Association between the Incidence of Sudden Cardiac Arrest and the Location of Culprit Lesions in STEMI Patients – Design of a Prospective Clinical Study

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ABSTRACT

Out-of-hospital cardiac arrest (OHCA) has a poor prognosis and is the most severe complication of any cardiac event. It is known from previous studies that the location of the culprit lesion in ST-segment elevation myocardial infarction (STEMI) patients with cardiac arrest may affect the post resuscitation survival rate. However, due to the low number of cases, the association between the localization of the culprit lesion within the coronary tree and the occurrence of cardiac arrest is not widely discussed, because resuscitated cardiac arrest patients are excluded from the vast majority of clinical trials. This is a prospective observational study that aims to develop a prediction model for OHCA in patients who present with STEMI, based on differences related to culprit lesion location. The primary objective of the study is to evaluate the differences related to the location of the culprit lesion in patients with STEMI who present OHCA versus patients without cardiac arrest.

Keywords: cardiac arrest, acute coronary syndromes, culprit lesion, left anterior descending artery

BACKGROUND

Acute myocardial infarction is the most severe manifestation of coronary artery disease, and together with the overall spectrum of ischemic heart diseases, it remains the main cause of mortality worldwide.[1,2] In European countries, the incidence of myocardial infarction ranges from 90 to 312 per 100,000 persons per year.[3] The in-hospital mortality of patients with ST-segment elevation myocardial infarction (STEMI) in European countries varies between 4 to 12%, while the 1-year mortality in case of patients diagnosed with STEMI and treated via angioplasty is around 10%.[4] Older women with STEMI have worse outcomes

compared to older males, and young men are more likely to survive than young women with the same pathology.[5] Advanced age and higher Killip class, longer time until revascularization and treatment strategy, history of myocardial infarction, diabetes mellitus, renal failure, a higher number of affected coronary arteries, and reduced left ventricular ejection fraction (LVEF) increase mortality in STEMI.[4]

Out-of-hospital cardiac arrest

Out-of-hospital cardiac arrest (OHCA) has poor prognosis and is the most severe complication of any cardiac event. The incidence of OHCA in Europe has been estimated at around 275,000 persons per year. The survival rate of OHCA is low; according to different studies, it varies from 11% to 39%.[6,7] Ischemic heart disease is the most frequent cause of OHCA.[8] In patients with resuscitated cardiac arrest complicating STEMI, the six-month survival rate is 54% owing to quick prehospital medical attendance, emergency revascularization, and specific care in the cardiovascular intensive care unit.[9] The factors that can trigger cardiac arrest may be coronary plaque rupture or erosion, or fragmentation and embolization of a thrombus. The survival rate is influenced by gender, hypertension, dyslipidemia, smoking status, age over 59 years, diabetes mellitus, location of arrest at home, and high levels of blood lactate.[7]

The management of cardiopulmonary resuscitation has a relatively low success rate. Therefore, the outcome of resuscitated cases after cardiac arrest with significant coronary stenosis remains poor. Important steps in postresuscitation care include early coronary artery reperfusion, together with other aggressive post-cardiac arrest therapeutic measures, which can double the rate of survival. It is known from previous studies that the location of the culprit lesion in STEMI patients with cardiac arrest may affect the post-resuscitation survival rate. However, due to the low number of cases, the association between the localization of the culprit lesion within the coronary tree and the occurrence of cardiac arrest is not widely discussed, because resuscitated cardiac arrest patients are excluded from the vast majority of clinical trials.[9]

According to current therapeutic guidelines, in case of patients who have electrocardiographic criteria for STEMI, the treatment method is immediate invasive coronary angiography and, if indicated, percutaneous coronary revascularization. Furthermore, immediate coronary angiography is also indicated in all patients with cardiac arrest in whom an acute coronary syndrome is suspected.

The most common localization of the culprit vessel in cardiac arrest survivors is the left anterior descendent artery (LAD) or the right coronary artery (RCA). The left circumflex artery (LCX) is less frequently identified as a culprit vessel, most likely because the area supplemented by the LCX is an electrically silent zone.[10]

The most common acute complication of myocardial infarction that could lead to cardiac arrest is ventricular fibrillation (VF) and extreme bradycardia that leads to asystole. VF generally occurs if the culprit lesion is located on the LAD, because it carries almost 50% of the blood of the coronary circulation, making it the largest coronary artery. Atherosclerosis or thrombotic occlusion of this vessel involves a large area of the anterior, septal, and apical portions of the cardiac muscle, leading to a serious impairment of cardiac performance.[11] LAD occlusion complicated with cardiac arrest due to VF is more likely associated with a favorable resuscitation outcome, because it is a shockable arrhythmia, making it possible to use a defibrillator. The occlusion of the RCA can result in inferior or right ventricular STEMI, often associated with hypotension, bradycardia, or atrioventricular block, which progress gradually from first degree to complete block, being associated with less favorable outcomes following resuscitation. Cardiac arrest caused by VF is associated with better prognosis compared to bradycardia-asystole. At the same time, occlusion of the LAD increases the predisposition for cardiac arrest due to VF, while RCA occlusion more often leads to fatal outcomes. Left ventricular hypertrophy and multivessel coronary disease is more frequent in patients with fatal infarction, due to the fact that this associated disease increases the electrical instability of the myocardium.[12–14]

The role of cardiac magnetic resonance in risk stratification and follow-up of STEMI patients

Cardiac magnetic resonance (CMR) has an important role in risk stratification, treatment, and long-term follow-up of patients with ischemic heart disease, including patients with STEMI. This noninvasive investigation method is the gold standard technique for assessing the structural and functional features of the left ventricle, as well as the volumes and the size of the replacement fibrosis. Myocardial salvage is a strong predictor of major adverse cardiac events (MACE) and clinical events 6 months after infarction.

Infarct size depends on several factors such as collateral blood flow, time, and efficiency of revascularization. Studies have demonstrated that the quantity of myocardial loss is variable, depending on several factors, thus the follow-up of patients with the use of CMR after coronary reper-

fusion is important for risk stratification and guiding the post-infarction therapies.[15]

STUDY HYPOTHESIS

We hypothesized that patients with acute STEMI, who present culprit lesions at the level of the LAD and a degree of stenosis of less than 50%, are more likely to present sudden cardiac arrest in prehospital settings compared to patients with similar lesions located in the LCX or the RCA. Therefore, the aim of the study is to develop a prediction model for OHCA in patients who present with STEMI at 12 hours from the onset of symptoms, based on differences related to culprit lesion location.

OBJECTIVES

The primary objective of the study is to evaluate the differences related to the location of the culprit lesion in patients with STEMI who present OHCA versus patients without cardiac arrest. Secondary objectives include: (1) to evaluate the impact of culprit lesion location within the coronary tree and the myocardial remodeling process, assessed at one month by using CMR imaging; (2) to assess the role of culprit lesion location on the rate of MACE during a follow-up of 6 and 12 months, respectively.

STUDY DESIGN

This is a clinical, prospective, non-randomized, observational study that will be conducted in the Clinic of Cardiology of the Emergency Clinical County Hospital of Târgu Mureş, Romania, in collaboration with the Laboratory of Advanced Research in Cardiac Multimodal Imaging of the Cardio Med Medical Center Târgu Mureş, Romania. The follow-up will be performed at 30 days after inclusion, as well as 6 and 12 months respectively.

Study population

In total, the study will include 200 patients with acute STEMI, who are admitted through the emergency department for emergency invasive coronary angiography, with or without indication for percutaneous coronary revascularization of the culprit lesions. All patients will undergo complete clinical examination, laboratory testing (full blood count, biochemical analysis, inflammatory biomarkers, and electrolyte levels), transthoracic echocardiographic assessment, 12-lead electrocardiography. Patient inclusion and exclusion criteria are listed in Table 1.

Study groups

The study population will be divided into two main groups: group 1 – patients with location of the culprit lesion at the level of the left anterior descending artery; group 2 – patients with culprit lesion location in the circumflex or the right coronary artery respectively. The main groups will further be divided into subgroups according to the presence or absence of out-of-hospital cardiac arrest, and according to the stenosis degree of the culprit lesion into <50% versus ≥50% stenosis (Figure 1).
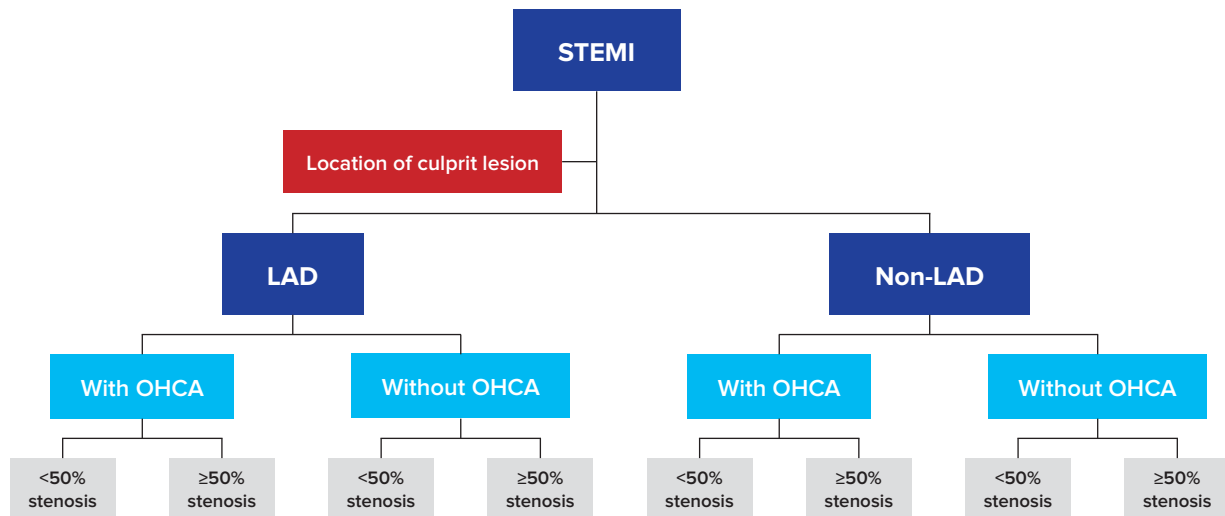
STUDY ENDPOINTS

The study endpoints include: (1) left ventricular function and remodeling assessed with CMR, according to location of culprit lesion within the coronary tree, in patients with STEMI, with versus without OHCA; (2) MACE rates at 6 and 12 months after the acute event, according to culprit lesion location. In this study, MACE are defined as the composite endpoint of cardiovascular death, reinfarction, repeated cardiac arrest, heart failure and hospitalizations related to cardiovascular causes.

STUDY PROCEDURES

At baseline, after obtaining the informed consent, all patients will undergo complete clinical assessment, laboratory testing, 12-lead ECG, transthoracic echocardiography, and invasive coronary angiography with or without performing percutaneous coronary revascularization of

TABLE 1. Study inclusion and exclusion criteria

Inclusion criteria
Age over 18 years
Acute ST elevation myocardial infarction, at 12 h from onset of symptoms, who undergo invasive coronary angiography, with or without indication of percutaneous revascularization of the culprit lesion

Exclusion criteria
Non-ST segment elevation acute coronary syndromes (unstable angina, NSTEMI)
Non-ischemic causes of cardiac arrest
Acute myocarditis
Allergy to iodine contrast agent
End-stage renal disease
Pregnant women
Active neoplastic diseases
Patient/patient family refusal to participate in the study

FIGURE 1. Group distribution of the study population according to the location of the culprit lesion within the coronary tree and the degree of stenosis. STEMI – ST-segment elevation myocardial infarction; LAD – left anterior descending artery; OHCA – out-of-hospital cardiac arrest

the culprit lesion, according to the current guidelines of the European Society of Cardiology regarding the management of patients with acute STEMI.

At the one-month follow-up, all patients will undergo assessment of cardiac function and structure, as well as evaluation of the myocardial scar and necrotic area, via CMR imaging with gadolinium tracing, as well as repeated clinical examination, ECG, echocardiography, and endpoint recordings.

The 6- and 12-month follow-up includes evaluation of the incidence of MACE rates, which in the present study are defined as the composite endpoint of cardiovascular death, reinfarction, repeated cardiac arrest, heart failure, and hospitalizations related to cardiovascular causes.

The study procedures are summarized in Table 2.

ETHICAL CONSIDERATIONS

All the study procedures will be conducted according to the ethical principles stated in the Declaration of Helsinki, and ethical approval from the Ethics Committee of both institutes where the study will be conducted

TABLE 2. Summary of the study protocol

	Baseline	1 month	6 months	12 months
Informed consent	■			
Screening for inclusion and exclusion criteria	■			
Demographic data	■			
Medical history	■			
Clinical examination	■	■	■	■
Records of vital signs	■	■	■	■
Pregnancy test	■			
Laboratory testing (CBC, biochemical analysis, inflammatory biomarkers, electrolyte levels)	■			
12-lead ECG	■	■	■	■
Transthoracic echocardiography	■	■	■	■
Invasive coronary angiography ± PCI of culprit lesion	■			
Cardiac MR	■	■		
Endpoint records	■	■	■	■

will be obtained. Signed written informed consent will be obtained from all patients included in the study, and in case of inability of consent from the patient, approval for study enrolment will be obtained from the patients' families.

CONCLUSIONS

In conclusion, the study will research the differences related to the location of the culprit lesion in patients with STEMI, who present OHCA versus patients without cardiac arrest, based on the hypothesis that STEMI patients with culprit lesions located at the level of the LAD, with a less than 50% stenosis, are more likely to present sudden cardiac arrest. At the same time, the study will develop a prediction model for OHCA in patients who present with STEMI, based on differences related to culprit location.

CONFLICT OF INTEREST

Nothing to declare.

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