon Time Improvement Project. *Cardiol Res*. 2016 Aug;7(4):152-156.
164. Wilson BH, Humphrey AD, Cedarholm JC, Downey WE, Haber RH, Kowalchuk GJ, et al. Achieving sustainable first door-to-balloon times of 90 minutes for regional transfer ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv*. 2013 Oct;6(10):1064-71.
165. Nguyen B, Fennessy M, Leya F, Nowak W, Ryan M, Freeberg S, et al. Comparison of primary percutaneous coronary intervention in patients with ST elevation myocardial infarction during and prior to availability of an in house STEMI system: Early experience and intermediate outcomes of the HARRT program for achieving routine D2B times < 60 minutes. *Catheter Cardiovasc Interv*. 2015 Aug;86(2):186-96.
166. Chen CC, Chiu IM, Cheng FJ, Wu KH, Li CJ. The impact of prolonged waiting time for coronary care unit admission on patients with non ST-elevation acute coronary syndrome. *Am J Emerg Med*. 2017 Aug 1;35(8):1078-81.
167. Bugiardini R, Cenko E, Ricci B, Vasiljevic Z, Dorobantu M, Kedev S, et al. Comparison of early versus delayed oral  $\beta$  blockers in acute coronary syndromes and effect on outcomes. *Am J Cardiol*. 2016 Mar 1;117(5):760-7.
168. Heitzler VN, Babić Z, Miličić D, Starčević B, Mirat J, Strozzi M, et al. Evaluation of importance of door-to-balloon time and total ischemic time in acute myocardial infarction with ST-elevation treated with primary percutaneous coronary intervention. *Acta Clin Croat*. 2012 Sep;51(3):387-95.
169. Khan A, Phadke M, Lokhandwala YY, Nathani PJ. A study of prehospital delay patterns in acute myocardial infarction in an urban tertiary care institute in Mumbai. *J Assoc Physicians India*. 2017 May 1;65(5):24-7.

170. El-Menyar A, Zubaid M, Shehab A, Bulbanat B, AlBustani N, Alenezi F, et al. Prevalence and impact of cardiovascular risk factors among patients presenting with acute coronary syndrome in the middle East. *Clin Cardiol.* 2011 Jan;34(1):51-8.
171. Kleiman NS, Lakkis N, Cannon CP, Murphy SA, DiBattiste PM, Demopoulos LA, et al. Prospective analysis of creatine kinase muscle-brain fraction and comparison with troponin T to predict cardiac risk and benefit of an invasive strategy in patients with non-ST-elevation acute coronary syndromes. *J Am Coll Cardiol.* 2002; 40:1044-50.
172. Franzosi MG, Santoro E, Zuanetti G, Baigent C, Collins R, Flather M, et al. Indications for ACE inhibitors in the early treatment of acute myocardial infarction-Systematic overview of individual data from 100,000 patients in randomized trials. *Circulation.* 1998 Jun 9;97(22):2002-12.
173. Hall AS, Murray GD, Ball SG. Follow-up study of patients randomly allocated ramipril or placebo for heart failure after acute myocardial infarction: AIRE extension (AIREX) Study. Acute infarction Ramipril efficacy. *Lancet.* 1997 May 24; 349 (9064):1493-7.
174. Labarthe DR, Dunbar SB. Global cardiovascular health promotion and disease prevention: 2011 and beyond. *Circulation.* 2012 May 29;125(21):2667–2676.
175. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet.* 2014 Aug 30;384(9945):766–781.
176. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract.* 2010 Jan 1;87(1):4–14.
177. Poljicanin T, Dzakula A, Milanović SM, Sekerija M, Ivanković D, Vuletić S. The changing pattern of cardiovascular risk factors: the CroHort study. *Coll Antropol.* 2012 Jan 2;36(Suppl 1):9–13.
178. Bartnik M, Ryden L, Ferrari R, Malmberg K, Pyorala K, Simoons M, et al. The prevalence of abnormal glucose regulation in patients with coronary artery disease across

- Europe. The Euro Heart Survey on diabetes and the heart. *Eur Heart J*. 2004;25(21):1880–1890. doi: 10.1016/j.ehj.2004.07.027.
179. Borch-Johnsen K, Neil A, Balkau B, Larsen S, Nissinen A, Pekkanen J, et al. Glucose tolerance and cardiovascular mortality: comparison of fasting and 2-hour diagnostic criteria. *Arch Intern Med*. 2001;161(3):397–405. doi: 10.1001/archinte.161.3.397.
180. Barr EL, Zimmet PZ, Welborn TA, Jolley D, Magliano DJ, Dunstan DW, et al. Risk of cardiovascular and all-cause mortality in individuals with diabetes mellitus, impaired fasting glucose, and impaired glucose tolerance: the Australian Diabetes, Obesity, and Lifestyle Study (AusDiab) *Circulation*. 2007;116(2):151–157.
181. Alhabib KF, Sulaiman K, Al-Motarreb A, Almahmeed W, Asaad N, Amin H, et al. Baseline characteristics, management practices, and long-term outcomes of Middle Eastern patients in the Second Gulf Registry of Acute Coronary Events (Gulf RACE-2) *Ann Saudi Med*. 2012;32(1):9–18.
182. Tsai CL, Magid DJ, Sullivan AF, Gordon JA, Kaushal R, Michael Ho P, et al. Quality of care for acute myocardial infarction in 58 U.S. emergency departments. *Acad Emerg Med*. 2010 Sep;17(9):940-50.
183. Buclin T, Van Melle G, Haller E, Yersin B, Berger JP. Diagnosis, clinical presentation and triage criteria of emergency patients admitted for chest pain: prospective study of 278 cases. *Schweiz Med Wochenschr*. 1988 Dec 17;118(50):1921-5.)
184. Tanzi P, Pelliccia F. Management of acute chest pain in the emergency department. *G Ital Cardiol (Rome)*. 2006 Mar;7(3):165-75.
185. Schewe JC, Kappler J, Dovermann K, Graeff I, Ehrentraut SF, Heister U, et al. Diagnostic accuracy of physician-staffed Emergency medical teams: a retrospective observational cohort study of prehospital versus hospital diagnosis in a 10-year interval. *Scand J Trauma Resusc Emerg Med*. 2019 Apr 2;27(1):36.

186. Hess EP, Wells GA, Jaffe A, Stiell IG. A study to derive a clinical decision rule for triage of emergency department patients with chest pain: design and methodology. *BMC Emerg Med.* 2008 Dec;8(1):1-0.
187. Gilutz H, Shindel S, Shoham-Vardi I. Adherence to NSTEMI Guidelines in the Emergency Department: Regression to Reality. *Crit Pathw Cardiol.* 2019 Mar;18(1):40-46.
188. Homma H, Niiyama Y, Sonoda H, Himuro N, Yamakage M. The Impact of Air Transport for Acute Coronary Syndrome Patients. *Air Med J.* 2019 Mar - Apr;38(2):73-77.
189. Kaul P, Ezekowitz JA, Armstrong PW, Leung BK, Savu A, Welsh RC, et al. Incidence of heart failure and mortality after acute coronary syndromes. *Am Heart J.* 2013 Mar;165(3):379-85. e2.
190. Piva e Mattos LA, Berwanger O, Santos ES, Reis HJ, Romano ER, Petriz JL, et al. Clinical outcomes at 30 days in the Brazilian Registry of Acute Coronary Syndromes (ACCEPT). *Arq Bras Cardiol.* 2013 Jan;100(1):6-13.
191. Santos ES, Timerman A, Baltar VT, Castillo MT, Pereira MP, Minuzzo L, et al. Dante Pazzanese risk score for non-st-segment elevation acute coronary syndrome. *Arq Bras Cardiol.* 2009 Oct;93(4):343-51, 336-44.
192. Heim I, Jonke V, Gostović M, Jembrek-Gostović M. Epidemiology of acute coronary syndrome in the City of Zagreb. *Acta Med Croatica.* 2009 Feb;63(1):105-9.
193. Aune E, Endresen K, Fox KA, Steen-Hansen JE, Roislien J, Hjelmessaeth J, et al. Effect of implementing routine early invasive strategy on one-year mortality in patients with acute myocardial infarction. *The American journal of cardiology.* 2010 Jan 1;105(1):36-42.
194. Brieger DB, Chew DP, Redfern J, Ellis C, Briffa TG, Howell TE, et al. Survival after an acute coronary syndrome: 18-month outcomes from the Australian and New Zealand SNAPSHOT ACS study. *Medical Journal of Australia.* 2015 Nov;203(9):368.

195. Stenestrand U, Wallentin L, Swedish Register of Cardiac Intensive Care Early statin treatment following acute myocardial infarction and 1-year survival. *Jama*. 2001 Jan 24;285(4):430-6.
196. Skelding KA, Boga G, Sartorius J, Wood GC, Berger PB, Mascarenhas VH, et al. Frequency of coronary angiography and revascularization among men and women with myocardial infarction and their relationship to mortality at one year: an analysis of the Geisinger myocardial infarction cohort. *Journal of interventional cardiology*. 2013 Feb;26(1):14-21.
197. Kleopatra K, Muth K, Zahn R, Bauer T, Koeth O, Jünger C, et al. Acute Coronary Syndromes Registry (ACOS) investigators. Effect of an invasive strategy on in-hospital outcome and one-year mortality in women with non-ST-elevation myocardial infarction. *International journal of cardiology*. 2011 Dec 15;153(3):291-5.
198. Ruano-Ravina A, Aldama-Lopez G, Cid-Alvarez B, Pinon-Esteban P, Lopez-Otero D, Calvino-Santos R, et al. Radial vs femoral access after percutaneous coronary intervention for ST-segment elevation myocardial infarction. Thirty-day and one-year mortality results. *Revista Española de Cardiología (English Edition)*. 2013 Nov 1;66(11):871-8.
199. Potočnjak I, Bodrožić-Džakić T, Šmit I, Trbušić M, Milošević M, Degoricija V. Gender-associated differences in acute heart failure patients presenting to emergency department. *Acta Clinica Croatica*. 2015 Nov 1;54(3.):257-65.
200. Hrvatski Zavod za Javno Zdravstvo. Izvješće o umrlim osobama u Hrvatskoj u 2017. godini. Zagreb Rujan 2018. [accessed 12.07.2019]. Available from: [https://www.hzjz.hr/wp-content/uploads/2018/09/Bilten\\_\\_Umrli-\\_2017-2.pdf](https://www.hzjz.hr/wp-content/uploads/2018/09/Bilten__Umrli-_2017-2.pdf)
201. Pocock SJ, Huo Y, Van de Werf F, Newsome S, Chin CT, Vega AM, et al. Predicting two-year mortality from discharge after acute coronary syndrome: An internationally-based risk score. *European Heart Journal: Acute Cardiovascular Care*. 2019 Dec 1;8(8):727-37.

202. McNamara RL, Kennedy KF, Cohen DJ, Diercks DB, Moscucci M, Ramee S, et al. Predicting in-hospital mortality in patients with acute myocardial infarction. *Journal of the American College of Cardiology*. 2016 Aug 9;68(6):626-35.



## **11. CURRICULLUM VITAE**

Musli (Mon) Gashi was born on June 5, 1968 in Osek Hyle – Gjakova, Republic of Kosova. In the school year 1987/88 he enrolled in Medical Faculty brunch general medicine at the University of Prishtina where he graduated on 02.02.1994. Immediately after graduating he worked as a physician at the humanitarian association “Mother Tereza” in Gjakova. On December 1, 1995 he started working as a school doctor in two primary schools in the municipality of Gjakova, where he worked until 01.10.1998. In 1998 he was accepted as assistant at the Faculty of Medicine in Prishtina in the field of Emergency Medicine where is still working. In 2004 he completed master's studies at the Medical Faculty University of Prishtina. In 2010 has enrolled in PhD studies program in English at the School of Medicine, University of Zagreb. Specialization in the field of Emergency Medicine has finished in 2007. During his specialization, he was trained by a team of professors and emergency medicine specialists from John Hopkins University in USA. From 2007 till now is working in Emergency Center in University Clinical Center of Kosova. He is the author and coauthor of several scientific and professional works. Is married, has a son. He lives in Prishtina.