Emergency Coronary Angiography After Out-of-Hospital Cardiac Arrest

Is It Essential or Futile?

Philippe Gabriel Steg, MD; Batric Popovic, MD

Out-of-hospital cardiac arrest (OHCA) encompasses a broad spectrum of causes and its prognosis is dismal. Identifying the cause and which patients are likely to survive is challenging.[1] The number of patients who survive OHCA is increasing as a result of public education programs, placement of automatic external defibrillators in public areas, and improvements in prehospital and hospital management. The most common cause is acute coronary syndrome and observational studies have found an association between the performance of early coronary angiography (with percutaneous coronary intervention [PCI], if indicated) and survival.[2] Given the dissemination of primary PCI and the increasing availability and access to angiography, the use of angiography and PCI have increased. The guidelines recommend performing immediate coronary angiography in survivors of OHCA with ST-segment elevation on the ECG (class I level of evidence B)[3,4] and advocate urgent angiography and PCI, if indicated, in patients with resuscitated cardiac arrest and without ST elevation but with a high suspicion of ongoing myocardial ischemia.

See Article by Patterson et al

In this issue of *Circulation: Cardiovascular Interventions*, Patterson et al[5] describe temporal trends in identification, management, and outcomes of acute coronary syndromes (ACS) patients presenting as OHCA in the United Kingdom, using the Myocardial Ischaemia National Audit Project. They note an increase in proportion of hospitalized ACS presenting as OHCA over a 5-year period. Patients with ST-segment elevation represented nearly two-thirds of the cases. The clinical profile of these patients has changed during this period with decreasing prevalence of cardiovascular risk factors and of known ischemic heart disease. Management also changed with increasing use of coronary angiography and PCI. As in previous observations, there was an association between the use of coronary angiography (with or without PCI) and a lower risk of in-hospital mortality regardless of the presence of ST-segment elevation. As noted in this report, there is a trend to extend the indications of coronary angiography to patients who survive OHCA but do not have ST-segment elevation. Whether this is justified remains uncertain. Despite the large sample size of this study and the careful attempts to adjust for potential confounders, the interpretation of these findings needs to account for several limitations.

The study cohort was ascertained retrospectively, and there was likely a major sample bias: the cohort represents only a third of all OHCA patients (ie, those who were transferred to the catheterization laboratory for suspected ACS). Many patients who are not in the cohort were managed in intensive care facilities and may have been more severe and may have had a lower index of suspicion for ACS as an underlying cause.

Additionally, although it was in part addressed by a time-varying covariate analysis, the study was also affected by survival bias, as is common in observational studies: undergoing coronary angiography implies that patients have survived up to that point, whereas some patients who might have undergone coronary angiography but died before its actual performance are counted in the group not treated with angiography.

The diagnosis of ACS can be difficult in the context of OHCA: ST-segment elevation on ECG is neither perfectly sensitive for determining an acute coronary occlusion nor specific,[6] as there are other causes of ST-segment elevation than acute coronary occlusion particularly in patients receiving an electric shock and with metabolic abnormalities as is common in OHCA. In patients without ST-segment elevation, the diagnosis is even more challenging, particularly as most patients surviving OHCA exhibit elevated levels of troponin indicative of type II myocardial injury secondary to shock, even in cases in which OHCA is of noncardiac origin. Although it is clear that ischemic heart disease accounts for a large fraction of OHCA, there are important noncardiac causes or other cardiac causes for which angiography and PCI are not expected to improve survival.[7] Even in patients who have genuine ischemic heart disease-related OHCA, a substantial fraction may have chronic ischemic heart disease with a previous myocardial infarction scar generating arrhythmias and no acute myocardial ischemia or occlusion.[7] Although these patients are expected to have severe coronary artery disease on angiography, it is unclear how and why angiography and PCI would improve their outcomes.

Confounding by indication is another concern: there was a clear association between factors predicting survival and those predicting use of coronary angiography and PCI. This

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Table. Ongoing Randomized Clinical Trials Comparing Early Coronary Angiography With Delayed Coronary Angiography in Patients With OHCA but Without ST-Segment Elevation

Unique Identifier*	Title	Country	Sample Size	Main Inclusion Criteria	Primary Outcome
NCT02309151	Direct or Subacute Coronary Angiography for Out-of-hospital Cardiac Arrest (DISCO)	Sweden	1006 participants	Witnessed OHCA Return of spontaneous circulation No ST elevation on ECG	30-d survival
NCT02387398	Early Coronary Angiography Versus Delayed Coronary Angiography (PEARL)	United States	240 participants	OHCA of presumed cardiac cause Return of spontaneous circulation No ST elevation on ECG	Safety and efficacy at 180 d Safety: association of major adverse events (rearrest, bleeding, pulmonary edema, hypotension, acute renal insufficiency, and pneumonia)
NCT02587494	Cardiac Catheterization in Cardiac Arrest	United Kingdom	75 participants	OHCA of presumed cardiac cause Initial rhythm: ventricular tachycardia/ventricular fibrillation Glasgow Coma Scale score of <8 on hospital admission No ST elevation on ECG	Composite of death and poor neurological outcomes (CPC score of 3–5) at 30 d.
NCT02641626	Coronariography in Out of Hospital Cardiac Arrest (COUPE)	Spain	166 participants	OHCA Prior rule out of an obvious noncardiac cause (head computed tomography scan and transesophageal echocardiography) Glasgow Coma Scale score of ≤8 after return of spontaneous circulation Hemodynamic stability No ST elevation on ECG	Survival with good neurological outcome for activities of daily living (CPC 1–2) at 30 d.
NCT02750462	Immediate Unselected Coronary Angiography Versus Delayed Triage in Survivors of Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation (TOMAHAWK)	Germany	558 participants	OHCA of possible cardiac cause Return of spontaneous circulation Hemodynamic stability No ST elevation on ECG	30-d survival
NCT02876458	Emergency Versus Delayed Coronary Angiogram in Survivors of Out-of-hospital Cardiac Arrest (EMERGE)	France	970 participants	OHCA Return of spontaneous circulation No ST elevation on ECG	Survival rate with no or minimal neurological sequel (CPC 1 or 2) at 180 d
ISRCTN96585404	Randomized Trial of Expedited Transfer to a Cardiac Arrest Centre for Non-ST Elevation Out-of-Hospital Cardiac Arrest (ARREST)	United Kingdom	860 participants	Witnessed OHCA Return of spontaneous circulation No ST elevation on ECG	30-d survival

CPC indicates cerebral performance category; and OHCA, out-of-hospital cardiac arrest.
*Unique identifiers registered in https://www.clinicaltrials.gov, or https://www.isrctn.com.

association is expected because clinicians likely often appropriately withhold coronary angiography in patients with a low probability of survival or neurological recovery. Finally, the strong association of coronary angiography and PCI with survival both in ST-segment elevation and non–ST-segment elevation is troubling and in fact, suggests residual confounding. In non–ST-segment–elevation myocardial infarction, the survival benefit of urgent angiography is more difficult to understand than in ST-segment–elevation myocardial infarction.

Given the established benefits of timely coronary recanalization in ST-segment–elevation myocardial infarction, and despite the lack of direct evidence from a randomized clinical

trial, few physicians would dispute the value of immediate coronary angiography in OHCA patients with ST elevation, accepting that some patients may have transient ST abnormalities after cardioversion, and therefore angiography does not always lead to primary PCI. Studies in this field have been observational and, therefore, are highly vulnerable to confounding. Nevertheless, these studies suggest that early revascularization after cardiac arrest in patients with ST-segment elevation is feasible, safe, associated with coronary flow restoration, and associated with improved clinical and neurological outcomes.[8,9]

Several features are highly suggestive of acute coronary occlusion as underlying cause of OHCA: chest pain preceding collapse, the presence of cardiovascular risk factors, an initial shockable rhythm (ventricular tachycardia or ventricular fibrillation), and the presence of ST elevation on the postresuscitation ECG are strongly associated with acute coronary occlusion.[7,10] Factors associated with better prognosis after OHCA include initial shockable rhythm, the action of a bystander witness, prompt cardiopulmonary resuscitation, and the prehospital return of spontaneous circulation.[11–13] Indeed, Blom et al[11] found that 41.4% of patients with a shockable first rhythm survived with favorable neurological outcome compared with only 2.7% of those with a nonshockable first rhythm.

Should We Extend the Indication of Coronary Angiography to All Resuscitated OHCA Patients?

Given the very poor prognosis of OHCA, the fact that ACS is a common cause, and the results of the observational reports, should we routinely use coronary angiography in all survivors of OHCA and should we do this in emergency? Although it is tempting to give patients the benefit of the doubt and some may consider the benefits of angiography as intuitively obvious, there are important potential downsides to emergency routine coronary angiography, which may be sometimes useless and even harmful. Immediate angiography is a resource-intensive and costly intervention, not without risks and may delay the implementation of critical, potentially lifesaving treatments. It requires patient mobilization at a time of hemodynamic instability and critical monitoring, exposure to contrast agents, vascular risks, bleeding risks from adjunctive antithrombotic medication, and in the patients who undergo PCI there is a documented increased risk of stent thrombosis.[14] In addition, performing emergent angiography may delay or hamper the prevention of brain injury with hypothermia and improved hemodynamic conditions. Yet, neurological status is one of the most important prognostic factors. This shifts clinical attention away from the patient's brain to their heart, even though most patients who experience OHCA die from neurological complications.[15] Scoring systems have been developed to assess neurological injury and may be useful for predicting outcomes. However, a major shortcoming of such scoring systems is their lack of reliability in the early hours after OHCA (ie, most are validated for assessment after 24 hours). It would be helpful to focus future research on the determination of a clinical scoring system that allows to predict survival, futility, or both. Until such scoring systems are available and allow rational triage, the recommendations of the European Association for PCI consensus advise a short emergency department or intensive care unit stop in patients without ST-segment–elevation myocardial infarction ECG criteria.[16] This approach is intended to allow time for the medical team to obtain sufficient information to exclude noncoronary causes and for additional testing if needed. This strategy helps preserve healthcare resources and minimize risks to the patient. But, in the absence of an obvious noncoronary cause, coronary angiography should be performed as soon as possible, within 2 hours. Therefore, there is currently a widespread push for emergency coronary angiography in the setting of OHCA.

The number of patients who survive to hospital admission after OHCA is increasing and determining the optimal allocation of limited resources among this group of patients is challenging. Observational studies are difficult to interpret given the potential biases and confounding. Several ongoing randomized clinical trials compare immediate coronary angiography with delayed coronary angiography in patients after OHCA, but without ST-segment elevation (Table). The results of these trials will be critical in providing unbiased evidence to guide practice. In addition, in our opinion, future research should also focus on producing triage models that can be used very early after admission to determine or rule out the chance of survival with good neurological outcomes.

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