Role of coronary angiography for out-of-hospital cardiac arrest survivors according to postreturn of spontaneous circulation on an electrocardiogram

Tae Rim Lee, MD, Sung Yeon Hwang, MD, Won Chul Cha, MD, Tae Gun Shin, MD, PhD, Min Seob Sim, MD, PhD, Ik Joon Jo, MD, PhD, Keun Jeong Song, MD, PhD, Joong Eui Rhee, MD, PhD, Yeon Kwon Jeong, MD, PhD

Abstract
Survivors of out-of-hospital cardiac arrest (OHCA) have high mortality and morbidity. An acute coronary event is the most common cause of sudden cardiac death. For this reason, coronary angiography is an important diagnostic and treatment strategy for patients with postcardiac arrest. This study aimed to identify the correlation between postreturn of spontaneous circulation (ROSC) on an electrocardiogram (ECG) and results of coronary angiography of OHCA survivors.

We collected data from our OHCA registry from January 2010 to November 2014. We categorized OHCA survivors into 2 groups according to post-ROSC ECG results. Emergent coronary artery angiography (CAG) (CAG performed within 12 hours after cardiac arrest) was performed in patients who showed ST segment elevation or new onset of left bundle branch block (LBBB) in post-ROSC ECG. For other patients, the decision for performing CAG was made according to agreement between the emergency physician and the cardiologist.

During the study period, 472 OHCA victims visited our emergency department and underwent cardiopulmonary resuscitation. Among 198 OHCA survivors, 82 patients underwent coronary artery intervention. Thirty-one (70.4%) patients in the ST segment elevation or LBBB group and 10 (24.4%) patients in the nonspecific ECG group had coronary artery lesions (P < .01). Seven (18.4%) patients in the nonspecific ECG group showed coronary spasm.

OHCA survivors without ST segment elevation or new onset LBBB still have significant coronary lesions in CAG. If there is no other obvious arrest cause in patients without significant changes in post ROSC ECG, CAG should be considered to rule out the possibility of coronary artery problems, including coronary spasm.

Abbreviations: CAG = coronary artery angiography, LBBB = left bundle branch block, MI = myocardial infarction, OHCA = out-of-hospital cardiac arrest, PCI = primary coronary intervention, RBBB = right bundle branch block, ROSC = return of spontaneous circulation, STsD = ST segment depression, STsE = ST segment elevation.

Keywords: acute myocardial infarction, cardiac arrest, coronary angiography, electrocardiogram, sudden cardiac death

1. Introduction
Patients with out-of-hospital cardiac arrest (OHCA) have high mortality and morbidity, even after return of spontaneous circulation (ROSC).[1] In contrast to in-hospital cardiac arrest, problems of the heart, especially myocardial infarction (MI), are the leading causes of the OHCA.[2–3] One of the treatment strategies of patients with postcardiac arrest syndrome (those who recover from cardiac arrest) is recognition and treatment of the cause of cardiac arrest and prevention of recurrence of cardiac arrest. Therefore, coronary angiography (CAG) and percutaneous coronary intervention (PCI) are important procedures for improving survival in patients with OHCA after ROSC. The 2015 American Heart Association and European Resuscitation Council guidelines[4,5] recommended that if ST segment elevation (STsE) or new onset of left bundle branch block (LBBB) is shown in an electrocardiogram (ECG) post-ROSC in a patient with cardiac arrest, emergent CAG and PCI should be performed. However, there is no definitive guideline for the other ECG group without STsE or LBBB on whether to perform emergent CAG and PCI. For this patient group, the usefulness of emergent CAG and PCI has been controversial.[6–14]

The sensitivity and specificity of ECG or cardiac markers, such as troponin I, for predicting possible cardiac causes for patients with OHCA are still unclear.[15,16] Recently, some reports[17,18] have shown an increasing trend of performing CAG in OHCA survivors, even without STsE on an ECG. However, there are insufficient data on the associations of post-ROSC ECG findings and CAG results.
Therefore, we conducted a retrospective, observational study on the relationship between post-ROSC ECG findings and CAG findings, including coronary spasm.

2. Methods

We included patients with OHCA who had CAG performed from January 2010 to November 2014 in Samsung Medical Center (SMC). The study hospital is a tertiary teaching hospital that is located in a metropolis. The emergency department (ED) is one of 30 local emergency centers in the metropolis and was designated by the Ministry of Health. The ED has 80,000 patient visits per year and approximately 100 OHCA visits per year.

2.1. OHCA protocol at SMC

During the study period, the decision for CAG was made according to our OHCA protocol. OHCA victims with post-ROSC ECG findings of STsE or new-onset LBBB (STsE group) underwent emergent CAG and PCI. Emergent CAG and PCI were defined as being performed within 12 hours after cardiac arrest in our protocol.[19] If there was no definitive coronary artery lesion in emergent CAG, secondary CAG with a spasm test was performed to identify coronary spasm. For OHCA victims without post-ROSC ECG findings of STsE or new-onset LBBB (nonspecific group), the decision of whether to perform CAG was made by the attending physician and through cardiology consultation after stabilization of the patient. While performing CAG, the spasm test was also performed to identify coronary artery spasm for victims without definitive coronary artery lesions. Therapeutic hypothermia was carried out in all OHCA victims without contraindications, regardless of performing CAG.

2.2. Data collection

This study was approved by the IRB of our institute (2013–12–038). The data were collected retrospectively from the SMC OHCA and SMC therapeutic hypothermia databases that included prospectively collected data from patient cohorts. The cohorts included all OHCA patient who had cardiopulmonary resuscitation (CPR), and treatment and prognosis data of SMC from 2010. Additional data of post-ROSC ECG and formal reports of CAG or PCI were collected from the medical record retrospectively. Post-ROSC ECGs were defined as 12-lead ECG that was recorded immediately after successful ROSC (ROSC > 20 min). ECG findings were classified into 5 categories as follows: STsE, ST segment depression (STsD), new-onset LBBB, right bundle branch block (RBBB), and others or no specific finding. These findings were classified by 1 emergency medicine staff member who did not know CAG or PCI results or patients’ treatment course. If an ECG finding was classified as LBBB, we searched for a previous ECG before cardiac arrest. If there was a previous ECG in our medical record, the emergency medicine staff member compared both ECGs to decide whether the post-ROSC ECG change was new onset. If there was no previous ECG in our medical record, an LBBB finding was classified as a new onset. According to the post-ROSC ECG results, we divided patients into 2 groups: STsE or LBBB group and nonspecific ECG group.

CAG results were collected from formal records that were written by the Department of Cardiology. In our institute, any coronary lesion was defined as when a coronary artery occlusion involved more than 50% of its diameter. An acute lesion was defined as observation of a thrombus or the guide wire passed easily.[6,20] Successful PCI was determined if the remnant lesion was less than 30% and the flow was TIMI grade 3[21] after PCI.[6,8,20] According to the CAG results, the patients were classified into 3 groups: abnormal CAG, normal CAG, and spasm groups.

2.3. Statistical analysis

We describe nominal variables as numbers and percentages. Continuous variables are shown as mean and standard deviation if they were normally distributed, and as median and interquartile range if they were not normally distributed. We compared demographic data, and CPR-associated data and CAG findings, between the STsE or LBBB groups and the nonspecific ECG group. We also compared demographic data between the normal and abnormal CAG groups. We used the chi-square test or Fisher’s exact test for nominal variables and used the t-test or Mann–Whitney U test for continuous variables. We considered that there was statistically significant difference if the P value was less than 0.05. We estimated the sensitivity, specificity, positive predictive value, and negative predictive value of CAG abnormalities according to post-ROSC ECG findings. We described these variables using 95% confidence intervals. We used STATA 11.0 (StataCorp, TX) for statistical analysis.

3. Results

A total of 472 patients with OHCA visited our ED during the study period. A total of 198 (41.9%) patients achieved successful ROSC. A total of 148 (31.4%) patients were admitted and 50 (10.6%) patients died in the ED. Among these patients who admitted, 44 were classified into the STsE or LBBB group and all of them had emergent CAG performed. Among 90 patients classified into the nonspecific ECG group, 19 had emergent CAG performed, 19 patients had delayed CAG, and the other 52 patients did not have CAG performed (Fig. 1). Table 1 shows the demographic and CPR data according to post-ROSC ECG findings. There were no significant differences in post-ROSC ECG findings between the STsE or LBBB group and the nonspecific ECG group. Table 2 shows the CAG findings according to post-ROSC ECG findings. Any coronary lesions, including acute lesions, and the number of successful PCIs were significantly more frequent in the STsE or LBBB group (P < .01 and P = .04, respectively). However, spasm of the coronary artery was observed only in the nonspecific ECG group. Table 3 shows the demographic data according to CAG abnormalities.

![Figure 1. Enrollment of patients.](image-url)
Davies et al.[22] found 74 coronary thrombi among 100 victims of sudden cardiac death due to coronary event are variable.

4. Discussion

Acute coronary syndrome is the most common cause of OHCA.[18,24] According to previous studies, reported percentages of sudden cardiac death due to coronary event are variable. Davies et al.[22] found 74 coronary thrombi among 100 victims, and another study reported 57% of cases of sudden coronary death, which showed acute coronary plaque changes.[23] In contrast, Warnes and Roberts[24] reported that there were only 13 cases of coronary thrombi in 70 sudden coronary death victims. However, among numerous possible causes for sudden cardiac arrest, the acute coronary syndrome is the most common cause.[25,26]

Successful emergent CAG is associated with an improved survival rate in OHCA victims with or without STsE.[8] Emergent CAG for OHCA with STsE or new LBBB is currently strongly recommended.[19,27] However, emergent CAG for OHCA victims with other nonspecific ECG findings is still controversial. A recent large, retrospective study in the US reported an increasing proportion of performing CAG in OHCA survivors with ventricular tachycardia (VT)/ventricular fibrillation (VF), even without STsE in ECG, and also showed improving survival to discharge.[17] The authors of this previous study also mentioned that a significant portion of patients with VF/VT cardiac arrest still did not undergo CAG and revascularization. However, performing CAG in OHCA survivors without STsE might be useful for identifying possible coronary artery lesions and establishing hemodynamic stability. This can be achieved by revascularization of possible culprit lesions or helping to trigger a search for other possible causes for cardiac arrest if CAG results are negative.[18]

While interpreting post-ROSC ECG findings, physicians need to be aware that there can be false positive cases because of

| Table 1 | Demographic data of the study groups. |
|---|---|
| | ST elevation or LBBB group (n = 44) | Nonspecific ECG group (n = 38) | P |
| Age, y | 55.09 ± 18.27 | 50.71 ± 16.01 | 0.25 |
| Sex, female | 23 (52.3) | 13 (34.2) | 0.10 |
| Comorbidity | | | |
| Diabetes | 9 (20.4) | 6 (15.8) | 0.58 |
| Hypertension | 20 (45.5) | 11 (29.7) | 0.14 |
| Heart disease | 9 (20.5) | 5 (13.2) | 0.38 |
| Renal disease | 4 (9.09) | 3 (7.89) | 0.84 |
| Malignancy | 6 (13.6) | 2 (5.26) | 0.20 |
| CPR | | | |
| No-flow time, min | 2 (0–5) | 4 (0–10) | 0.41 |
| BLS time, min | 10.22 ± 9.09 | 10.71 ± 9.55 | 0.49 |
| ACLS time, min | 9 (3–28) | 13 (0–28) | 0.53 |
| Initial rhythm | 25 (10–38) | 21 (12–38) | 0.51 |
| VF | 29 (65.9) | 23 (60.5) | 0.66 |
| Asystole | 8 (18.2) | 7 (18.4) | |
| 1-month survival | 34 (77.3) | 31 (81.6) | 0.63 |

Table 2

| Electrocardiogram findings and coronary angiography results in the groups. |
|---|---|
| | ST elevation or LBBB group (n = 44) | Nonspecific ECG group (n = 38) | P |
| ECG findings | | | |
| ST elevation | 42 (95.4) | | |
| LBBB | 2 (4.5) | | |
| ST depression | 12 (27.3) | 3 (15.8) | 0.01 |
| RBBB | 0 (0.0) | 1 (2.6) | 0.01 |
| Non-specific findings | 25 (56.8) | | |
| CAG findings | | | |
| Any lesion | 31 (70.5) | 10 (26.4) | <0.01 |
| One-vessel occlusion | 14 (31.8) | 5 (13.2) | | |
| Two-vessel occlusion | 8 (18.2) | 2 (5.3) | |
| Three-vessel occlusion | 9 (20.5) | 3 (7.9) | |
| Acute lesion | 19 (43.2) | 0 (0.0) | 0.01 |
| Successful PCI | 16 (36.4) | 6 (15.8) | 0.04 |
| Spasm | 0 (0) | 5 (13.2) | <0.01 |

We did not perform statistical analysis in the spasm group because the number of patients was too small.

| Table 3 | Demographic characteristics according to coronary angiography results. |
|---|---|
| | Abnormal CAG group (n = 41) | Normal CAG group (n = 34) | Spasm group (n = 7) |
| Age, y | 56.60 ± 17.28 | 46.94 ± 16.60 | 60.00 ± 11.87 |
| Sex, female | 19 (46.3) | 15 (44.12) | 2 (28.6) |
| ECG findings | | | |
| ST elevation | 30 (73.2) | 12 (35.3) | 0 (0.0) |
| LBBB | 1 (2.4) | 1 (2.9) | 0 (0.0) |
| ST depression | 6 (14.6) | 4 (11.8) | 2 (28.6) |
| RBBB | 0 (0.0) | 1 (2.9) | 0 (0.0) |
| Non-specific findings | 4 (9.8) | 16 (47.1) | 7 (71.4) |
| Comorbidity | | | |
| Diabetes | 10 (24.4) | 4 (11.8) | 0.16 |
| Hypertension | 20 (48.8) | 9 (26.5) | 0.14 |
| Heart disease | 6 (14.6) | 7 (20.6) | 0.49 |
| Renal disease | 3 (7.3) | 3 (11.8) | 0.51 |
| Malignancy | 5 (12.2) | 1 (2.9) | 0.14 |
| CPR | | | |
| No-flow time, min | 2 (0–5) | 6 (1–10) | 0.64 |
| BLS time, min | 9.14 ± 8.97 | 12.32 ± 9.94 | 0.15 |
| ACLS time, min | 12 (4–33) | 14 (6–28) | 0.45 |
| CPR time, min | 25 (10–38) | 25 (14–40) | 0.51 |
| Initial rhythm | 14 (6–29) | 25 (14–40) | 0.51 |
| VF | 20 (48.8) | 27 (79.4) | 5 (71.4) |
| PEA | 12 (29.3) | 5 (14.7) | 1 (14.3) |
| Asystole | 9 (21.9) | 2 (5.8) | 1 (14.3) |
| 1-month survival | 28 (68.3) | 30 (88.2) | 0.04 |

We did not perform statistical analysis in the spasm group because the number of patients was too small.
ischemia-reperfusion injury occurring during OHCA.\textsuperscript{11} In one study with 129 OHCA victims, analysis of ST-segment changes in post-ROSC ECG showed a low sensitivity and negative predictive value for identifying patients with probable coronary artery lesions.\textsuperscript{12,13} In OHCA survivors, other cardiac markers, such as creatine kinase-mb or troponin, are not reliable indicators for determining coronary artery problems as a cause of sudden cardiac arrest.\textsuperscript{28,29} However, according to a study published in 1994,\textsuperscript{6} clinical and electrocardiographic data, such as chest pain or ST-segment elevation, have poor predictive value for coronary artery occlusion. Another study also showed that 66\% of OHCA victims without ECG changes in STsE or new LBBB had significant coronary artery lesions.\textsuperscript{8} The negative predictive value of STsE or LBBB for acute coronary heart disease has been reported to vary from 42\% to 83\%.\textsuperscript{6,8,20,30}

In our study, 19 of 44 (43.2\%) patients with acute lesions had STsE or new LBBB in post-ROSC ECG. The incidence of acute coronary lesions in this group is low compared with that in previous studies, but there was a significant higher proportion of acute coronary lesions than in the nonspecific ECG group. A relatively high negative predictive value (84.2\%) was observed in our study. This high value might have been caused by a difference in CAG selection criteria or composition of both study groups. A negative predictive value that is not 100\% is considered to have great clinical significance. Sideris et al\textsuperscript{31} reported that with combined/extended ECG criteria, including ST-segment changes, LBBB, a wide QRS, and RBBB, are easily applicable and might help to identify patients who could gain benefits from emergent CAG after ROSC. With their combined/extended criteria, sensitivity, and negative predictive values for selection of OHCA victims with AMI was 100\%.

Coronary artery spasm is also a major cause of sudden cardiac arrest in OHCA survivors.\textsuperscript{12-20} In our study, 7 (18.4\%) patients from the nonspecific ECG group showed coronary artery spasm in CAG. Post-ROSC ECG findings were ST-segment depression in 2 patients and the other ECG findings were nonspecific. If CAG was not performed in these patients with coronary spasm, appropriate treatment was not carried out. We did not perform emergent CAG in OHCA victims without STsE or new LBBB in post-ROSC ECG. These patients underwent delayed or elective CAG by the decision of the attending physician. The number of patients with coronary artery spasm was too small to conduct subsequent analysis. However, we consider that to rescue patients with coronary spasm, which leads to sudden cardiac arrest, CAG could be performed to determine the cause of cardiac arrest and to properly treat patients. However, future studies will be required to investigate the appropriate timing of when to perform CAG in these patients without STsE or new LBBB in post-ROSC ECG. Post-ROSC ECG alone should not be considered as a strict selection criterion for performing emergent CAG in OHCA victims without obvious arrest cause other than cardiac causes.\textsuperscript{11}

Therefore, acute coronary problems are difficult to predict in OHCA survivors based on clinical and electrocardiographic data alone. According to our study results of coronary artery spasm, we might not identify the cause of cardiac arrest if we do not perform CAG in patients without STsE or new LBBB.

### 5. Limitations

This study was designed as a nonrandomized, observational, retrospective study based on prospectively collected data in a registry. All of the OHCA survivors who showed STsE or new-onset LBBB in post-ROSC ECG underwent emergent CAG. For other patients whose post-ECG did not show STsE or new-onset LBBB, the decision for performing CAG was made by specialists from emergency medicine or cardiology faculties. This might have caused selection bias. However, to reduce such bias, we classified our patients into 2 groups according to post-ROSC ECG by 1 emergency physician who was blinded to the patients’ CAG results, treatment course, and prognosis. Except for 1 patient whose next of kin refused to perform PCI, other excluded patients appeared to have an obvious noncardiac cause. The effect of selection bias might not be significant.

This study was conducted in single center and the number of OHCA survivors who underwent PCI was relatively small. Even though a small number of patients were analyzed, we found 7 patients with coronary spasm in the nonspecific ECG group. This might be the reason why we need to perform CAG in OHCA victims without STsE or new-onset LBBB. Further investigation might be required to determine the appropriate timing for when to perform PCI for OHCA survivors who do not show STsE or new-onset LBBB.

### 6. Conclusions

CAG results of OHCA survivors with changes in the ECG, such as STsE or new-onset LBBB, are highly associated with acute coronary lesions. However, a significant number of patients from the nonspecific ECG group show coronary lesions, including
coronary spasm. We consider that ST-elevation myocardial infarction: long-term survival and neurological outcome. Int J Cardiol 2013;166:236–41.

[14] Zimmermann S, Flachs kampf FA, Allf A, et al. Out-of-hospital cardiac arrest and percutaneous coronary intervention for ST-elevation myocardial infarction: long-term survival and neurological outcome. Int J Cardiol 2013;166:236–41.

[15] Dumas F, Manzo-Silberman S, Fichter J, et al. Can early cardiac troponin I measurement help to predict recent coronary occlusion in out-of-hospital cardiac arrest survivors? Crit Care Med 2012;40:1777–84.

[16] Zanutti D, Armillini L, Nucifora G, et al. Predictive value of electrocardiogram in diagnosing acute coronary artery lesions among patients with out-of-hospital cardiac arrest. Resuscitation 2013;84: 1250–4.

[17] Patel N, Patel NJ, Macon CJ, et al. Trends and outcomes of coronary angiography and percutaneous coronary intervention after out-of-hospital cardiac arrest associated with ventricular fibrillation or pulseless ventricular tachycardia. JAMA Cardiol 2016;1:890–99.

[18] Noc M, Fajadet J, Lassen JF, et al. Invasive coronary treatment strategies for out-of-hospital cardiac arrest: a consensus statement from the European association for percutaneous cardiovascular interventions (EAPCI)/STEMI for life (SFL) groups. EuroIntervention 2014;10:31–7.

[19] O’Connor RE, Brady W, Brooks SC, et al. Part 10: acute coronary syndromes: 2010 American Heart Association Guidelines for Cardiovascular Pulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122:877–817.

[20] Anyfantakis ZA, Baron G, Aubry P, et al. Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest. Am Heart J 2009;157:312–8.

[21] Chesebro JH, Knatterud G, Roberts R, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial Phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation 1987;76:142–54.

[22] Davies MJ, Thomas A. Thrombosis and acute coronary-artery lesions in sudden cardiac ischemic death. N Engl J Med 1984;310:1137–40.

[23] Farb A, Tang AL, Burke AP, et al. Sudden coronary death. Frequency of active coronary lesions, inactive coronary lesions, and myocardial infarction. Circulation 1995;92:1701–9.

[24] Warnes CA, Roberts WC. Sudden coronary death: comparison of patients with to those without coronary thrombus at necropsy. Am J Cardiol 1984;54:1206–11.

[25] Eisenberg MS, Mengert TJ. Cardiac resuscitation. N Engl J Med 2001;344:1304–13.

[26] Zipes DP, Wellens HJ. Sudden cardiac death. Circulation 1998;98: 2334–51.

[27] Peberdy MA, Callaway CW, Neumar RW, et al. Part 9: post-cardiac arrest care: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122:8768–86.

[28] Mullner M, Hirschl MM, Herkner H, et al. Creatine kinase-mb fraction and cardiac troponin T to diagnose acute myocardial infarction after cardiopulmonary resuscitation. J Am Coll Cardiol 1996;28:1220–5.

[29] Hollenbeck RD, McPerson JA, Mooney MR, et al. Early cardiac catheterization is associated with improved survival in comatose survivors of cardiac arrest without STEMI. Resuscitation 2014;85:88–95.

[30] Noc M. Urgent coronary angiography and percutaneous coronary intervention as a part of postresuscitation management. Crit Care Med 2008;36:5454–7.

[31] Sideris G, Vosli S, Dillinger JG, et al. Value of post-resuscitation electrocardiogram in the diagnosis of acute myocardial infarction in out-of-hospital cardiac arrest patients. Resuscitation 2011;82:1148–53.

[32] Miller DD, Waters DD, Szlachcic J, et al. Clinical characteristics associated with sudden death in patients with variant angina. Circulation 1982;66:588–92.

[33] Mark DB, Califf RM, Morris KG, et al. Clinical characteristics and long-term survival of patients with variant angina. Circulation 1984;69:880–8.

[34] Yasue H, Takizawa A, Nagao M, et al. Long-term prognosis for patients with variant angina and influential factors. Circulation 1988;78:1–9.

[35] Igarashi Y, Tamura Y, Suzuki K, et al. Coronary artery spasm is a major cause of sudden cardiac arrest in survivors without underlying heart disease. Coron Artery Dis 1993;4:177–85.

[36] MacAlpin RN. Cardiac arrest and sudden unexpected death in variant angina: complications of coronary spasm that can occur in the absence of severe organic coronary stenosis. Am Heart J 1993;125:1011–7.