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ORIGINAL RESEARCH

Cardiology

Cardiologists appropriately exclude resuscitated out-of-hospital cardiac arrests from emergency coronary angiography

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Abstract

Objective: Emergency coronary angiography after resuscitated out-of-hospital cardiac arrest as a selective or non-selective diagnostic procedure with or without intervention continues to be the subject of debate. This study sought to determine if cardiologists reliably select patients using clinical judgement for emergency coronary angiography without missing acutely ischemic cases requiring revascularization.

Methods: Presenting clinical details and ECGs (within 2 hours) from 52 consecutive out-of-hospital cardiac arrest patients who underwent non-selective coronary angiography were compiled retrospectively. Three out-of-hospital cardiac arrest-experienced interventional cardiologists, blinded to patient outcome, independently determined working diagnosis, and decision for emergency coronary angiography using clinical judgement. Sensitivity of the cardiologists' decision was assessed with respect to the outcome of acute revascularization. Inter-rater differences, consensus in clinical assessment, and influence of working diagnosis were also investigated.

Results: Sensitivity of individual cardiologist's decision for emergency coronary angiography with respect to acute revascularization was very high (adjusted overall sensitivity = 95.8%, 95% CI = 89–100, cardiologist range = 93%–100%), and perfect for the consensus of 2 or more cardiologists (100%, 95% CI = 79.4–100). There was no statistical difference in the sensitivity of this decision between cardiologists ($P < 0.05$), and inter-rater agreement was moderate (78% overall agreement, $K = 0.56$).

Conclusions: Experienced cardiologists recommend emergency coronary angiography in all resuscitated out-of-hospital cardiac arrest requiring acute revascularization and appropriately excluded one-third of patients. Rather than advocating a non-selective, or conversely, a restrictive strategy with respect to coronary angiography after out-of-hospital cardiac arrest, the findings support an individualized approach by a

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multidisciplinary emergency team that includes experienced cardiologists. The results should be confirmed in a larger prospective study.

KEYWORDS
coronary angiography, out-of-hospital cardiac arrest, percutaneous coronary intervention

1 | INTRODUCTION

1.1 | Background

Out-of-hospital cardiac arrest affects an estimated 20,000 individuals each year in Australia with a crude incidence of 102.5 per 100,000 population.[1] Only 21% to 36% of those who receive attempted resuscitation by ambulance personnel have return of spontaneous circulation on arrival to hospital.[1] The leading cause of non-traumatic out-of-hospital cardiac arrest is acute myocardial infarction resulting from an acutely occluded coronary artery. Australian guidelines recommend emergency coronary angiography with percutaneous coronary intervention as indicated in patients with ST-segment elevation on the post-resuscitation ECG or a high clinical suspicion of ischaemia.[2] However, due to the complex diagnostic and prognostic setting, determining suitability for emergency coronary angiography in the absence of ST-segment elevation is difficult because standard indicators such as clinical history and cardiac biomarkers are often unknown or difficult to interpret. Retrospective data have consistently shown that if all non-traumatic out-of-hospital cardiac arrests are taken for emergency coronary angiography (non-selective approach), 74%–82% with ST-segment elevation and 26%–46% of those without ST-segment elevation will undergo acute revascularization for an occluded coronary artery.[3,4] Several prospective clinical trials are currently underway in an attempt to provide definitive evidence for the selective versus non-selective angiography debate.[5] The recent COACT trial found no difference in survival at 90 days between emergency versus delayed coronary angiography in non-ST-segment elevation patients with a shockable arrest rhythm who were unconscious on hospital arrival.[6]

1.2 | Importance

The time-sensitive aim in undertaking emergency coronary angiography is to revascularize a culprit lesion responsible for the out-of-hospital cardiac arrest to prevent further myocardial injury. Conversely, coronary angiography may be deferred when there is no expected benefit. Whether cardiologists, as part of the multidisciplinary emergency management team, achieve these aims appropriately using a selective approach based on clinical judgement is currently unknown. There is no single benchmark to assess the appropriateness of emergency coronary angiography in the setting of out-of-hospital cardiac arrest; however, for the purposes of this study acute revascularization was chosen as the gold standard against which to assess a selective cardiologist-led approach.

1.3 | Goals of this investigation

This study sought to determine if experienced interventional cardiologists use clinical judgement to reliably select patients for emergency coronary angiography without missing acutely ischemic cases requiring revascularization. The primary objective investigated whether the decision for emergency coronary angiography, based on the initial clinical summary and ECG, is highly sensitive for acute revascularization. Secondary objectives included (1) inter-rater differences, (2) cardiologist consensus in clinical assessment, and (3) influence of working diagnosis.

2 | METHODS

2.1 | Study design and setting

This clinical evaluation study was conducted at the Lyell McEwin Hospital, a tertiary teaching hospital in South Australia. Institutional ethical review was not sought for the study because it met criteria for exemption from such review according to institutional policy. The standards for reporting diagnostic accuracy studies (STARD 2015) were followed.[7]

South Australia has a single state-wide emergency medical services system where out-of-hospital cardiac arrest patients are treated by paramedics on-scene and a 12-lead ECG is taken out-of-hospital after achieving stable return of spontaneous circulation. A "Code STEMI" may be called either in the ambulance by an intensive care paramedic, or by a physician in the emergency department to activate the on-call interventional cardiologist and cardiac catheterization team. The Lyell McEwin Hospital is the single cardiac arrest center for northern Adelaide and services a population of 398,000. Both the South Australian Ambulance Service and Lyell McEwin Hospital follow the 2010 (now 2015) ANZCOR resuscitation guidelines endorsed by the Australian Resuscitation Council and the New Zealand Resuscitation Council.[2] Emergency physicians routinely refer out-of-hospital cardiac arrest patients without obvious non-cardiac cause for review by the cardiology team before activating "code STEMI." The decision to proceed with coronary angiography is ultimately made by the interventionist.

During the study inclusion period (2011–2013), hospital protocol required all out-of-hospital cardiac arrest patients with return of spontaneous circulation to undergo emergency coronary angiography via code STEMI (non-selective approach) unless there was a clear, non-cardiac cause of arrest, evidence of futility, or contraindication. Since this time, a selective approach has been adopted by the hospital, and subsequent patients were not eligible for inclusion due to selection bias.

The Bottom Line

Coronary angiography after out-of-hospital cardiac arrest has been associated with improved outcome, but the optimal timing is unknown. This retrospective analysis of 52 out-of-hospital cardiac patients demonstrated that experienced interventional cardiologists accurately identified patients who required emergency revascularization based on clinical summary and ECG.

2.2 | Selection of participants

The hospital out-of-hospital cardiac arrest registry was searched to identify patients admitted during the non-selective era of 2011–2013 who underwent coronary angiography (emergency or delayed >6 hours). The registry collects comprehensive patient data from consecutive patients in accordance with the Utstein template,[8] including findings from coronary angiography. Cases were excluded on the following grounds: (1) no coronary angiography indicated due to obvious non-cardiac cause, evidence of futility, or contraindication on initial hospital assessment, failed cardiac catheterization attempt, (2) identifiable case (eg, unusually young age, transfer from remote hospital), and (3) no ECG available.

2.3 | Measurements

For all included patients, the initial clinical summary from up to the first 2 hours post-arrival was copied from the medical record and de-identified. At minimum, the summary included the ambulance case card, emergency department clinical record, and observations, arterial blood gas result(s) and post-return of spontaneous circulation ECGs. References to treating physicians, patient management, and working diagnosis were removed. The initial clinical summary reflects the information available to the on-call interventionist at initial consultation prior to the decision for emergency coronary angiography, or within the first 2 hours for patients with delayed coronary angiography.

Three interventional cardiologists were selected to participate in this study and all had >5 years experience as interventional team leaders with previous experience in other centers. Each cardiologist independently reviewed the initial clinical summary for each patient and used clinical judgment to complete a case report form. Working diagnosis was categorized as likely ischemia, other cardiac cause, and non-cardiac cause. Recommendation for coronary angiography was dichotomized into emergency (<6 hours post-arrest) or not emergency (delayed 6–24 hours, within next office hours, or not indicated). Results were re-identified and linked with complete registry data.

2.4 | Outcomes

The primary outcome was sensitivity of the experienced cardiologist-led decision for emergency coronary angiography, based on the initial clinical summary and ECG, with respect to the real-life outcome of acute revascularization (percutaneous coronary intervention, including planned or failed percutaneous coronary intervention, or coronary artery bypass grafting, coronary artery bypass grafting). Secondary outcomes included (1) inter-rater differences, (2) cardiologist consensus in decision making, and (3) influence of working diagnosis.

2.5 | Analysis

Normally distributed continuous data are presented as mean ± SD and comparisons between groups made using Student *t* test. Categorical data are presented as frequency and percentage and comparisons between groups made using Fisher's exact test and Pearson chi-square test, as appropriate.

The cardiologist's decision for emergency coronary angiography was evaluated as a diagnostic test. Ideally, the cardiologist would always recommend emergency coronary angiography in patients who required acute revascularization. Thus, the sensitivity of the decision (probability that the cardiologists select emergency coronary angiography when the patient requires acute revascularization) was identified as the important test characteristic.

Sensitivity and specificity of the decision for emergency coronary angiography with respect to acute revascularization was calculated for each cardiologist individually, as well as combined. Related-samples Cochran's Q test was used to assess differences in the distributions of sensitivity and specificity between cardiologists. If the *P*-value was <0.5, post hoc McNemar's tests with Bonferroni correction ($P < 0.0125$) were used to identify significant differences between cardiologist pairwise. Combined cardiologist sensitivity and specificity were calculated and adjusted for clustering on patient using the variance inflation factor, which takes into account the cluster size-weighted average cluster size and the intra-class correlation coefficient.[9]

Agreement between individual cardiologist decision and acute revascularization was evaluated using McNemar's tests and combined agreement was evaluated using logistic generalized estimating equation (GEE) models to account for clustering. Post hoc McNemar's exact conditional tests found sufficient power (>0.80) to detect significant agreement.

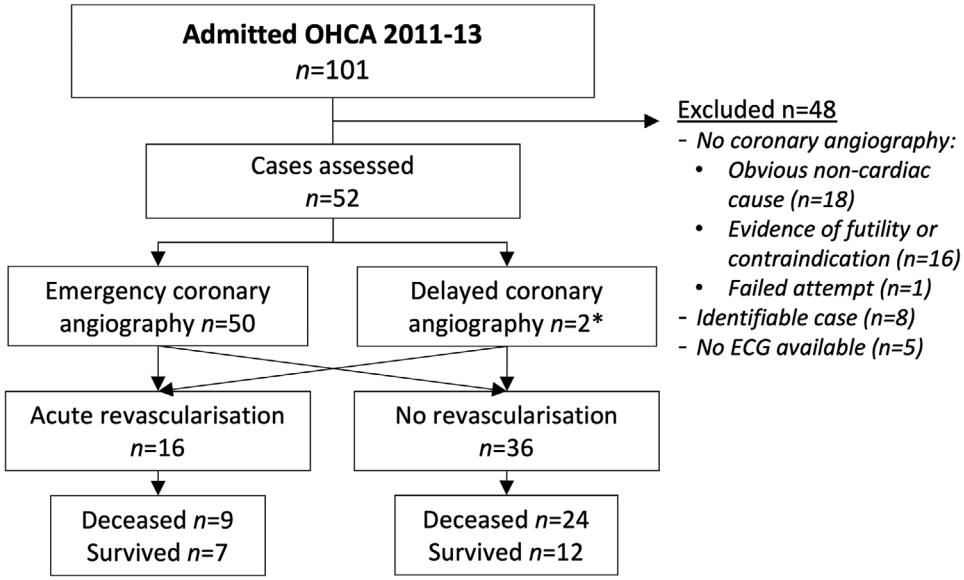

FIGURE 1 Flow diagram of real-life treatment pathway and outcome of patients included in the final cohort for analysis. *One case with missed post-return of spontaneous circulation ST-elevation and acute thrombus considered too unstable for percutaneous coronary intervention was included in the acute revascularization group for study purposes

Inter-rater agreement was measured using Randolph's free-marginal multi-rater kappa, where κ-values of 0–0.2, 0.21–0.4, 0.41–0.6, 0.61–0.8, and 0.81–1.0 represent poor, low, moderate, good, and very good levels of agreement, respectively.[10,11]

A 2-tailed $P < 0.05$ was considered statistically significant, except where stated. Analyses were performed using SPSS 24 (IBM SPSS Statistics, Armonk, NY), and SAS 9.4 (SAS Institute, Cary, NC).

3 | RESULTS

3.1 | Characteristics of study subjects

A search of the hospital out-of-hospital cardiac arrest registry identified 101 patients admitted between 2011 and 2013, and of those, 52 were included (Figure 1). The final cohort was predominately male, aged 58 ± 15 years, bystander-witnessed arrest in 65%, shockable rhythm in 69%, return of spontaneous circulation within 20 minutes in 28%, ST-segment elevation in 33%, and 37% survived to hospital discharge all with good neurological recovery (cerebral performance category 1–2). Coronary angiography revealed coronary artery dissection in 63%, 29% received percutaneous coronary intervention, and 37% were diagnosed with an acute myocardial infarction according to the fourth universal definition (Table 1).[12] Percutaneous coronary intervention was only performed in patients with a diagnosis of acute myocardial infarction. One case with missed post-return of spontaneous circulation ST-segment elevation, delayed coronary angiography, and acute thrombus considered too unstable for percutaneous coronary intervention, was re-categorized into the acute revascularization group for study analyses. No cases had failed revascularization attempts or plans for coronary artery bypass grafting.

3.2 | Main results

The primary study endpoint, sensitivity of the decision for emergency coronary angiography with respect to acute revascularization, is presented in Table 2. We considered the results of all cardiologists individually as well as pooled together. Adjusted overall sensitivity was very high (95.8%, 95% CI = 89–100). Both cardiologists 1 and 2 recommended no emergency coronary angiography in separate cases requiring acute revascularization; however, they each specified that additional diagnostic tests were required to assist with the decision making process. Agreement between the individual decision and outcome of acute revascularization was significant for each cardiologist as well as overall ($P < 0.01$).

3.3 | Secondary outcomes

3.3.1 | Inter-rater differences

There was no statistical difference in overall sensitivity between cardiologists with respect to acute revascularization (related-samples Cochran's Q test, $P > 0.05$), but there was a significant difference in specificity between cardiologist 2 and 3 (post-hoc McNemar's test with Bonferroni correction, $P < 0.01$). Inter-rater agreement of the selection of emergency versus no emergency coronary angiography was moderate (78% overall agreement, $K = 0.56$). In 63% of cases, there was 100% agreement.

TABLE 1 Medical history, arrest characteristics, management, and outcome of patients included in analysis (n = 52)

Patient characteristics	
Male sex	34 (65)
Age (y)	58 ± 15
Independent living	50 (96)
Known ischemic heart disease	18 (35)
Diabetes	16 (31)
Hypertension	33 (64)
Family history cardiac disease	13 (25)
Current smoker	16 (31)
Dyslipidemia	21 (40)
Witnessed arrest	
Bystander	34 (65)
EMS	4 (8)
Unwitnessed	14 (27)
Bystander CPR (excludes EMS-witnessed)	34 (71) (n = 48)
Shockable rhythm	36 (69)
Time to return of spontaneous circulation ≤20 mins	14 (28) (n = 50*)
Post-return of spontaneous circulation ST-segment elevation	17 (33)
Spontaneous circulation on arrival	42 (81)
Business hours	39 (75)
Coronary angiogram	
Emergency	51 (98)
Delayed (>6 h)	1 (2)
Arrest to coronary angiography (min)	120 [99–146]
Presenting hospital to coronary angiography (min)	66 [52–87]
Obstructive coronary artery disease	33 (63)
Percutaneous coronary intervention	15 (29)
Etiology	
Cardiac ischemic	18 (35)
Cardiac other	23 (44)
Non-cardiac	11 (21)
Acute myocardial infarction	19 (37)
Survived	19 (37)
Cerebral performance category 1–2 (''good outcome'')	19 (37)

Abbreviations: CPR, cardiopulmonary resuscitation; EMS, emergency medical services; ROSC, return of spontaneous circulation.
Data presented as n (%), mean ± SD or median [interquartile range].
*ROSC time unknown in 2 cases.

3.3.2 | Consensus

Consensus in clinical management was defined as when 2 or more cardiologists selected the same approach. Sensitivity of the consensus decision for emergency coronary angiography was 100% (95% CI = 79.4–100) with respect to acute revascularization (Figure 2). None of the cases chosen by consensus for no emergency coronary angiography required acute revascularization.

TABLE 2 Sensitivity and specificity of cardiologist selection of emergency coronary angiography according to acute revascularization

Assessor	Sensitivity True positive rate	Specificity True negative rate
Cardiologist 1	93.8 (69.8–99.8)	44.4 (27.9–61.9)
Cardiologist 2	93.8 (69.8–99.8)	61.1 (43.5–76.9)
Cardiologist 3	100 (79.4–100)	30.6 (16.4–48.1)
Overall	95.8 (89–100)	45 (35–55.7)

3.3.3 | Influence of working diagnosis

Table 3 presents the number of cases each cardiologist diagnosed as "likely ischemic," "other cardiac," and "non-cardiac," as well as the proportion in each category they selected for emergency coronary angiography. The diagnosis made by cardiologist 3 and consensus (diagnosis made by 2 or more cardiologists) was "likely ischemic" for all patients who required acute revascularization, and all such patients were selected for emergency coronary angiography. Cardiologists 1 and 2 diagnosed one case each that required acute revascularization as "other cardiac" and did not select emergency coronary angiography. As documented above, both cases were assessed as requiring additional diagnostic tests to assist with the decision making process.

4 | LIMITATIONS

Our study was a single-center observational cohort study, and as such, the results should be interpreted in the light of inherent limitations. Bias may have been introduced because over one third (30/82) of presumed cardiac cases were excluded because (1) coronary angiography was not performed due to evidence of futility or contraindication, (2) cases were considered identifiable, and (3) ECGs were missing. However, of the 16 cases excluded for the first reason above, the final etiology was cardiac ischemic in 2 deceased patients, both of whom had multiple comorbidities with poor neurological prognosis; other diagnoses in this group included cardiac non-ischemic (n = 7), non-cardiac (n = 5), and unknown (n = 2). The initial clinical summary was collated from the medical record and reflects up to 2 hours post-arrival, but this may not be an accurate representation of what information is available or communicated to the on-call interventionists at initial consultation and handover. Our results are from experienced interventionists and may not be applicable to more junior clinicians.

Unlike other similar studies, our primary outcome was not analyzed with respect to acute myocardial infarction. This was because the diagnostic criteria for acute myocardial infarction in out-of-hospital cardiac arrest are not entirely clear (ie, non-acute myocardial infarction

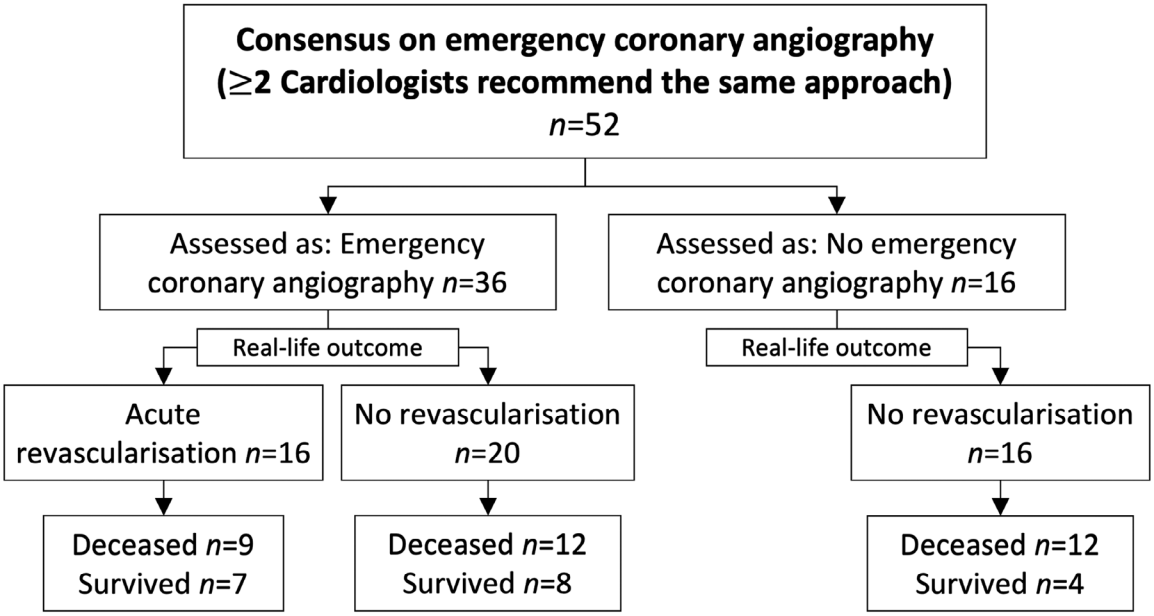

FIGURE 2 Flow diagram of emergency versus no emergency coronary angiography recommended by 2 or more cardiologists (consensus) with revascularization outcome and survival to hospital discharge

patients may still have troponin rise; history of chest pain is often unknown, etc), and because acute myocardial infarction may exclude patients with other non-obstructive ischemic diagnoses such as global ischemia in the setting of multiple lesions, and spasm. We acknowledge that acute revascularization is a subjective measure but there is as yet no single gold standard for assessing appropriateness of emergency coronary angiography in this setting.

5 | DISCUSSION

Experienced cardiologists used clinical judgment to reliably select retrospective out-of-hospital cardiac arrest patients for emergency coronary angiography without missing acutely ischemic cases requiring revascularization. Although revascularization of an acutely occluded coronary artery is not the only reason why a patient may be selected for emergency coronary angiography, it nonetheless remains a time-critical endpoint useful for assessing appropriateness. If a selective clinician-led approach had been used in the study cohort, 16 (31%) patients could potentially have avoided emergency coronary angiography. Interventional cardiologists may be involved early in the decision making process after resuscitated out-of-hospital cardiac arrest because they appropriately identify patients in whom emergency coronary angiography can be safely deferred. The Australian emergency care system is similar in design and function to others outside Australia, making our findings readily generalizable.

Out-of-hospital cardiac arrest represents a complex diagnostic and prognostic setting where the trigger may be multifactorial with several plausible causes. It was outside the scope of this study to investigate factors influencing the decision for emergency coronary angiography.

TABLE 3 Selection of emergency coronary angiography by experienced cardiologists according to their working diagnosis based on the initial clinical summary and ECG

Working diagnosis	n	Selected for emergency coronary angiogram(%)
Cardiologist 1		
Likely ischemic	32	31 (97)
Other cardiac	16	4 (25)
Non-cardiac	4	0 (0)
Cardiologist 2		
Likely ischemic	37	28 (76)
Other cardiac	11	1 (9)
Non-cardiac	4	0 (0)
Cardiologist 3		
Likely ischemic	40	40 (100)
Other cardiac	3	1 (33)
Non-cardiac	9	0 (0)
Consensus diagnosis		
Likely ischemic	38	34 (89)
Other cardiac	9	2 (22)
Non-cardiac	3	0 (0)
No consensus	2	0 (0)

However, the results found that two or more cardiologists (consensus) made the same diagnosis of "likely ischemic" with a recommendation for emergency coronary angiography in all patients who required acute

revascularization. No patients with a "non-cardiac" working diagnosis were selected for emergency coronary angiography, again confirming this cardiologist-led approach.

There are no other studies that have assessed the performance of clinical judgment in this area. Studies assessing clinical prediction rules demonstrate that post-return of spontaneous circulation ST-segment elevation alone is not a useful marker for emergency coronary angiography with a sensitivity of 64%–88% for acute myocardial infarction,[4,15] and only 56%–70% for percutaneous coronary intervention,[3,4,14] lower than the current study. Intracranial hemorrhage may also present with post-return of spontaneous circulation ST-segment elevation in up to 78% of patients, but rarely in two contiguous leads.[16] Elevated cardiac troponin on admission is another key diagnostic indicator for acute myocardial infarction; however, it performs poorly in the setting of out-of-hospital cardiac arrest because global ischemia also results in myocardial damage.[17,18] Only a few studies have gone further and investigated other clinical markers but applicability is limited due to inclusion criteria.[19–21] A clinical score >1 based on pre-arrest chest pain (1 patient), shockable rhythm (1 patient), and post-return of spontaneous circulation ST-segment elevation in any lead (2 patients) had a sensitivity of 93% for acute myocardial infarction.[19] Although scoring systems are useful clinical aids to improve diagnostic accuracy, clinical judgment appears to perform better in this setting.

The results of this study do not dismiss emergency coronary angiography without acute revascularization as a negative finding. Rather, coronary angiography provides a single procedure that aids in the time-critical diagnosis of ischemic versus non-ischemic heart disease, pulmonary embolism, and cardiomyopathy. In the setting of post-return of spontaneous circulation ST-segment elevation, an emergency coronary angiography without intervention will likely result in one of many useful diagnoses including Takotsubo cardiomyopathy, myocarditis, spontaneous coronary artery dissection, myocardial infarction with non-obstructive coronary arteries, and type II myocardial infarction, to name a few.

In summary, our study tested whether interventional cardiologists identify out-of-hospital cardiac arrest patients who might benefit from emergency coronary angiography using clinical judgment. Experienced cardiologists from our institution recommended emergency coronary angiography in all patients who required acute revascularization, as well as appropriately excluding a proportion of patients. A prospective multicenter cohort investigating the qualitative aspects of judgment rational that includes emergency physicians and cardiologists with varying levels of experience should be performed to confirm and broaden the applicability of these findings. An individualized approach to coronary angiography after out-of-hospital cardiac arrest may be appropriate when experienced interventionists, who understand the risks and benefits of coronary angiography and acute revascularization, are involved early in the decision making process.

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AUTHOR CONTRIBUTIONS

CZ, MRW, and MAA conceived and designed the study. MRW and SW extracted the preliminary data. SR, KM, and CZ provided the data assessments. MRW performed the data collection and analysis under supervision of CZ, JFB, and MAA. MRW drafted the manuscript and all authors contributed substantially to its revision. MRW takes responsibility for the paper as a whole.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

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