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One-year clinical impact of cardiac arrest in patients with first onset acute ST-segment elevation myocardial infarction

Ki Hong Lee [a], Myung Ho Jeong [a,*], YoungkeunAhn [a], Sung Soo Kim [a], Shi Hyun Rhew [a], Young Wook Jeong [a], Soo Young Jang [a], Jae Yeong Cho [a], Hae Chang Jeong [a], Keun-Ho Park [a], Nam Sik Yoon [a], Doo Sun Sim [a], Hyun Ju Yoon [a], Kye Hun Kim [a], Young Joon Hong [a], Hyung Wook Park [a], Ju Han Kim [a], Jeong Gwan Cho [a], Jong Chun Park [a], Myeong Chan Cho [b], Chong Jin Kim [c], Young Jo Kim [d], KAMIR (Korea Acute Myocardial Infarction Registry) Investigators

[a] Chonnam National University Hospital, Gwangju, South Korea
[b] Chungbuk National University Hospital, Chungju, South Korea
[c] East West Neo Medical Center, Seoul, South Korea
[d] Yeungnam University Hospital, Daegu, South Korea

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ABSTRACT

Background: Cardiac arrest complicating acute ST elevation myocardial infarction (STEMI) is known to be associated with increased in-hospital mortality. However, little is known about the long-term outcomes after cardiac arrest complicating first onset STEMI in contemporary percutaneous coronary intervention (PCI) era.
Methods: We analyzed 7942 consecutive patients who were diagnosed with STEMI and had no previous history of MI. They were divided into two groups according to the presence of cardiac arrest (group I, patients with cardiac arrest; n = 481, group II, patients without cardiac arrest; n = 7641).
Results: In a stepwise multivariate model, previous history of chronic kidney disease, high serum level of glucose and low high density lipoprotein-cholesterol was an independent predictor of cardiac arrest complicating STEMI. Group I had significantly higher in-hospital mortality (adjusted hazard ratio [HR] 3.06, 95% confidence interval [CI] 2.08–4.51, $p < 0.001$) and 30-day mortality after hospital discharge (adjusted HR 2.92, 95% CI 1.86–4.58, log-rank $p < 0.001$). However, there was no significant increase in mortality beyond 30 days (6-month, adjusted HR 1.46, 95% CI 0.45–4.77, log rank $p = 0.382$; 1-year, adjusted HR 1.84, 95% CI 0.83–4.05, log-rank $p = 0.107$). Also, there were no significant differences in 6-month and 1-year major adverse cardiac events in 30-day survivors. Performing PCI was associated with decreased 12-month mortality in 30-day survivors.
Conclusions: Although patients with cardiac arrest complicating first onset STEMI had higher in-hospital and 30-day mortality after hospital discharge, cardiac arrest itself did not have any residual impact on mortality as well as clinical outcomes.

1. Introduction

Coronary heart disease especially ST-segment elevation myocardial infarction (STEMI) is the most common cause of cardiac arrest [1]. Cardiac arrest is also the leading cause of death worldwide [2]. Cardiac arrest complicating first onset STEMI has been known to be associated with increased in-hospital and short-term mortality [3,4]. Tremendous efforts were tried to improve survival rate after cardiac arrest, and increasing evidence supports a role for hospital based intensive treatments to improve survival rate after cardiac arrest [5–9]. Percutaneous coronary intervention (PCI) became a pivotal step in patients with STEMI as treatment strategy in the current era, and evidence based guidelines indicate that PCI can improve survival rate after cardiac arrest [7–9]. In the thrombolytic therapy era, patients with cardiac arrest caused by ventricular arrhythmia had higher in-hospital mortality as well as higher 1-year mortality of 30-day survivors [3]. However, little has been known about the impact of cardiac arrest on mortality in the contemporary PCI era. Therefore, we evaluated the impact of cardiac arrest complicating STEMI on the clinical outcomes as well as mortality.

2. Methods

2.1. Study population

There were 14,885 consecutive patients who enrolled in the Korea Acute Myocardial Infarction Registry (KAMIR) from November 2005 to February 2008. A total of 7942

* Corresponding author at: Principal Investigator of Korea Acute Myocardial Infarction Registry, Director of Heart Research Center Nominated by Korea Ministry of Health and Welfare, Chonnam National University Hospital, 42 Jaebongro, Dong-gu, Gwangju 501-757, South Korea. Tel.: +82 62 220 6243; fax: +82 62 228 7174.
E-mail addresses: myungho@chollian.net, mhjeong@chonnam.ac.kr (M.H. Jeong).

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patients consisted of the study population who met all the inclusion criteria. The criteria for inclusion consisted of the witnessed cardiac arrest by EMS providers or physicians, and the diagnosis of ST-segment elevation myocardial infarction. The criteria for exclusion included the diagnosis of non-ST-segment elevation myocardial infarction, previous history of myocardial infarction (MI), and non-successful resuscitation after cardiac arrest. Also, patients with an arrest caused by trauma, submersion, drug overuse, asphyxia, exsanguination, suicide, cerebrovascular accidents, subarachnoid hemorrhage or any other identifiable non-cardiac causes such as sepsis and malignant tumor were excluded. They were divided into two groups according to the presence or absence of cardiac arrest (group I, patients with cardiac arrest; n = 481, group II, patients without cardiac arrest; n = 7641).

The KAMIR, launched in November 2005, is a Korean prospective multicenter data collection registry reflecting real-world treatment practices and outcomes in Asian patients diagnosed with acute MI (AMI) [10]. The registry includes 50 community and teaching hospitals with facilities for primary PCI and on-site cardiac surgery. The KAMIR is supported by a research grant from the Korean Circulation Society in commemoration of its 50th anniversary. Data were collected by a trained study coordinator using a standardized case report form and protocol. The study protocol was approved by the ethics committee at each participating institution.

2.2. Medical treatment and PCI procedure

All patients received 300 mg of aspirin and 300 to 600 mg loading dose of clopidogrel, and heparin. The maintenance dose was 100 mg/day for aspirin and 75 mg/day for clopidogrel. Aspirin and clopidogrel were administered to all patients for ≥6 months as per existing guidelines. During hospital admission, the patients received medical treatment including beta blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers and statins. After discharge, the patients continued receiving the same kinds of medications that they received in-hospital period except for some intravenous or temporary medications.

Coronary artery stenting was performed using the standard technique. The decision for predilatation, direct stenting, and postadjunctive balloon inflation, and the administration of glycoprotein IIb/IIIa inhibitors were left to the discretion of individual operators. Clinical follow-up was performed at 1, 6, 12 months and when angina-like symptoms occurred.

2.3. Study definition and end points

Cardiac arrest was defined as the cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation. Initial rhythm at the time of resuscitation was classified as shockable (ventricular tachycardia/ventricular fibrillation) and non-shockable (pulseless electrical activity/asystole). AMI was diagnosed by the presence of characteristic clinical presentation, serial changes on electrocardiogram suggesting infarction, and increased cardiac enzymes. STEMI was diagnosed by a suggestive symptom with ST elevation >2 mm in ≥2 precordial leads, ST elevation >1 mm in ≥2 limb leads, or new left bundle branch block on the 12-lead electrocardiogram with a concomitant increase of at least one cardiac enzyme. Cardiogenic shock was a systolic blood pressure <90 mm Hg with evidence of tissue hypoperfusion. Cerebrovascular accident (CVA) was defined as a new focal neurologic defect with proof of brain image. Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2. New onset heart failure was defined as newly developed New York Heart Association class III/IV dyspnea, orthopnea, rales greater than one-third lung fields, elevated jugular venous pressure, or pulmonary congestion on chest X-ray thought to be related to cardiac dysfunction. Major bleeding was defined as an absolute hematocrit drop of ≥15%, any intracranial bleeding, bleeding events associated with causing death, the need for surgery, or transfusion, or any clinically relevant bleeding, as judged by the investigator. Recurrent MI was defined as recurrent symptoms with new electrocardiographic changes compatible with MI or cardiac markers at least twice the upper limit of normal. Target-vessel revascularization (TVR) was defined as any repeated intervention driven by the lesions located in the treated vessel within and beyond the target limits.

Study end points were mortality at each time point. In-hospital complications were composed of in-hospital death, cardiogenic shock, new onset atrial fibrillation, CVA, new onset heart failure, and major bleeding. Major adverse cardiac events (MACEs) were defined as the composite of all-cause death, MI, and repeated PCI or coronary artery bypass grafting (CABG) during 12 months of clinical follow-up.

2.4. Statistical analysis

All statistical analyses were done with SPSS 18.0 (Statistical Package for the Social Sciences, SPSS-PC Inc, Chicago, IL, U.S.A.). For continuous variables, the differences between groups were evaluated by an unpaired t test or Mann–Whitney rank-sum test. For discrete variables, differences were expressed as counts and percentages and were analyzed with a chi-square test (or Fisher's exact test) between groups as appropriate. We constructed the Kaplan–Meier curves for mortality at each time point, and the difference between the groups was assessed by log-rank test. Multivariate regression analysis was used to find the predictors for cardiac arrest complicating STEMI. Cox proportional hazards regression was used to compute the impact of mortality at each time point. We controlled for all available variables considered potentially relevant in all regression analysis: age, gender, hypertension, diabetes mellitus, dyslipidemia, smoking, left ventricular ejection fraction, use of platelet glycoprotein IIb/IIIa inhibitors, medications, laboratory findings, door-to-balloon time and performing PCI. Best cut-off values of continuous variables which had significant effects ($p < 0.1$) in univariate analysis were assessed by the receiver operating curve and entered into the regression model if those variables had significant area under the receiver operating characteristic curve (AUC > 0.5). All analyses were 2-tailed, with clinical significance defined as values of $p < 0.05$.

3. Results

3.1. Baseline clinical characteristics

A total of 7942 first onset STEMI patients were analyzed. Cardiac arrest was developed at out-of hospital (n = 242, 3.0%), in-hospital (n = 273, 3.4%), and both out-of and in-hospital (n = 34, 0.4%). They presented initial rhythm at the time of resuscitation as shockable (n = 384, 80.8%) or non-shockable (n = 91, 19.2%). Previous history of CVA (8.1% vs. 5.7%, p = 0.006) and CKD (2.5% vs. 1.2%, p = 0.010) was more common in group I than group II. Left ventricular ejection fraction was significantly lower in group I (45.0% vs. 50.0%, p < 0.001). Serum level of glucose was higher in group I, whereas that of total cholesterol, high-density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol and high sensitivity C-reactive protein were higher in group II (Table 1).

In-hospital and discharge medications were analyzed in patients who did not die at the day of hospital arrival. During hospital admission, beta blocker (63.7% vs. 73.2%, p < 0.001) and angiotensin converting enzyme inhibitor (66.5% vs. 72.6%, p = 0.016) were more commonly prescribed in group II, whereas glycoprotein IIb/IIIa inhibitors (22.0% vs. 15.5%, p = 0.002) were more commonly used in group I. At hospital discharge, beta-blocker (73.6% vs. 79.5%, p = 0.010) and angiotensin converting enzyme inhibitor (71.1% vs. 77.7%, p = 0.006) were more commonly prescribed in group II (Table 1).

3.2. Procedural characteristics

The primary PCI rate was higher in patients with cardiac arrest (79.5% vs. 74.7%, p = 0.020). When excluding the patients who died at the day of hospital arrival, the overall PCI rate during hospital admission was similar between the 2 groups (87.2% vs. 89.5%, p = 0.164). Door-to-balloon time was shorter in group I (95.0 vs. 107.0 min, p < 0.001). There were no differences in the prevalence of multi-vessel disease, lesion severity, and stent type length, or the stent diameter. However, the left main coronary artery was more common the culprit artery in group I (3.8% vs. 1.9%, p = 0.008). Pre-procedural Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 was more common in group I (61.1% vs. 52.4%, p < 0.001), and the achievement of post-procedural TIMI flow grade 3 was less common in group I (80.2% vs. 91.8%, p < 0.001) (Table 2).

3.3. Clinical outcomes

In-hospital mortality was higher in group I than group II before (32.1% vs. 4.5%, p < 0.001) and after excluding the patients who died at the day of hospital arrival (17.8% vs. 2.9%, p < 0.001). The incidence of cardiogenic shock, CVA, new onset heart failure, and major bleeding was more common in group I than group II. However, there were no differences in the rate of cardiac death, total death, MI, TVR, CABG as well as the composite of MACEs at 6-month clinical outcomes post-1 month. Also, there were no differences in the rate of cardiac death, total death, MI, TVR, CABG as well as the composite of MACEs at 12-month clinical outcomes post-1 month (Table 3).

Subgroup analysis for mortality in patients with cardiac arrest was done according to the initial rhythm at the time of resuscitation. Patients with initial rhythm as non-shockable showed significantly higher in-hospital mortality than the patients with initial rhythm as shockable before (29.8% vs. 42.7%, p < 0.019) and after excluding the patients who died at the day of hospital arrival (15.3% vs. 30.2%, p = 0.006).