

How Much Is Enough ... What More Is Needed?

Kapledo Lotun, MD; Karl B. Kern, MD

Optimal care for the fortunate few resuscitated after out-of-hospital cardiac arrest remains uncertain. An aggressive approach to simultaneously cool and cath such patients on arrival at the hospital is favored by some interventional cardiologists.^{1–11} Others remain unconvinced that such therapy is beneficial or needed.^{12–14}

See Article by Waldo et al

See Article by Geri et al

See Article by Vyas et al

See Article by Stær-Jensen et al

In this issue of *Circulation: Cardiovascular Interventions* are 4 reports regarding immediate coronary angiography and its role in postresuscitation care.^{15–18}

Vyas et al report on 4029 postcardiac arrest patients from the Cardiac Arrest Registry to Enhance Survival (CARES) database between January 2010 and December 2013.¹⁵ CARES is a large national prospective emergency medical systems-based registry involving over 800 emergency medical service agencies in 21 states with a catchment area of over 80 million people. The emphasis of this registry has been in-field cardiac arrest and resuscitation variables, but some postresuscitation variables were added in 2010 as optional data elements, including data on the performance of coronary angiography post arrest. A small number of patients treated at hospitals without cardiac catheterization facilities were excluded. The final study population consisted of 4029 out-of-hospital cardiac arrest patients resuscitated from an initial rhythm of ventricular fibrillation or pulseless ventricular tachycardia and admitted to 374 hospitals in the United States. This is the largest cohort published to date which examines the association of coronary angiography post arrest and survival. Nearly half (48.5%) underwent early coronary angiography, as directed by the attending cardiologist's preference, though no other information was provided about the decision for or against angiography. Because the database concentrates on resuscitation variables, information about the postresuscitation electrocardiographic presence of ST-segment-elevation

was not available on about half of the study patients. Hence, the authors could provide no meaningful data for the patient subgroups with and without ST-segment-elevation. However, because of the large size of their database, the authors were able to perform a propensity-matched analysis that has not been possible in any previous report. This statistical approach is helpful to limit the selection or indication bias that is typical with cohort studies examining the association between early coronary angiography post arrest and survival. Vyas et al, using this propensity-matched format, found that early coronary angiography was associated with a 50% increase in survival to hospital discharge (odds ratio 1.52 [95% confidence interval 1.28–1.80]) and favorable neurological outcome (odds ratio 1.47 [95% confidence interval 1.25–1.71]). This confirms several earlier reports that were not able to use propensity matching.^{3–11} Additional statistical analyses found that coronary revascularization was the main mediator of the survival benefit associated with early coronary angiography. This is an important insight. The real benefit of early coronary angiography is to identify who needs timely coronary revascularization. The most pronounced example is the patient with an acutely occluded coronary artery that results in out-of-hospital cardiac arrest. Not only do such patients need to be resuscitated and reestablish spontaneous systemic circulation, but they also need prompt coronary reperfusion to salvage myocardial tissue and function. The definition of early coronary angiography used by Vyas in this report was broad, including all those who had catheterization within 24 hours of admission. Given this broad definition, it is even more impressive that coronary angiography and revascularization were associated with good outcomes and begs the question what if...what if such was truly early as in <2 hours from admission?

The second report in this issue is from the well-known investigative group in Paris, which has published extensively on the value of coronary angiography post cardiac arrest.^{8,19,20} Geri et al report here on a 14-year cohort (2000–2013) of 1722 consecutive nontraumatic, out-of-hospital cardiac arrest patients, who were resuscitated and subjected to a local policy of early coronary angiography for all patients without an obvious noncardiac cause for their cardiac arrest.¹⁶ They evaluated survival, both short-term (30 days) and long-term (10 years), among those who did not receive coronary angiography (n=628), those receiving coronary angiography but not revascularization (n=615), and those undergoing coronary angiography and subsequent revascularization (n=479). Initial evaluation showed coronary angiography, and coronary angiography revascularization was associated with progressively increased survival rates at 30 days and at 10 years. Propensity-score matching further confirmed this association with both short- and long-term outcomes. This second report in this issue

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From the Sarver Heart Center, University of Arizona, Tucson.

Correspondence to Karl B. Kern, MD, Professor of Medicine, Division of Cardiology, Sarver Heart Center, University of Arizona, 1501 N. Campbell Ave, Tucson, AZ 85724. E-mail kernk@email.arizona.edu

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is the largest single-center experience reported to date and again, because of the large number of patients, was able to do propensity matching to help overcome some of the inherent indication biases of nonrandomized cohort studies. Together these 2 reports add a total of 5751 patients to the published experience examining the use of coronary angiography post arrest, which essentially doubles the prior experience.² Even more importantly, both have raised the bar of evidence by using propensity-score matching and, as expected, have shown slightly less impressive odds ratios or hazard ratios, but still statistically significant differences in favor of early coronary angiography and revascularization. The report from France shows that this association between coronary angiography and intervention with improved survival is maintained for at least 10 years.

The third article in this issue by Waldo et al attempts to derive a risk stratification schema to identify the presence of an acute coronary lesion among those resuscitated from cardiac arrest (both out-of-hospital and in-hospital) and having coronary angiography.¹⁷ The heterogeneity of cardiac arrest patients makes it difficult to predict the presence of coronary artery disease and its implication in cardiac arrest. The recognition that coronary artery disease is often the precursor to cardiac arrest has led to its inclusion in the guidelines for emergent angiography and revascularization. Unfortunately, all cardiac arrests are not necessarily cardiac in origin, and thus, refining the set of patient who will need emergent angiography is the next step in the management of these patients. Waldo et al make a valiant effort to study these patients and come up with a model to stratify who will likely have an acute coronary lesion and benefit from emergent angiography. It is a good beginning and complements the prior proposal of Sideras et al,²¹ but unfortunately still falls somewhat short of what is needed for clinical decision-making. Their point system with a minimum of 1 and maximum of 5 includes a history of angina (1 point), a history of heart failure (1 point), a shockable rhythm (1 point), and the presence of a ST-segment-elevation myocardial infarction (2 points). They conclude that >1 point is highly suggestive of presence of an acute culprit lesion.

The fourth report published in this issue is an unselective, consecutive series of resuscitated, out-of-hospital cardiac arrest patients undergoing immediate coronary angiography by Staer-Jensen and the Oslo University group.¹⁸ They examine whether the first postresuscitation ECG is useful in selecting which patient needs immediate coronary angiography. They found that 1 out of 7 postresuscitated patients without ST elevation had an acutely occluded coronary. They also showed that while 31% of those with VF/VT had an occluded coronary, so did 22% (ie, 1 out of 5) with PEA or asystole. They concluded that lack of ST-segment-elevation on the initial postresuscitation ECG does not identify who should and should not undergo immediate coronary angiography, and though only a minority of such patients have an acutely occluded coronary, the number is not trivial (somewhere between 1 out of 5 and 1 out of 7) per their report.

Do we now have enough information to know how to best treat the postarrest patient, particularly those without ST-segment-elevation?

It seems to us that the ongoing debate and uncertainty stems from the ambiguity about who benefits from early coronary angiography after resuscitation from cardiac arrest. We continue to believe that it is all patients with an acutely occluded epicardial coronary artery. Cardiac arrest is the initial presentation of coronary artery disease in a substantial proportion of cardiac patients. We agree with Geri et al,¹⁶ as well as with Staer-Jensen et al,¹⁸ that the surface ECG is a poor postarrest predictor of an acutely occluded coronary. Attempts to identify which postarrest patients would specifically benefit from an early coronary angiography, including the schematic reported here by Waldo et al, still require validation in separate populations from which the risk stratification system was developed.¹⁷ Forty percent of the population from whom the Waldo schematic is developed had in-hospital cardiac arrest, where the pathogenesis of cardiac arrest is less likely to be acute coronary ischemia. Furthermore, the reliability of obtaining a history of angina or heart failure from a comatose postarrest patient arriving by ambulance without family members may be difficult. The Waldo model also relies exclusively on the concept that an acute culprit lesion is responsible for cardiac arrest. Though we agree this is the most common scenario, the concept of ischemic burden and global ischemia in patients with multiple lesions as a cause of cardiac arrest, rather than an acute culprit, will be unaccounted for in this model.

Vyas et al note in their analysis that the association between early cath and better outcomes did not hold up for those without ST-segment-elevation.¹⁵ However, they note in their methodology that in their attempt to propensity match such patients, over 62% of such patients did not have any information concerning their ECG post resuscitation. Exclusion of such a large proportion of their population makes this conclusion seem premature. Geri et al note that their local practice does not use the postresuscitation ECG in selecting who should have early coronary angiography and that they continue to think all postarrest patients without an obvious non-cardiac cause should undergo early coronary angiography.¹⁶ However, both studies agreed that the value of early coronary angiography is in providing early revascularization, that is, generally immediate percutaneous coronary intervention.

The report by Staer-Jensen reaffirms that a significant minority of the post resuscitated without ST elevation have a coronary lesion, including an acutely occluded coronary artery requiring immediate revascularization for optimal long-term outcomes.¹⁸

Both the European Society of Cardiology and the American Heart Association, combined with the Foundation of the American College of Cardiology, have strongly recommended that postarrest patients with ST-segment-elevation should undergo immediate coronary angiography at admission, whether comatose or awake (Class 1 recommendation).^{22,23} The European Society of Cardiology guidelines also recommend early coronary angiography be considered for those without ST-segment-elevation (Class 2A recommendation), though the American Heart Association/American College of Cardiology guidelines are silent on this issue. Recently, the European Association for Percutaneous Cardiovascular Interventions Stent for Life group published an algorithm for considering early coronary angiography for the postarrest

patient without ST-segment-elevation. They suggest a short stop in the Emergency Department to further evaluate for non-cardiac causes, but if negative, then proceeding without further delay (within 2 hours) with coronary angiography.²⁴ The Interventional Council of the American College of Cardiology has just published an alternative approach recommending early coronary angiography for those post arrest without ST-segment-elevation, outlining unfavorable characteristics that could be considered before proceeding to the cath laboratory.²⁵

We have also published 2 cohort series from the International Cardiac Arrest Registry (INTCAR) Cardiology subgroup,^{26,27} suggesting that early coronary angiography performed in postarrest patients without ST-segment-elevation does increase survival and favorable neurological outcome and that the angiographic findings in this patient subgroup may explain these results. We found in our series that one in 4 patients without ST-segment-elevation after cardiac arrest has an acutely occluded coronary at angiography.²⁷ Timely reperfusion, typically with percutaneous coronary intervention, not only saves myocardium, but should also improve survival.

With such guidelines, previously published series, and now these 4 new reports in this issue of *Circulation: Cardiovascular Interventions*, what more do we need before we embrace this postresuscitation concept of early coronary angiography?

Despite the consistency of these cohort studies, the cardiology interventional community seems to not only want, but even demand, a randomized controlled trial of early coronary angiography post arrest before it is willing to fully accept this approach.²⁸ The good news is that such studies are underway. Two pilot randomized controlled trials have either just begun or will start in the next few months, one in Europe and one in the United States. The Direct or Subacute Coronary Angiography for Out-of-Hospital Cardiac Arrest (DISCO) trial (NCT02309151) is underway in Scandinavia, and the multicentered Pilot Randomized Clinical Trial of Early Coronary Angiography Versus No Early Coronary Angiography for Post-Cardiac Arrest Patients Without ECG ST Segment Elevation (PEARL) trial (NCT02387398) is just about to begin in the United States. Though both trials are admittedly small, with anticipated randomization of ≈ 300 patients each, the organizers have prospectively communicated to make them reasonably similar to maximize the opportunity for combining results in a potential meta-analysis.

In a few years, we will be able to stop asking “do we have enough data” and “are we there now.”²⁸ Hopefully, then we can begin to move forward as an interventional community in providing the best possible postcardiac arrest care to all patients fortunate enough to be resuscitated from out-of-hospital cardiac arrest.

Disclosures

None.

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