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Coronary Angiography Predicts Improved Outcome Following Cardiac Arrest: Propensity-adjusted Analysis

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Objectives: Determine if clinical parameters of resuscitated patients predict coronary angiography (CATH) performance and if receiving CATH after cardiac arrest is associated with outcome. *Introduction:* CATH is associated with survival in patients suffering out-of-hospital cardiac arrest (OHCA) from ventricular fibrillation or ventricular tachycardia(VF/VT). Its effect on outcome in other cohorts is unknown. *Methods:* Chart review of resuscitated cardiac arrest patients between 2005 and 2007. Exclusion criteria: immediate withdrawal of care, hemodynamic collapse, or neurologic exam under sedation. Clinical parameters included Glasgow Coma Scale (GCS) arrest location, presenting rhythm, age, and acute ischemic ECG changes (new left bundle branch block or ST-elevation myocardial infarction-STEMI). Logistic regression identified clinical parameters predicting CATH. The association between CATH and good outcome (discharge home or to acute rehabilitation facility) was determined using logistic regression adjusting for likelihood of receiving CATH via propensity score. *Result:* Of the 241 patients, 96 (40%) received CATH. Significant disease (≥70% stenosis) of ≥1 coronary arteries was identified in 69% of patients including 57% of patients without acute ischemic ECG changes. Unadjusted predictors of CATH were sex, method of arrival, OHCA, presenting rhythm, acute ischemic ECG changes, and GCS. Propensity adjusted logistic regression demonstrated an association between CATH and good outcome (OR 2.16; 95% CI 1.12, 4.19; $P < 0.02$). *Conclusion:* CATH is more likely to be performed in certain patients and identifies a significant number of high-grade stenoses in this population. Receiving CATH was independently associated with good outcome.

Keywords: heart arrest; resuscitation; catheterization; ventricular fibrillation

Introduction

Cardiac arrest is a devastating clinical situation for which the odds of survival are low. Because cardiac arrest represents the most extreme form of heart failure, acute cardiac interventions may improve the odds of survival. For example, the importance of prompt coronary angiography (CATH) is well established in patients presenting with acute ischemic electrocardiogram (ECG) changes such as ST-elevation myocardial infarction (STEMI) or new left bundle branch block (LBBB).[1-3] Delays in revascularization during acute coronary syndromes may be associated with worse outcomes.[1-3] Early CATH is associated with improved survival after out-of-hospital cardiac arrest (OHCA) with ventricular fibrillation or ventricular tachycardia (VF/VT) and/

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or acute ischemic ECG changes (STEMI or new LBBB).[4-7] Despite these data, there are no specific recommendations for routine performance of CATH after cardiac arrest.

Although coronary artery disease is common in patients with cardiac arrest, acute coronary syndromes may be difficult to predict by clinical criteria.[8] Furthermore, a variety of non-cardiac variables may influence the likelihood of performing CATH in a patient after cardiac arrest.[9,10] In the absence of a randomized trial of CATH in the post-cardiac arrest period, rigorous analysis of observational data are required to assess the effect of CATH on good outcomes. This study examined (1) what demographic and clinical variables predict CATH after cardiac arrest and (2) whether performing CATH is associated with good outcome after adjusting for the propensity of receiving CATH. We also investigated the diagnostic and therapeutic yield of CATH.

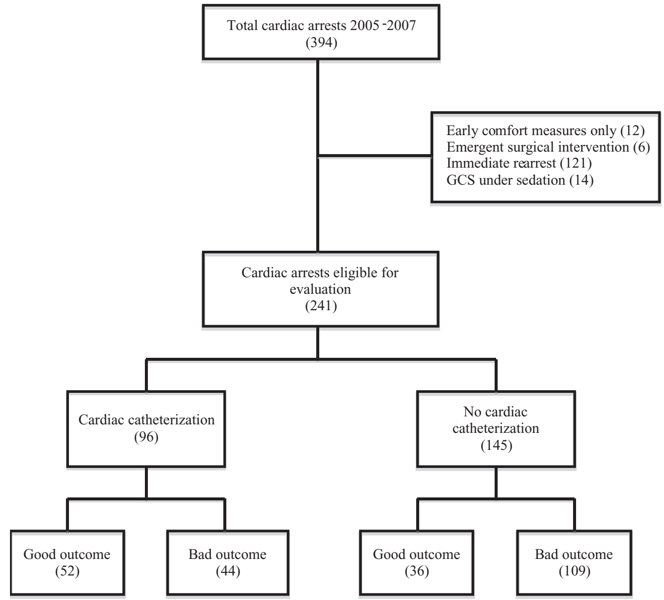

Figure 1. Flowchart of patients with cardiac arrest from 2005 to 2007. A good outcome was defined as discharge to the patient's home or to an acute rehabilitation center. GCS indicates Glasgow Coma Scale.

Methods

The University of Pittsburgh Institutional Review Board approved this study. We completed a retrospective chart review of consecutive adult patients who suffered cardiac arrest (defined as receiving defibrillation or chest compressions for pulseless arrhythmia) and presented to our tertiary care facility between January 1, 2005 and December 31, 2007. We considered all patients who were successfully resuscitated from either OHCA or in-hospital cardiac arrest (IHCA) as potential candidates for cardiac catheterization. Contraindications included: early withdrawal of care or "comfort measures only" (CMO), first score on the Glasgow Coma Scale (GCS) obscured by a sedative or paralytic agent, planned emergent surgical intervention, or immediate rearrest. Patients with CMO or withdrawal of care status determined within the first 6 hours were considered "early" CMO or withdrawal of care. Patients with contraindications were excluded from the analysis (Figure 1).

Demographic (age, gender, location of arrest, year of arrest, method of arrival, and presenting rhythm) and clinical examination data (presence of STEMI or new LBBB, history of cardiac disease, performance of echocardiography, use of therapeutic hypothermia, and GCS) were abstracted from the medical records. Etiology of arrest was considered to be non-cardiac if the patient suffered one of the following: acute airway obstruction, decannulated tracheostomy, hanging victims, or medical toxidrome deemed by a toxicologist as the etiology of arrest. All other arrests were considered cardiac in etiology. In our facility, hypothermia treatment is provided to patients who remain comatose after successful resuscitation from cardiac arrest. Cardiac interventions (catheterization, stents placed, coronary artery bypass grafting [CABG], left ventricular assistance device [LVAD], transplant and intra-aortic balloon pump [IABP]) each patient received were also recorded. A diseased vessel was defined as $\geq$70% occlusion and a positive CATH was defined as $\geq$1 diseased vessel. Early CATH was defined as receiving CATH within 24 hours of arrival. Similar to prior research, neurologic outcome was classified as "Good" if the patient was discharged to home or acute rehabilitation facility. All other neurologic outcomes (discharge to chronic rehabilitation facility, skilled nursing facility, hospice, or death) were classified as "Bad."[11]

Statistical Analysis

Cardiac arrest patients undergoing CATH differ from those that do not with respect to demographic and clinical characteristics. Because these same characteristics may be predictive of good clinical outcomes and patients are not randomized to receive angiography, we used a propensity score analysis to assess the association between CATH and clinical outcomes.[12] This analysis allowed us to adjust for these potential confounders by comparing rates of good outcome between patients receiving and not receiving CATH at similar levels of demographic and clinical covariates. We first used a logistic regression model that predicted early CATH based on 13 demographic and clinical exam characteristics (Table 1). Demographic (age, gender, year of arrest, method of arrival, location of arrest, and presenting rhythm) and clinical examination data (presence of STEMI or new LBBB, history of cardiac disease, echocardiography, use of therapeutic hypothermia, and GCS) were included in the propensity score calculation. The c-statistic for this model was 0.89, indicating a good ability to predict patients receiving and not receiving CATH. We used the predicted probability of receiving CATH as the propensity score for each patient. Patients were then stratified by quartile of increasing propensity score. To verify that our propensity scores would adequately adjust for differences between those receiving and not receiving CATH, we ran logistic models predicting CATH for each of the 13 predictors of CATH adjusting for the quartiles of propensity scores. Attenuation of the predictor's adjusted odds ratio (OR) to the null value and inclusion of 1 in the confidence interval would indicate "effective" propensity scores in balancing covariate differences between the 2 groups. As a crude stratified analysis, we then compared the rate of good clinical outcome between patients receiving and not receiving CATH within each propensity score quartile using Fisher exact test. We then performed a multiple logistic regression to estimate the overall odds ratio of good clinical outcome for CATH adjusting for propensity score quartile. In addition, we used descriptive statistics to evaluate CATH results across patients characterized by presenting rhythm. The effect of early (day of arrest) versus delayed catheterization was compared using Fisher Exact test. Length of stay between the CATH groups was compared using a t test. Analyses were performed using STATA version 10.0 (STATA Corporation, College Station, Tex) and all tests were 2-sided with $\alpha = .05$.

Results

Of the 394 cardiac arrest participants, 153 met exclusion criteria, primarily because of rapid rearrest (121/153, 79%; Figure 1). A total of 241 patients were analyzed. Clinical features of the population are listed in Table 1. Eleven of the 241 arrests (5%) were considered non-cardiac in etiology. Coronary artery disease was present in 52% of patients overall and did not differ between CATH (49%) and no CATH (53%; $P = .53$) groups.

Predictors of Receiving CATH

Unadjusted predictors of CATH were male gender (OR 1.71; 95% CI 1.01, 2.91), transfer from outside hospital (OR 1.94; 95% CI 1.01, 3.72), OHCA (OR 2.83; 95% CI 1.63, 4.89), pulseless electrical activity (PEA; OR 0.30; 95% CI 0.16, 0.58), asystole (OR 0.17; 95% CI 0.08, 0.37), unknown initial rhythm (OR 0.14; 95% CI 0.04, 0.45), STEMI or new LBBB (OR 26.25; 95% CI 8.98, 76.76), performance of echocardiography (OR 2.08; 95% CI 1.17, 3.69), abnormal eye GCS (OR 0.53; 95% CI 0.31, 0.91), abnormal verbal GCS (OR 0.23; 95% CI 0.11, 0.48), and abnormal motor GCS (OR 0.41; 95% CI 0.24, 0.69; Table 1). There were no significant differences between participants with CATH and those without CATH with respect to age, year, history of cardiac disease, and use of therapeutic hypothermia. All patients with LBBB received CATH. Of the 15 STEMI patients, 4 did not receive CATH because of poor neurologic status. Adjusting for propensity score quartiles, the odds ratios of all predictors moved closer to 1.0 and their confidence intervals included the null value of 1.0, with the exception of STEMI or new LBBB (OR 4.02; 95% CI 1.12, 14.43).

Propensity Score Analysis: CATH and Good Clinical Outcome

Just over half of patients receiving CATH experienced a good clinical outcome (54.2%), compared to 24.8% of patients not receiving CATH (Table 2). The same trend in better outcomes for the CATH group was observed within propensity quartiles with the exception of the first quartile where the

Table 1. Patient Characteristics Predicting CATH Performance

Characteristics	n (%), All cases, 241 (100%)	Performance of CATH, n (%) Yes, (n = 96)	No, (n = 145)	*P*-value	OR for Performing CATH (95%CI) Unadjusted	Adjusted for Propensity Score
Demographics						
Age (years)				.664		
Mean ± standard deviation	60.6 ± 15.9	61.2 ± 13.9	60.3 ± 16.6		1.0 (0.99, 1.02)	0.99 (0.98, 1.02)
Gender				.044		
Female	107 (45%)	35 (37%)	72 (50%)		1	1
Male	134 (55%)	61 (64%)	73 (50%)		1.71 (1.01, 2.91)	1.18 (0.61, 2.25)
Year of arrest				.375		
2005	69 (29%)	23 (24%)	46 (32%)		1	1
2006	91 (38%)	37 (39%)	54 (37%)		1.37 (0.71, 2.63)	0.84 (0.37, 1.91)
2007	81 (34%)	36 (38%)	45 (31%)		1.6 (0.82, 3.11)	1.00 (0.43, 2.31)
Method of Arrival				<.001		
EMS	59 (24%)	25 (26%)	34 (23%)		1	1
Transfer from outside hospital	102 (42%)	60 (63%)	42 (29%)		1.94 (1.01, 3.72)	1.54 (0.73, 3.27)
Inpatient	75 (31%)	9 (9%)	66 (46%)		0.19 (0.07, 0.44)	0.53 (0.19, 1.50)
In ED	5 (2%)	2 (2%)	3 (2%)		0.91 (0.14, 5.83)	0.91 (0.12, 6.89)
OHCA				<.001		
Yes	135 (56%)	68 (71%)	67 (46%)		2.83 (1.63, 4.89)	1.34 (0.68, 2.65)
No	106 (44%)	28 (29%)	78 (54%)		1	1
Presenting Rhythm				<.001		
VF/VT	93 (39%)	57 (60%)	36 (25%)		1	1
PEA	74 (31%)	24 (25%)	50 (34%)		0.30 (0.16, 0.58)	0.66 (0.31, 1.43)
Asystole	52 (22%)	11 (11%)	41 (28%)		0.17 (0.08, 0.37)	0.69 (0.26, 1.82)
Unknown	22 (9%)	4 (4%)	18 (12%)		0.14 (0.04, 0.45)	0.59 (0.15, 2.25)
Clinical exam						
STEMI or new LBBB				<.001		
Yes (either)	46 (20%)	42 (44%)	4 (3%)		26.25 (8.98, 76.76)	4.02 (1.12, 14.43)
No (neither)	189 (78%)	54 (56%)	135 (97%)		1	1
History of cardiac disease				.526		
Yes	122 (51%)	46 (49%)	76 (53%)		0.84 (0.50, 1.42)	0.91 (0.47, 1.76)
No/ unknown	115 (49%)	48 (51%)	67 (47%)		1	1
Echocardiography				.012		
Yes	160 (66%)	73 (76%)	87 (60%)		2.08 (1.17, 3.69)	1.64 (0.78, 3.37)
No	80 (33%)	23 (24%)	57 (40%)		1	1
Therapeutic Hypothermia						
Yes	79 (33%)	32 (33%)	47 (32%)	.882	1.04 (0.60, 1.80)	0.88 (0.45, 1.73)
No	162 (67%)	64 (67%)	98 (68%)		1	1
Eye GCS						
1-3	152 (63%)	52 (54%)	100 (69%)	.020	0.53 (0.31, 0.91)	0.84 (0.43, 1.63)
4	89 (37%)	44 (46%)	45 (31%)		1	1
Verbal GCS						
1-4	202 (84%)	69 (72%)	133 (92%)	<.001	0.23 (0.11, 0.48)	0.65 (0.28, 1.51)
5	39 (16%)	27 (28%)	12 (8%)		1	1
Motor GCS						
1-5	151 (63%)	48 (50%)	103 (71%)	.001	0.41 (0.24, 0.69)	0.61 (0.31, 1.18)
6	90 (37%)	48 (50%)	42 (29%)		1	1

NOTES: EMS = emergency medical services; in ED = cardiac arrest occurred in the emergency department; GCS = Glasgow Coma Score; LBBB = new left bundle branch block; OHCA = out-of-hospital cardiac arrest; STEMI = ST-segment elevation myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

Table 2. Comparison of the Percentage With Good Clinical Outcome for Patients who Received CATH and Those Who did not

	% Good Outcome		
	CATH	No CATH	*P*-value
Overall unadjusted	52/96 (54.2%)	36/145 (24.8%)	<.0001
Quartiles of Propensity Score			
First quartile	0/1 (0%)	8/57 (14%)	1.0
Second quartile	6/16 (38%)	13/42 (31%)	.7
Third quartile	15/25 (60%)	10/33 (30%)	.03
Fourth quartile	31/54 (57%)	5/13 (38%)	.3

NOTE: CATH = cardiac catheterization with coronary angiography.

Table 3. Catheterization Results in Patients With ECG Changes of STEMI or new LBBB

	All Rhythms (n = 46)	VF/VT (n = 27)	PEA (n = 11)	Asystole (n = 7)	Unknown (n = 1)
Received CATH	42 (91%)	27 (100%)	8 (73%)	6 (86%)	1 (100%)
Among those receiving CATH					
Positive CATH	39 (93%)	25 (93%)	7 (88%)	6 (100%)	1 (100%)
1 vessel	16 (38%)	13 (48%)	1 (13%)	2 (33%)	0 (0%)
2 vessels	11 (26%)	6 (22%)	3 (38%)	2 (33%)	0 (0%)
3 vessels	7 (17%)	4 (15%)	1 (13%)	2 (33%)	0 (0%)
4 vessels	3 (7%)	0 (0%)	2 (25%)	0 (0%)	1 (100%)
5 vessels	2 (5%)	2 (7%)	0 (0%)	0 (0%)	0 (0%)
Stent	29 (63%)	21 (78%)	4 (36%)	3 (43%)	1 (100%)
CABG	5 (11%)	4 (15%)	1 (9%)	0 (0%)	0 (0%)
LVAD	2 (4%)	0 (0%)	1 (9%)	0 (0%)	1 (100%)
Transplant	2 (4%)	0 (0%)	2 (18%)	0 (0%)	0 (0%)
IABP	16 (35%)	6 (22%)	5 (45%)	4 (57%)	1 (100%)

NOTES: CATH = cardiac catheterization with coronary angiography; positive CATH = lesion ≥70% present on CATH; CABG = coronary artery bypass graft; IABP = intra-aortic balloon pump; LVAD = mechanical left-ventricular assist device; PEA = pulseless electrical activity; VF/VT = ventricular fibrillation or ventricular tachycardia.

likelihood of receiving CATH was very small. In the overall propensity-adjusted logistic regression, receiving CATH increased the likelihood of having a good clinical outcome (OR 2.16; 95% CI 1.12, 4.19; $P < .02$). In exploratory analysis, early CATH (day of arrest, n = 63) was not associated with improved survival when compared to later CATH (63% vs. 67% (n = 33), respectively; $P = .66$), nor was it associated with good outcome (52% vs. 58%; $P = .67$). Hospital length of stay did not differ between the CATH (15 days) and no CATH groups (11 days; $P = .18$).

The findings of catheterization are described in Tables 3 and 4. Even in patients without acute ischemic ECG changes, CATH revealed significant coronary artery lesions in 57%. Only 2 patients had failed revascularization attempts via CATH. Overall, 14% of patients required IABP, 7% received CABG, 2% received LVAD, and 3% received cardiac transplant following their cardiac arrest.

Discussion

Our study demonstrates that demographic and clinical variables available immediately post cardiac arrest are associated with CATH. Specifically, gender, OHCA, acute ischemic electrocardiographic changes, and echocardiography are positively associated with receiving CATH after cardiac arrest. An initial rhythm of PEA, asystole, or lower than maximal eye, verbal, or motor GCS are negatively associated with receipt of CATH. These data also reveal a bias for taking patients with superior neurological

Table 4. Catheterization results in Patients Without ECG Changes of STEMI or new LBBB

	All Rhythms (n = 195)	VF/VT (n = 66)	PEA (n = 63)	Asystole (n = 45)	Unknown (n = 21)
Received CATH	54 (28%)	30 (45%)	16 (25%)	5 (11%)	3 (14%)
Among those receiving CATH					
Positive CATH	31 (57%)	17 (57%)	9 (56%)	3 (60%)	2 (66%)
1 vessel	13 (24%)	8 (27%)	3 (19%)	2 (40%)	0 (0%)
2 vessels	7 (13%)	2 (7%)	3 (19%)	0 (0%)	2 (66%)
3 vessels	5 (9%)	3 (10%)	1 (6%)	1 (20%)	0 (0%)
4 vessels	4 (7%)	3 (10%)	1 (6%)	0 (0%)	0 (0%)
5 vessels	2 (4%)	1 (3%)	1 (6%)	0 (0%)	0 (0%)
Stent	19 (10%)	10 (16%)	5 (9%)	1 (2%)	3 (15%)
CABG	11 (6%)	9 (14%)	1 (2%)	1 (2%)	0 (0%)
LVAD	4 (2%)	2 (3%)	1 (2%)	1 (2%)	0 (0%)
Transplant	6 (3%)	5 (8%)	0 (0%)	1 (2%)	0 (0%)
IABP	18 (10%)	11 (17%)	3 (5%)	3 (7%)	2 (10%)

NOTES: CATH = cardiac catheterization with coronary angiography; positive CATH = lesion ≥70% present on CATH; CABG = coronary artery bypass graft; IABP = intra-aortic balloon pump; LVAD = mechanical left-ventricular assist device; PEA = pulseless electrical activity; VF/VT = ventricular fibrillation or ventricular tachycardia.

status to CATH. Normal eye, verbal, and motor GCS scores are independent predictors of CATH performance. Moreover, 4 STEMI patients in our population did not receive CATH because of unfavorable neurological status. Importantly, Levy et al demonstrated that an initially poor GCS did not predict a poor neurologic outcome with certainty.[13] Prior studies have also demonstrated that the use of hypothermia after cardiac arrest improves neurologic outcome in patients who are comatose after initial resuscitation.[11,14] Some argue that because cardiac arrest caries a high mortality from neurological, rather than cardiac sequelae, CATH should be reserved for those patients who demonstrate neurological improvement.[10] Given the priority of early reperfusion to reduce morbidity and mortality,[1-3] this practice might deprive some patients who might recover neurologically of their potential survival. Furthermore, the use of therapeutic hypothermia may confound this argument, because patients may not reveal their neurological trajectory until up to several days after return of spontaneous circulation.[13,15] A combination of these potent therapies increased the number of patients enjoying a good outcome following cardiac arrest by 30%.[7] These data should be considered when evaluating post-cardiac arrest patients for CATH and may prompt clinicians to consider its use in patients who may not traditionally receive it.

Even after adjusting for clinical factors associated with CATH performance, receiving CATH after cardiac arrest was independently associated with good neurological outcome following cardiac arrest. In these data, there was no difference in outcomes between groups receiving early and later CATH. This may be due to the small sample size. Although it is generally accepted that early CATH is indicated in patients with STEMI or new LBBB, the role of early CATH in other post-cardiac arrest patients remains to be determined. One potential benefit of early CATH is the ability to define coronary anatomy, because early identification of coronary versus non-coronary causes of cardiac arrest in an otherwise undifferentiated patient would result in different therapeutic strategies. Notably, 14% of the patients in this study required IABP therapy during the post-arrest period. A significant number of patients also required CABG, left ventricular assist device, or cardiac transplantation after CATH.

A criticism of prior studies investigating the use of prompt CATH to improve survival has been extensive exclusion criteria and highly selective patient populations.[4-6,8,16] In this study, improved survival and outcome were associated with CATH in cardiac arrest patients regardless of arrest location, presenting rhythm, presence of STEMI or new LBBB, or neurological status. CATH was independently associated with good neurological outcome.

Finally, many patients suffering cardiac arrest have significant coronary artery disease. These data agree with prior literature suggesting 60% to 80% of cardiac arrests are a result of cardiovascular disease.[4,816,17] Those participants without STEMI or new LBBB also had significant coronary lesions in 56% to 66% of cases. These data suggest the burden of coronary artery disease is high in this population and support CATH in this population. Given that CATH is independently associated with good neurologic outcome, the high coronary artery disease burden in this population, the benefits of early reperfusion, and improved therapies for brain resuscitation following cardiac arrest, CATH should be considered along with hypothermia in all post-cardiac arrest patients.

This study has several limitations. First, it is limited to a retrospective chart review. Data could have been inaccurately reported in the patient record. Patients could have been missed, but we believe this to have been minimized by our inclusive search strategy. Third, the cohort of IHCA patients may not be representative of other hospitals, because ours has a tiered Rapid Response System with a reduced rate of IHCA.[18] Finally, the outcome assessed was discharge to home or acute rehabilitation facility as a surrogate for long-term neurological status. However, we have previously noted that discharge disposition is similar to Cerebral Performance Category classification.[19]

Conclusions

Demographic and clinical variables, including neurologic exam, predict performance of CATH after cardiac arrest. When adjusted for these variables, performance of CATH is independently predictive of good neurological outcome. Post-cardiac arrest CATH reveals a high incidence of significant coronary artery disease.

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