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Early coronary angiography and percutaneous coronary intervention are associated with improved outcomes after out of hospital cardiac arrest

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ABSTRACT

Aim: Early coronary angiography (CAG) and percutaneous coronary intervention (PCI) are associated with better outcomes in subjects resuscitated from out-of-hospital cardiac arrest (OHCA). We sought to determine the relative contributions of early CAG and PCI to outcomes and adverse events after OHCA.
Methods: We analyzed 599 OHCA subjects from a prospective two-center registry. Hospital survival, functional outcomes and adverse events were compared between subjects undergoing early CAG (within 24 h) with or without PCI and subjects not undergoing early CAG. We adjusted for propensity to perform early CAG and PCI and for post-resuscitation illness severity and care.
Results: Early CAG subjects had improved rates of hospital survival (56.2% versus 31.0%, OR 2.85 [95% CI 2.04–4.00]; $p < 0.0001$) and better functional outcomes compared to no early CAG. Early PCI was associated with improved survival compared to early CAG without PCI (65.6% versus 45.5%, OR 2.29 [95% CI 1.41–3.69]; $p < 0.001$). After multivariate adjustment and propensity matching, early PCI remained significantly associated with improved survival compared with early CAG without PCI and no early CAG, but early CAG without PCI was no longer significantly associated with improved outcome compared with no early CAG. Early CAG and early PCI were not associated with an increase in transfusions or acute kidney injury.
Conclusions: Early CAG and PCI are associated with improved survival and functional outcomes after OHCA, but only early PCI was associated with a significant benefit after statistical adjustment. Our analysis supports the performance of immediate CAG to determine the need for PCI in selected patients following resuscitation from OHCA.

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CAG, coronary angiography; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; CXR, chest X-ray; ECG, electrocardiography; HCT, head computed tomography scan; MI, myocardial infarction; mRS, modified Rankin scale; MSOF, multi-system organ failure; OHCA, out-of-hospital cardiac arrest; PCAC, Pittsburgh cardiac arrest category; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation; STE, ST-segment elevation; TH, therapeutic hypothermia; UPMC, University of Pittsburgh Medical Center; VF, ventricular fibrillation; VT, ventricular tachycardia.

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1 Introduction

Out-of-hospital cardiac arrest (OHCA) affects almost 360,000 Americans each year, with an associated mortality rate of approximately 90% [1,2]. Coronary artery disease (CAD) is one of the leading causes of OHCA, and up to 70% of subjects undergoing coronary angiography (CAG) after OHCA are found to have obstructive CAD [3]. Acute coronary occlusion is common among OHCA subjects undergoing CAG, especially in the presence of ST-segment elevation (STE) on electrocardiogram (ECG) [4–8]. Up to 25–30% of OHCA subjects without STE on ECG have acute coronary occlusion and/or undergo percutaneous coronary intervention (PCI), and the ECG alone is insensitive for identification of acute coronary lesions after OHCA [3–6,8]. The prevalence of acute coronary occlusion found at CAG after OHCA is comparable to subjects with acute coronary syndromes (ACS) without STE, a population in which an early invasive strategy is recommended by guidelines [9].

Observational studies demonstrate significantly higher survival in comatose OHCA subjects undergoing CAG, with or without STE on ECG [8,10–14]. Most evidence suggests that early CAG (within 6–24 h of OHCA) is superior to delayed or no CAG, and the majority of benefit of CAG occurs in patients who receive revascularization [5,6,12–14]. Current guidelines recommend emergent CAG in OHCA subjects with STE on ECG, suspected acute myocardial infarction (MI) or evidence of hemodynamic or electrical instability, independent of the presence of coma [1]. Observational studies after OHCA are fraught with selection bias: subjects selected for CAG have more favorable case features and receive more aggressive overall care, which may account for some of the association with improved outcomes [5,6,11–13,15]. Prior studies have adjusted for post-resuscitation injury severity and bundled care components or the propensity to undergo CAG, but none has adjusted for all relevant variables [5,6,13]. Rates of adverse events associated with early CAG have not been systematically examined in OHCA subjects.

We hypothesized that the observed benefits of early CAG would be driven primarily by PCI, but *peri*-procedural risks would be present in all subjects undergoing early CAG. Given the inherent biases and confounding surrounding early CAG in this population, we corrected for baseline differences which influence the propensity to perform CAG, differences in the severity of post-cardiac illness (including brain injury and shock severity) and other components of bundled post-arrest care. Finally, we examined the association between early CAG and procedural complications that could be affected by timing and urgency of the procedure in this unstable patient population.

2 Methods

2.1 Study design and population

This study was approved by the Institutional Review Board at the University of Pittsburgh based on minimal risk to subjects, as part of an ongoing quality-improvement project described previously [16]. Consecutive adult subjects resuscitated from OHCA of presumed cardiac etiology admitted between January 8, 2005, and November 7, 2013 to the University of Pittsburgh Medical Center (UPMC) Presbyterian and Mercy Hospitals, two urban tertiary-care medical centers, were identified using an existing registry of post-cardiac arrest subjects, coupled with the cardiac catheterization laboratory database of CAG procedures at each hospital [16,17]. Subjects were entered into these databases prospectively. Subjects who died or failed to achieve return of spontaneous circulation in the emergency department were excluded, as were subjects with a clear non-cardiac etiology of OHCA. No patients were receiving ongoing resuscitation at the time of CAG.

2.2 Study definitions

Early CAG was defined as within 24 h of return of spontaneous circulation (ROSC) based on timing of urgent CAG in subjects with STEMI or high-risk non-STE ACS [18,19]. Post-cardiac arrest illness severity was measured using the Pittsburgh Cardiac Arrest Category (PCAC), a validated ordinal scale that ranks subjects from low (I) to high (IV) injury severity based on the neurological exam and severity of cardiovascular and respiratory failure within the first 6 h after ROSC [16,20]. We considered clinical data that was available prior to CAG as potentially influencing the propensity to perform the procedure, including initial troponin and ECG if present prior to CAG, as well as pre-CAG results of chest radiograph (CXR) and computed tomography of the head (HCT) (Supplemental Table 1). CXR was classified as compatible with edema if the radiography report noted "bilateral infiltrates,", "vascular congestion", "congestive heart failure" or "edema." Edema on HCT was defined as a grey-white ratio <1.2 [21]. We documented the use of vasopressors, inotropes and therapeutic hypothermia (TH) in the post-resuscitation phase. During the time of this study, the recommended goal temperature when using TH was 33 °C.

The decision to perform early CAG involved a multidisciplinary process including an interventional cardiologist and an Emergency Medicine or Critical Care Medicine physician from the Post Cardiac Arrest Service, incorporating the clinical presentation, post-cardiac arrest illness severity and perceived likelihood of poor neurological outcome. The decision to perform PCI was made by the interventional cardiologist for the suspected culprit lesion. Based on intention-to-treat principles, subjects were classified as receiving PCI regardless of whether the intervention was successful. Successful PCI was defined as TIMI-2 or 3 flow at the end of the procedure. When TIMI flow was not explicitly stated we accepted statements such as "successful," "good flow," or report of >50% reduction in stenosis as a surrogate for success.

2.3 Study outcomes

The primary outcome was survival to hospital discharge. Secondary outcome measures reflecting functional outcome at hospital discharge included cerebral performance category (CPC: 1–2 considered favorable), modified Rankin scale (mRS: 0–3 considered favorable) and discharge destination (home and inpatient rehabilitation considered favorable) [22].

Adverse events were defined as occurring within 72 h of CAG (or admission if no CAG was performed), even if not directly linked to the procedure. Severe acute kidney injury was defined as a doubling of creatinine (within 72 h), a rise in creatinine of >2 mg/dl in those subjects with initial creatinine >2 mg/dl, or the new use of dialysis. We excluded subjects with documented stage 4 chronic kidney disease, end-stage renal disease or chronic dialysis from this analysis. Hemoglobin decrease was defined as the difference between the initial hemoglobin and the lowest value in the subsequent 72 h, and the need for transfusion of packed red blood cells was defined as within 72 h after CAG.

2.4 Statistical analysis

Categorical descriptive variables were compared between groups using chi-squared test and continuous variables were compared using Student's *t*-test for means; Mann-Whitney *U* test was used to compare medians when data were not normally-distributed. Separate propensity (P) scores were derived using multivariable logistic regression including variables present prior to the decision to perform CAG and PCI (Supplemental Table S1) with the dependent variable being the decision to perform early CAG (regardless of PCI status) or early PCI (a separate propensity