

Early Coronary Angiography and Survival After Out-of-Hospital Cardiac Arrest

Ankur Vyas, MD; Paul S. Chan, MD, MSc; Peter Cram, MD, MBA;
Brahmajee K. Nallamothu, MD, MPH; Bryan McNally, MD, MPH; Saket Girotra, MD, SM

Background—Although out-of-hospital cardiac arrest is common because of acute myocardial infarction, it is unknown whether early coronary angiography is associated with improved survival in these patients.

Methods and Results—Using data from the Cardiac Arrest Registry to Enhance Survival (CARES), we identified 4029 adult patients admitted to 374 hospitals after successful resuscitation from out-of-hospital cardiac arrest because of ventricular fibrillation, pulseless ventricular tachycardia, or unknown shockable rhythm between January 2010 and December 2013. Early coronary angiography (occurring within one calendar day of cardiac arrest) was performed in 1953 (48.5%) patients, of whom 1253 (64.2%) received coronary revascularization. Patients who underwent early coronary angiography were younger (59.9 versus 62.0 years); more likely to be men (78.1% versus 64.3%), have a witnessed arrest (84.6% versus 77.4%), and have ST-segment–elevation myocardial infarction (32.7% versus 7.9%); and less likely to have known cardiovascular disease (22.8% versus 35.0%), diabetes mellitus (11.0% versus 17.0%), and renal disease (1.8% versus 5.8%; $P < 0.01$ for all comparisons). In analysis of 1312 propensity score–matched pairs, early coronary angiography was associated with higher odds of survival to discharge (odds ratio 1.52 [95% confidence interval 1.28–1.80]; $P < 0.0001$) and survival with favorable neurological outcome (odds ratio 1.47 [95% confidence interval 1.25–1.71]; $P < 0.0001$). Further adjustment for coronary revascularization in our models significantly attenuated both odds ratios, suggesting that revascularization was a key mediator of the survival benefit.

Conclusions—Among initial survivors of out-of-hospital cardiac arrest caused by VF or pulseless VT, we found early coronary angiography was associated with higher odds of survival to discharge and favorable neurological outcome. (*Circ Cardiovasc Interv.* 2015;8:e002321. DOI: 10.1161/CIRCINTERVENTIONS.114.002321.)

Key Words: cardiac arrest ■ cardiac catheterization ■ coronary angiography ■ diabetes mellitus
■ out-of-hospital cardiac arrest

Out-of-hospital cardiac arrest is common, affecting nearly 300 000 people annually in the United States, and is associated with low survival rates of $< 10\%$.¹ Although acute myocardial infarction (MI) is a frequent cause of cardiac arrests because of ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), the effectiveness of a strategy of early coronary angiography and revascularization is unclear in this setting because cardiac arrest patients were excluded from clinical trials of early coronary intervention in acute MI.^{2–5}

Several observational studies have previously reported higher rates of survival in patients who receive early coronary angiography after initial resuscitation from out-of-hospital cardiac arrest.^{6–11} However, these studies were limited by single-center and retrospective study designs, often lacked a control group that did not receive coronary angiography, and used statistical methods that did not account for indication

See Editorial by Lotun and Kern

bias. Nonetheless, quantifying the benefit of early coronary angiography in patients with out-of-hospital cardiac arrest has important implications, given current guidelines recommend regionalizing postcardiac arrest care in specialized centers that are capable of performing coronary angiography and percutaneous coronary intervention.¹² Moreover, although professional societies recommended immediate coronary angiography in out-of-hospital cardiac arrest with ST-segment–elevation MI (STEMI) and in patients who do not have obvious noncoronary causes but no ST-elevation, it remains unclear whether these have been applied into practice.¹³

To address this gap in knowledge, we leveraged data from the Cardiac Arrest Registry to Enhance Survival (CARES)—a large national prospective registry of out-of-hospital cardiac

Received November 22, 2014; accepted July 31, 2015.

From the Division of Cardiology, Department of Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City (A.V., S.G.); Division of Cardiology, Department of Internal Medicine, Saint Luke's Mid America Heart Institute, Kansas City (P.S.C.); Division of General Internal Medicine, Department of Internal Medicine, Mt Sinai/UHN Hospitals, Toronto, ON Canada (P.C.); Veterans Affairs Ann Arbor Health Services Research and Development Center of Excellence and the Division of Cardiology, Department of Internal Medicine, University of Michigan, Ann Arbor (B.K.N.); and Department of Emergency Medicine, Emory University School of Medicine, Atlanta (B.M.).

The Data Supplement is available at <http://circinterventions.ahajournals.org/lookup/suppl/doi:10.1161/CIRCINTERVENTIONS.114.002321/-DC1>.

Correspondence to Ankur Vyas, MD, University of Iowa Hospitals and Clinics, Division of Cardiovascular Medicine, 200 Hawkins Dr, Int. Med. E316-1 GH, Iowa City, IA 52242. E-mail ankurvayas7@gmail.com

© 2015 American Heart Association, Inc.

Circ Cardiovasc Interv is available at <http://circinterventions.ahajournals.org>

DOI: 10.1161/CIRCINTERVENTIONS.114.002321

WHAT IS KNOWN

- Acute myocardial infarction is a common cause of out-of-hospital cardiac arrest.
- ECG criteria have poor negative predictive value in diagnosing acute myocardial infarction in resuscitated patients.

WHAT THE STUDY ADDS

- In patients successfully resuscitated from an out-of-hospital cardiac arrest as a result of a shockable rhythm, early coronary angiography is associated with higher odds of survival to discharge and favorable neurological outcome.
- The benefit of early coronary angiography is largely mediated by revascularization.
- Randomized controlled trials are needed to confirm this potential benefit.

arrests to examine the association of early coronary angiography (performed within one calendar day of cardiac arrest) and survival. We used a matched propensity score analysis to explicitly account for indication bias. Given that patients with cardiac arrest are at risk for significant neurological disability, we also examined survival with favorable neurological outcome. Finally, we examined whether the benefit of early coronary angiography on our study outcomes was mediated by greater use of revascularization in the early coronary angiography group.

Methods

Data Source

CARES is a large prospective registry of out-of-hospital cardiac arrest in the United States that was established in 2004 as a collaboration between the Emory University School of Medicine and the Center for Disease Control and Prevention. Since inception, CARES has grown to involve over 800 emergency medical service (EMS) agencies and 1300 hospitals across 23 states, encompassing a catchment area of over 80 million people. Details of CARES' study population, data collection, data reporting, and EMS and cardiac arrest protocols have been previously reported.^{14–16} In brief, CARES collects data on all 9-1-1 activated out-of-hospital cardiac arrest events of nontraumatic pathogenesis, which involve attempted resuscitation by EMS or first responder units. Data collection in the registry is based on the Utstein template and includes patient demographics, cardiac arrest characteristics, EMS response, and in-hospital outcomes at enrolling sites.¹⁵ In January 2010, a few optional elements were added to the CARES data collection form, which included whether the patient underwent coronary angiography during hospital stay. The current study was based on data collected since that time.

Study Population

We identified 21 269 patients aged ≥ 18 years with an out-of-hospital cardiac arrest because of VF, pulseless VT, or unknown shockable rhythm between January 1, 2010, and December 31, 2013. Because patients who died in the field were not eligible to receive coronary angiography, we restricted our sample to patients who had sustained return of spontaneous circulation of at least 20 minutes and survived to hospital admission (n=8134). Given that data on coronary angiography was an optional data element, we excluded 3668 patients from sites that did not report data on performance of coronary angiography.

We also excluded patients treated at hospitals that did not perform coronary angiography on any cardiac arrest patient and were also confirmed to not have a cardiac catheterization laboratory using the American Hospital Association 2010 data set (n=65 patients at 29 hospitals). This was done to ensure that coronary angiography was available at all study hospitals. Finally, because we were interested in examining whether coronary angiography performed within one day of cardiac arrest was associated with improved survival, we also excluded patients for whom data on the date of coronary angiography (n=370) or survival (n=2) were missing. Our final study population comprised 4029 patients with out-of-hospital cardiac arrest as a result of shockable rhythms at 374 hospitals (Figure 1).

Study Variables

The primary exposure variable was performance of early coronary angiography—defined as coronary angiography performed within 1 calendar day of the cardiac arrest.

Patient-level data included subject age (categorized as 18–54, 55–64, 65–74, ≥ 75), sex, race (white, black, other, or unknown), initial cardiac arrest rhythm (VF, VT, or unknown shockable rhythm), location of arrest (home, public location, or healthcare facility), whether cardiac arrest was witnessed by someone other than a first responder or the EMS provider, provision of bystander cardiopulmonary resuscitation, use of an automated external defibrillator, and initiation of hypothermia in the field or in the hospital. Information was also available regarding additional data elements—placement of an advanced airway in the field, medical comorbidities (heart disease, diabetes mellitus, hypertension, stroke, hyperlipidemia, renal disease, respiratory disease, and cancer), and whether the initial diagnosis was STEMI. However, reporting on these latter variables, as well as race, was optional and, therefore, not consistently reported from all sites. We used indicator variables for missing data.

Study Outcomes

Our primary outcome was survival to discharge. Our secondary outcome was survival to discharge with favorable neurological outcome. Neurological status at discharge was assessed using the previously described and validated cerebral performance category score.¹⁷ A cerebral performance category score of 1 denotes mild or no neurological disability; 2, moderate neurological disability; 3, severe neurological disability; 4, coma or vegetative state; and 5, brain death. Based on prior work, which found prognostic postdischarge differences in survival between patients with a discharge cerebral performance category score of 1 versus 2, we defined favorable neurological outcome as a cerebral performance category score of 1 (ie, none or mild neurological disability).¹⁸

Statistical Analysis

We compared baseline characteristics according to whether patients underwent early coronary angiography using the 2-sample *t* test for continuous variables and the χ^2 test for categorical variables. We also compared unadjusted rates of survival to discharge and favorable neurological outcome between the 2 groups and calculated unadjusted odds ratios (OR).

To account for indication bias, we performed a matched 1:1 propensity score analysis to examine the association between early coronary angiography and survival. To accomplish this, we first constructed a nonparsimonious multivariable logistic regression model to determine each patient's propensity of receiving early coronary angiography. All covariates listed in the Study Variables section were included in the model. Next, we used a greedy matching algorithm (ie, without replacement) to match patients who did and did not receive early coronary angiography, using a caliper width that was $< 20\%$ of the standard deviation of the logit of the propensity score.¹⁹ To ensure that both study groups were well balanced after propensity matching, we calculated a standardized difference for each covariate and compared them before and after propensity matching. Standardized differences measure the difference in the means between 2 groups expressed in units of standard deviation and help assess the degree of imbalance of

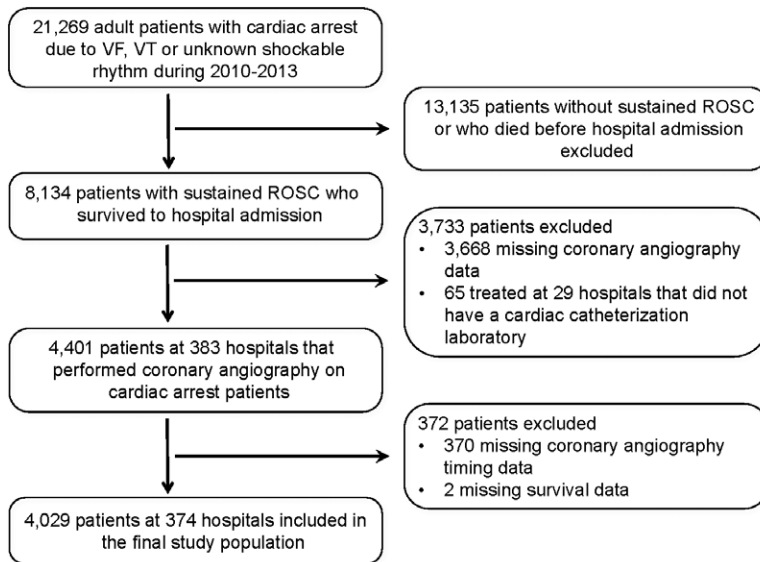


Figure 1. Study cohort. ROSC indicates return of spontaneous circulation; VF, ventricular fibrillation; and VT, ventricular tachycardia.

a variable between 2 compared groups. Unlike P values, standardized differences are not influenced by sample size.²⁰ A standardized difference of <10% suggests successful matching on propensity scores. Finally, we used the Cochran–Mantel–Haenszel test to examine the association between early coronary angiography and our study outcomes of survival to discharge and favorable neurological outcome.

Also, because hospitals may differ in their tendency to offer coronary angiography to cardiac arrest survivors, we examined whether the benefit of early angiography on survival was mediated by greater use of coronary revascularization in the early coronary angiography group. We constructed a multivariable logistic regression to examine the association between early coronary angiography and our study outcomes while adjusting for all variables listed in the Study Variables section. We then examined whether the strength of the association between early coronary angiography and our study outcomes was attenuated after additionally adjusting for receipt of coronary revascularization (percutaneous coronary intervention or coronary artery bypass graft surgery).

To determine whether the association between early coronary angiography and survival outcomes was only confined to STEMI patients, we repeated our analysis after restricting our cohort to patients who did not have STEMI. We reestimated propensity scores for this cohort by constructing a separate multivariable logistic regression model and conducted a similar matched propensity score analysis as described earlier.

To explore the role of unmeasured confounders (X), we performed additional sensitivity analysis. We assumed an unmeasured confounder to be associated with survival with an OR of 1.5 and a prevalence of 10% in the reference (delayed or no coronary angiography) group. We used the method of Lin et al²¹ to calculate the prevalence of X in the exposed cohort that would make the effect of early coronary angiography on survival nonsignificant. We then repeated the above calculations assuming an OR of 2.0 and 3.0, respectively, between X and survival. We also repeated the above analysis for survival with favorable neurological outcome.

All statistical analysis was performed using SAS 9.3 (SAS System for Windows, version 9.3. Cary, NC: SAS Institute. 2002–2010). Graphs were generated using GraphPad Prism version 6.0d for Mac OS X (GraphPad Software, La Jolla, CA, <http://www.graphpad.com>). The institutional review board at University of Iowa approved the study protocol and waived the requirement for informed consent.

Results

Among 4029 patients successfully resuscitated from an out-of-hospital cardiac arrest caused by VF or pulseless VT included

in our study, early coronary angiography was performed in 1953 (48.5%) patients. Patients in the early angiography group were younger (59.9 years versus 62.0 years), more likely to be male (78.1% versus 64.3%), have a witnessed cardiac arrest (84.6% versus 77.4%), and have an initial diagnosis of STEMI (32.7% versus 7.9%). In contrast, patients with early coronary angiography were less likely to receive an advanced airway in the field (57.1% versus 68.1%), be treated with therapeutic hypothermia in the hospital (56.4% versus 60.7%), or have underlying heart disease, diabetes mellitus, stroke, and renal disease ($P < 0.01$ for all comparisons; Table 1).

Overall, 2718 (67.5%) patients survived to hospital discharge, and 1968 (48.8%) survived with a favorable neurological outcome. Compared with patients who did not, patients who underwent early coronary angiography had a higher unadjusted rate of survival to discharge (76.0% versus 59.4%; OR 2.16, 95% confidence interval [CI] 1.89–2.47; $P < 0.0001$), as well as survival with favorable neurological outcome (58.7% versus 39.6%; OR 2.18, 95% CI 1.92–2.47; $P < 0.0001$; Tables 2 and 3).

To account for indication bias, we estimated the propensity of receiving early coronary angiography for each patient using a multivariable logistic regression model (c -statistic = 0.746; Appendix Table I in the Data Supplement). A total of 2624 patients (1312 in each group) were successfully matched using propensity scores. Compared with patients who were matched, patients who were unmatched were older, more likely to be women, of black race, have STEMI and a greater burden of comorbidities, but less likely to have a witnessed arrest and receive hypothermia (Appendix Table II in the Data Supplement). Among matched patients, we confirmed that matching was successful in achieving covariate balance between the 2 groups as demonstrated by standardized differences of <10% for all covariates (Figure 2; Appendix Table III in the Data Supplement). In propensity-matched analysis, early coronary angiography remained strongly associated with higher odds of survival to discharge (OR 1.52, 95% CI 1.28–1.80; $P < 0.0001$), as well as survival with favorable neurological outcome (OR 1.47, 95% CI 1.25–1.71; $P < 0.0001$).

Table 1. Baseline Characteristics of Study Patients

Characteristic	Early Coronary Angiography		P Value
	Yes	No	
N	1953	2076	
Age, y (mean±SD)	59.9±12.1	62.0±16.4	<0.0001
Age, y			<0.0001
18–54	648 (33.2)	608 (29.3)	
55–64	637 (32.6)	504 (24.3)	
65–74	441 (22.6)	467 (22.5)	
≥75	227 (11.6)	497 (23.9)	
Female	428 (21.9)	741 (35.7)	<0.0001
Race			<0.0001
White	1088 (55.7)	1104 (53.2)	
Black	182 (9.3)	297 (14.3)	
Other	86 (4.4)	91 (4.4)	
Unknown	597 (30.6)	584 (28.1)	
Location of arrest			<0.0001
Home	1054 (54.0)	1249 (60.2)	
Public	794 (40.7)	612 (29.5)	
Healthcare facility	105 (5.4)	215 (10.4)	
Arrest witnessed			<0.0001
Yes	1653 (84.6)	1605 (77.3)	
No	300 (15.4)	470 (22.6)	
Unknown	0 (0.0)	1 (0.1)	
Bystander CPR	924 (47.3)	1035 (49.9)	0.11
AED used	643 (32.9)	718 (34.6)	0.27
Initial cardiac arrest rhythm			0.98
VF	1347 (69.0)	1426 (68.7)	
VT	105 (5.4)	112 (5.4)	
Unknown shockable rhythm	501 (25.7)	538 (25.9)	
Hypothermia care in field	595 (30.5)	658 (31.7)	0.40
Hypothermia care in hospital			0.02
Yes	1102 (56.4)	1261 (60.7)	
No	813 (41.6)	784 (37.8)	
Unknown	38 (2.0)	31 (1.5)	
Advanced airway placed in field			<0.0001
Yes	1115 (57.1)	1414 (68.1)	
No	741 (37.9)	546 (26.3)	
Unknown	97 (5.0)	116 (5.6)	
STEMI			<0.0001
Yes	639 (32.7)	163 (7.9)	
No	361 (18.5)	655 (31.6)	
Unknown	953 (48.8)	1258 (60.6)	
Co-morbidities			
Heart disease	445 (22.8)	727 (35.0)	<0.0001
Diabetes mellitus	214 (11.0)	353 (17.0)	<0.0001
Hypertension	471 (24.1)	521 (25.1)	0.002
Hyperlipidemia	128 (6.6)	93 (4.5)	<0.0001
Renal disease	35 (1.8)	121 (5.8)	<0.0001

(Continued)

Table 1. Continued

Characteristic	Early Coronary Angiography		P Value
	Yes	No	
Respiratory disease	81 (4.2)	179 (8.6)	<0.0001
Stroke	25 (1.3)	85 (4.1)	<0.0001
Cancer	43 (2.2)	83 (4.0)	<0.0001
Unknown	703 (36.0)	641 (30.9)	

All numbers in table represent number (percent) unless otherwise specified. *P* values derived using 2 sample *t* test for continuous age and Chi-square test for all other variables. AED indicates automatic external defibrillator; CPR, cardiopulmonary resuscitation; SD, standard deviation; STEMI, ST-segment-elevation myocardial infarction; VF, ventricular fibrillation; and VT, ventricular tachycardia.

In the overall cohort, 1253 (64.2%) patients underwent coronary revascularization in the early coronary angiography group compared with 227 (10.9%) patients in the group that did not undergo early coronary angiography. In both groups, patients who underwent coronary revascularization had higher rates of survival to discharge (79.7% versus 69.2% in the early coronary angiography group and 92.5% versus 55.1% in the group that did not receive early coronary angiography) and favorable neurological outcome (61.5% versus 53.6% in the early coronary angiography group and 77.5% versus 34.9% in the group that did not receive early coronary angiography) compared with patients who did not receive coronary revascularization. After additional adjustment of coronary revascularization in a sequential model, we found that the association of early coronary angiography with survival to discharge was markedly attenuated (OR 1.59, 95% CI 1.35–1.86; *P*<0.0001 to OR 1.12, 95% CI 0.94–1.35; *P*=0.21). Similarly, the association between early coronary angiography and favorable neurological outcome was attenuated (OR 1.59, 95% CI 1.36–1.86; *P*<0.0001 to OR 1.25, 95% CI 1.05–1.49; *P*=0.01), suggesting that coronary revascularization, in large part, mediated the observed benefit of early coronary revascularization.

We also examined whether the benefit of early coronary angiography was consistent in patients without STEMI. After restricting the analyses to only patients who did not have STEMI on their ECG, a total of 620 patients were successfully matched (310 in each group) after reestimating propensity scores in this cohort. The association between early coronary angiography and survival to hospital discharge became nonsignificant (OR 1.29, 95% CI 0.87–1.90; *P*=0.2). However, survival with favorable neurological outcome remained strongly associated with early coronary angiography (OR 1.60, 95% CI 1.14–2.26; *P*<0.01; Table 3).

Finally, we examined the role of unmeasured confounders in sensitivity analysis. We found that the association between early coronary angiography and survival to discharge would become nonsignificant if an unmeasured confounder *X* with an OR of 1.5 with survival was 7× more prevalent (69%) in the exposed cohort compared with the unexposed cohort (10%). For an OR of 2.0, an unmeasured confounder would need to be 4× more prevalent (41%), whereas for an OR of 3.0, the unmeasured confounder would need to be 2.5× more prevalent (27%) in the exposed cohort compared with its prevalence in the non-exposed cohort to eliminate the effect of early coronary angiography on survival (Appendix Table IV in the Data Supplement). The findings were similar with favorable neurological outcome.

Table 2. Summary of Study Outcomes

Outcome	Early Coronary Angiography		P Value
	Yes	No	
N	1953	2076	
Survival to discharge	1484 (76.0)	1234 (59.4)	<0.0001
Neurological outcome			<0.0001
Good cerebral performance	1147 (58.7)	821 (39.6)	
Moderate disability	246 (12.6)	261 (12.6)	
Severe disability	67 (3.4)	94 (4.5)	
Coma, vegetative state	22 (1.1)	54 (2.6)	
Unknown	2 (0.1)	4 (0.2)	

All numbers in table represent number (percent) unless otherwise specified.

Discussion

In a large prospective cohort of patients with out-of-hospital cardiac arrest caused by VF and pulseless VT who survived to hospital admission, we found that approximately half the patients underwent coronary angiography within 1 calendar day of cardiac arrest. Early coronary angiography was associated with $\approx 50\%$ greater odds of survival to discharge and survival with favorable neurological outcome. The observed benefit of early coronary angiography was largely mediated by coronary revascularization and was consistent in the subgroup of patients who did not have an initial diagnosis of STEMI.

Our results differ from previous observational studies that have examined the association between early coronary angiography and survival after out-of-hospital cardiac arrest in several important ways. First, patients who do not receive early coronary angiography are generally sicker compared with patients who receive early coronary angiography, which can lead to indication bias. Indeed, we found that patients in our study who did not receive early coronary angiography were older, had a higher prevalence of comorbidities, and were less likely to have a witnessed cardiac arrest compared with patients who underwent early coronary angiography. Previous studies have not consistently used methods to account for indication bias and therefore may have overestimated the effect of early coronary angiography on survival.²² In contrast, we used a matched propensity score design to account for indication bias. Second, most of the prior studies were small, retrospective, conducted in single centers, or lacked a standardized definition of cardiac arrest.^{7,9,22} Moreover, many of these studies included only patients who were identified as having a STEMI

or did not have a control group and therefore were limited in drawing inferences.^{9,10,23} In contrast, CARES is the largest registry of out-of-hospital cardiac arrest in the United States that prospectively enrolls all out-of-hospital cardiac arrest patients from participating EMS agencies. The registry is based on the Utstein template with standardized definition of cardiac arrest, clinical variables, and study outcomes. As a result, patients enrolled in our study are more likely to be representative of out-of-hospital cardiac arrest victims in the community.

The importance of early coronary angiography is underscored by the fact that acute MI is the most common pathogenesis of out-of-hospital cardiac arrest, especially because of VF and pulseless VT.^{9,24} Moreover, previous studies have shown that clinical and electrocardiographic criteria are unreliable in identifying coronary ischemia in cardiac arrest. In a French study of 435 patients with out-of-hospital cardiac arrest all of whom underwent coronary angiography, nearly 70% (301) patients did not have ST-elevation on ECG after resuscitation. However, 58% of such patients had at least 1 significant coronary lesion during coronary angiography (negative predictive value = 42%).¹⁰ Therefore, a strategy of routine coronary angiography has considerable appeal in this patient population, even if they do not have electrocardiographic evidence of a STEMI.

It is noteworthy that 50% of patients with cardiac arrest caused by shockable rhythms did not undergo early coronary angiography, despite surviving to hospital admission. The low utilization of early coronary angiography in this population may reflect the lack of a strong evidence base supporting improved outcomes, given that cardiac arrest patients were largely excluded from randomized controlled trials of early revascularization in patients with acute MI. Furthermore, treating physicians may be reluctant to refer patients for invasive procedures when prognosis for neurological recovery is unclear. In this study, we found that early coronary angiography was associated with improved outcomes in patients with out-of-hospital cardiac arrest because of shockable rhythms, and this benefit was because of greater use of early revascularization. Although we used statistical methods to account for indication bias, causal interpretation is limited because of the observational nature of our study. However, given our study findings and the potential to improve survival in out-of-hospital cardiac arrest victims, there is an urgent need for randomized controlled trials to confirm the benefit of coronary angiography in patients with out-of-hospital cardiac arrest,

Table 3. Unadjusted and Adjusted Association of Early Coronary Angiography With Survival to Discharge and Favorable Neurological Outcome

Cohort	Survival to Discharge		Favorable Neurological Outcome	
	OR	95% CI	OR	95% CI
Unadjusted (before matching), (N=4029)*	2.16	1.89–2.47	2.18	1.92–2.47
Propensity matched, (N=2624)—all patients†	1.52	1.28–1.80	1.47	1.25–1.71
Propensity matched for patients identified as not having a STEMI, (N=620)†	1.29	0.87–1.90	1.60	1.14–2.26

CI indicates confidence interval; OR, odds ratio; and STEMI, ST-segment–elevation myocardial infarction.

*Odds ratios and P values derived using logistic regression.

†Odds ratios derived using Cochran–Mantel–Haenszel statistics stratifying by matched pairs; P values derived using McNemar's test.

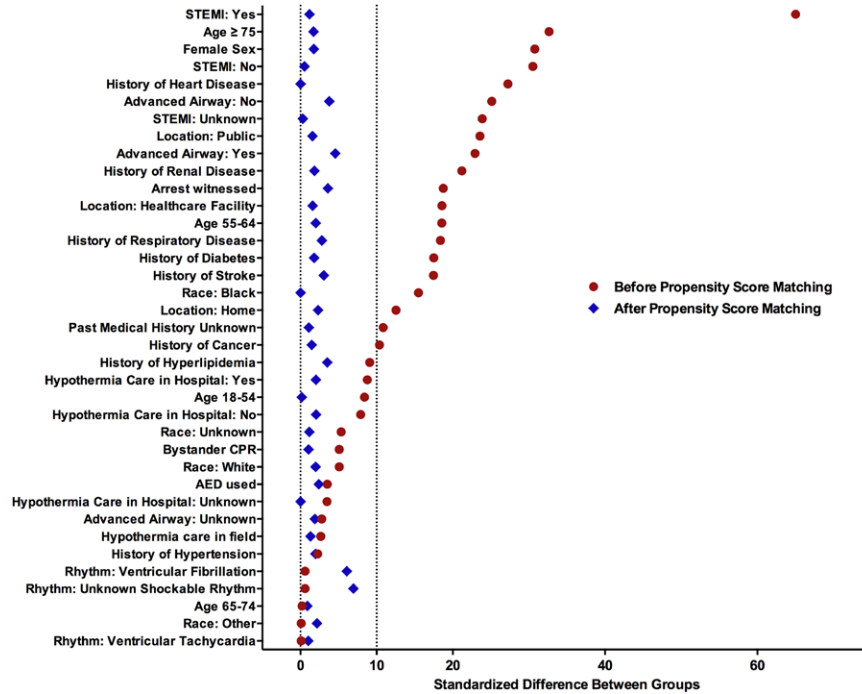


Figure 2. Standardized differences between cohorts before and after propensity score matching. Before propensity matching, there were significant differences in several variables between patients who did and did not receive early coronary angiography (standardized differences >10%). After propensity matching, the standardized difference for all variables was <10%, suggesting that propensity matching was successful in achieving covariate balance. Variables are presented in the descending order of magnitude of standardized differences before propensity matching. AED indicates automatic external defibrillator; CPR, cardiopulmonary resuscitation; SD, standard deviation; and STEMI, ST-segment–elevation myocardial infarction.

including its timing (immediate [<2 hours], early [<24 hours], or after neurological prognostication), especially in patients who are not identified to have ST-elevation on admission.

Our study findings should be interpreted in light of the following limitations. First, assignment of patients to early coronary angiography was not random, and indication bias would be of concern in such analysis. Although we used a matched propensity score analysis to account for indication bias and achieved balance on measured covariates after matching on propensity scores, potential for residual confounding from unmeasured patient-level variables remains. For example, variables that may influence selection of early coronary angiography and survival (such as resuscitation response time, neurological status at the time of admission, presence of shock) were unavailable. Likewise, details of coronary angiography (eg, percent stenosis, number of vessels treated) and related complications were not available. Further studies will require putting these findings in the context of these other key variables that may play a role in both the decision to perform early coronary angiography and the outcomes for patients. Second, although our matching algorithm was successful in achieving covariate balance, only 65% of our sample was successfully matched. Patients who remained unmatched were sicker compared with matched patients, and therefore, our findings may not generalize to such patients. Third, unlike 30-day survival, survival to hospital discharge may be influenced by hospital discharge practices (eg, discharge to hospice). However, this is less likely to be an issue given that early coronary angiography was also associated with favorable neurological outcome in this study. Fourth, it is possible that the association

between early coronary angiography and our study outcomes is confounded by other unmeasured hospital processes of care (eg, quality of postresuscitation care), which may have led to improved outcomes. However, we found that the effect of early coronary angiography on improving survival and neurological outcome was largely mediated by greater use of coronary revascularization in this group. Fifth, some variables (eg, STEMI and comorbidities) were missing in a large proportion of patients because sites were not required to report these variables. Moreover, race variable was also missing in a subset of patients because several EMS agencies are reluctant to report this variable. Variables with missing values were coded as unknown in our propensity score model, which may have introduced bias. Finally, our study only included hospitals that performed coronary angiography on at least one cardiac arrest survivor. Whether patients admitted to hospitals lacking cardiac catheterization laboratory should be transferred to hospitals with these facilities was not addressed in this study.

Conclusions

In conclusion, we found that early coronary angiography is associated with higher rates of survival and favorable neurological outcome in patients successfully resuscitated from an out-of-hospital cardiac arrest caused by VF or VT. Given the observational nature of the data, further research with randomized controlled trials is needed to confirm this potential benefit.

Sources of Funding

CARES registry funded by American Red Cross, American Heart Association, Medtronic Foundation, Zoll Corporation. This study

is supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health under awards K08HL122527 (Dr Girotra) and 1R01HL123980 (Dr Chan).

Disclosures

Dr Chan received research funding from the American Heart Association. Dr McNally received research funding from American Red Cross, American Heart Association, Medtronic Foundation, and Zoll Corporation. The other authors report no conflicts.

References

- Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Baha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER III, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation*. 2014;129:e28–e292. doi: 10.1161/01.cir.0000441139.02102.80.
- John RM, Tedrow UB, Koplan BA, Albert CM, Epstein LM, Sweeney MO, Miller AL, Michaud GF, Stevenson WG. Ventricular arrhythmias and sudden cardiac death. *Lancet*. 2012;380:1520–1529. doi: 10.1016/S0140-6736(12)61413-5.
- O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX, Anderson JL, Jacobs AK, Halperin JL, Albert NM, Brindis RG, Creager MA, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Kushner FG, Ohman EM, Stevenson WG, Yancy CW; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127:e362–e425. doi: 10.1161/CIR.0b013e3182742cf6.
- Jneid H, Anderson JL, Wright RS, Adams CD, Bridges CR, Casey DE Jr, Ettinger SM, Fesmire FM, Ganiats TG, Lincoff AM, Peterson ED, Philippides GJ, Theroux P, Wenger NK, Zidar JP. 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina/non-ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2012;60:645–681. doi: 10.1016/j.jacc.2012.06.004.
- Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, Neumann FJ, Robertson DH, DeLucca PT, DiBattiste PM, Gibson CM, Braunwald E; TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy)—Thrombolysis in Myocardial Infarction 18 Investigators. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med*. 2001;344:1879–1887. doi: 10.1056/NEJM200106213442501.
- Callaway CW, Schmicker RH, Brown SP, Albrich JM, Andrusiek DL, Aufderheide TP, Christenson J, Daya MR, Falconer D, Husa RD, Idris AH, Ornato JP, Rac VE, Rea TD, Rittenberger JC, Sears G, Stiell IG; ROC Investigators. Early coronary angiography and induced hypothermia are associated with survival and functional recovery after out-of-hospital cardiac arrest. *Resuscitation*. 2014;85:657–663. doi: 10.1016/j.resuscitation.2013.12.028.
- Zanuttini D, Armellini I, Nucifora G, Carchietti E, Trillò G, Spedicato L, Bernardi G, Proclemer A. Impact of emergency coronary angiography on in-hospital outcome of unconscious survivors after out-of-hospital cardiac arrest. *Am J Cardiol*. 2012;110:1723–1728. doi: 10.1016/j.amjcard.2012.08.006.
- Waldo SW, Armstrong EJ, Kulkarni A, Hoffmayer K, Kinlay S, Hsue P, Ganz P, McCabe JM. Comparison of clinical characteristics and outcomes of cardiac arrest survivors having versus not having coronary angiography. *Am J Cardiol*. 2013;111:1253–1258. doi: 10.1016/j.amjcard.2013.01.267.
- Spaulding CM, Joly LM, Rosenberg A, Monchi M, Weber SN, Dhainaut JF, Carli P. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med*. 1997;336:1629–1633. doi: 10.1056/NEJM199706053362302.
- Dumas F, Cariou A, Manzo-Silberman S, Grimaldi D, Vivien B, Rosencher J, Empana JP, Carli P, Mira JP, Jouven X, Spaulding C. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac Arrest) registry. *Circ Cardiovasc Interv*. 2010;3:200–207. doi: 10.1161/CIRCINTERVENTIONS.109.913665.
- Sunde K, Pytte M, Jacobsen D, Mangschau A, Jensen LP, Smedsrud C, Draegni T, Steen PA. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation*. 2007;73:29–39. doi: 10.1016/j.resuscitation.2006.08.016.
- Nichol G, Aufderheide TP, Eigel B, Neumar RW, Lurie KG, Bufalino VJ, Callaway CW, Menon V, Bass RR, Abella BS, Sayre M, Dougherty CM, Racht EM, Kleinman ME, O'Connor RE, Reilly JP, Ossmann EW, Peterson E; American Heart Association Emergency Cardiovascular Care Committee; Council on Arteriosclerosis, Thrombosis, and Vascular Biology; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Cardiovascular Nursing; Council on Clinical Cardiology; Advocacy Committee; Council on Quality of Care and Outcomes Research. Regional systems of care for out-of-hospital cardiac arrest: a policy statement from the American Heart Association. *Circulation*. 2010;121:709–729. doi: 10.1161/CIR.0b013e3181c8db7db.
- Noc M, Fajadet J, Lassen JF, Kala P, MacCarthy P, Olivecrona GK, Windecker S, Spaulding C; European Association for Percutaneous Cardiovascular Interventions (EAPCI); Stent for Life (SFL) Group. Invasive coronary treatment strategies for out-of-hospital cardiac arrest: a consensus statement from the European association for percutaneous cardiovascular interventions (EAPCI)/stent for life (SFL) groups. *EuroIntervention*. 2014;10:31–37. doi: 10.4244/EIJV10I1A7.
- McNally B, Stokes A, Crouch A, Kellermann AL; CARES Surveillance Group. CARES: Cardiac Arrest Registry to Enhance Survival. *Ann Emerg Med*. 2009;54:674–683.e2. doi: 10.1016/j.annemergmed.2009.03.018.
- McNally B, Robb R, Mehta M, Vellano K, Valderrama AL, Yoon PW, Sasson C, Crouch A, Perez AB, Merritt R, Kellermann AL; Centers for Disease Control and Prevention. Out-of-hospital cardiac arrest surveillance—Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1, 2005–December 31, 2010. *MMWR Surveill Summ*. 2011;60:1–19.
- Sasson C, Magid DJ, Chan P, Root ED, McNally BF, Kellermann AL, Haukoos JS; CARES Surveillance Group. Association of neighborhood characteristics with bystander-initiated CPR. *N Engl J Med*. 2012;367:1607–1615. doi: 10.1056/NEJMoa1110700.
- A randomized clinical trial of calcium entry blocker administration to comatose survivors of cardiac arrest. Design, methods, and patient characteristics. The Brain Resuscitation Clinical Trial II Study Group. *Control Clin Trials*. 1991;12:525–545.
- Chan PS, Nallamothu BK, Krumholz HM, Spertus JA, Li Y, Hammill BG, Curtis LH; American Heart Association Get with the Guidelines—Resuscitation Investigators. Long-term outcomes in elderly survivors of in-hospital cardiac arrest. *N Engl J Med*. 2013;368:1019–1026. doi: 10.1056/NEJMoa1200657.
- Normand ST, Landrum MB, Guadagnoli E, Ayanian JZ, Ryan TJ, Cleary PD, McNeil BJ. Validating recommendations for coronary angiography following acute myocardial infarction in the elderly: a matched analysis using propensity scores. *J Clin Epidemiol*. 2001;54:387–398. doi: 10.1016/S0895-4356(00)00321-8.
- Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46:399–424. doi: 10.1080/00273171.2011.568786.
- Lin DY, Psaty BM, Kronmal RA. Assessing the sensitivity of regression results to unmeasured confounders in observational studies. *Biometrics*. 1998;54:948–963. doi: 10.2307/2533848.
- Reynolds JC, Callaway CW, El Khoudary SR, Moore CG, Alvarez RJ, Rittenberger JC. Coronary angiography predicts improved outcome following cardiac arrest: propensity-adjusted analysis. *J Intensive Care Med*. 2009;24:179–186. doi: 10.1177/0885066609332725.
- Garot P, Lefevre T, Eltchaninoff H, Morice MC, Tamion F, Abry B, Lesault PF, Le Tarneq JY, Pougès C, Margenet A, Monchi M, Laurent I, Dumas P, Garot J, Louvard Y. Six-month outcome of emergency percutaneous coronary intervention in resuscitated patients after cardiac arrest complicating ST-elevation myocardial infarction. *Circulation*. 2007;115:1354–1362. doi: 10.1161/CIRCULATIONAHA.106.657619.
- Farb A, Tang AL, Burke AP, Sessums L, Liang Y, Virmani R. Sudden coronary death. Frequency of active coronary lesions, inactive coronary lesions, and myocardial infarction. *Circulation*. 1995;92:1701–1709.