Percutaneous Coronary Intervention Reduces Mortality in Out-of-Hospital Cardiac Arrest after Acute Coronary Syndrome: An Outcomes-Based Study from the Nationwide Inpatient Sample Database

Christine S. M. Lau[1,2], Mahyar Pourriahi[1,2], Amanda Ward[2], Kedar P. Kulkarni[1,2], Krishnaraj Mahendraraj[1], Ronald S. Chamberlain[1,2,3,4]*

[1]Department of Surgery, Saint Barnabas Medical Center, Livingston, NJ, USA
[2]Saint George's University School of Medicine, St. George, Grenada
[3]Department of Surgery, New Jersey Medical School, Rutgers University, Newark, NJ, USA
[4]Department of Surgery, Banner MD Anderson Cancer Center, Gilbert, AZ, USA
Email: *Ronald.Chamberlain@bannerhealth.com

Abstract

Introduction: Mortality following cardiac arrest (CA) is extremely high, with rates as high as 91.5% after out-of-hospital cardiac arrest (OHCA) and 76.1% after in-hospital cardiac arrest (IHCA). This study assessed the clinical profile and outcomes of a large cohort of patients undergoing primary percutaneous coronary intervention (PCI) for OHCA to determine its effect on clinical outcomes and mortality. **Methods**: 247,456 patients with OHCA due to acute coronary syndrome (ACS) were abstracted from the Nationwide Inpatient Sample database (2001-2011). **Results**: Among 247,456 OHCA patients, 11,111 (4.5%) had PCI while 236,345 (95.5%) did not. Patients who underwent PCI were younger than those who did not receive PCI (64 vs. 66 years), $p < 0.001$. Caucasians (79.6%) and males (66.5%) were more likely to undergo PCI, while significantly fewer African Americans (AA) (7.7%) and Hispanics (6.5%) received PCI, $p < 0.001$. A significantly greater percentage of patients with private insurance (35.5%) or Medicare (47.4%) underwent PCI, $p < 0.001$. Overall mortality was significantly lower among those undergoing PCI (28.3% vs. 65.4%), $p < 0.001$. Multivariate analysis identified age >65 years, female gender, AA or Hispanic race, advanced cancer, and liver dysfunction as independent factors associated with increased mortality, while PCI conferred a survival advantage in OHCA, $p < 0.001$. **Conclusion**: Treatment with PCI was associated with a significant decrease in mortality. PCI was performed most often in Caucasians, males, patients > 50 years old, and those with Medicare. PCI significantly reduces mortality in OHCA patients and should be considered in all OHCA patients. Further investigation and

development of methods to overcome the apparent socioeconomic barriers to PCI is required.

Keywords

Cardiac Arrest, Percutaneous Coronary Intervention, NIS

1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a leading cause of death in the industrialized world [1] [2] [3]. Over 350,000 people experience OHCA each year in the United States (US), while an additional 200,000 patients experience in-hospital cardiac arrest (IHCA) [4] [5] [6]. The Global Registry of Acute Coronary Events (GRACE) Registry found that cardiac arrest was an independent prognostic factor for in-hospital mortality [3] [7]. Despite advancements in resuscitation guidelines and techniques, survival rates remain low for both OHCA (9.5%) and IHCA (23.9%) [3] [6] [8] [9].

Coronary artery disease (CAD) plays a major role in acute coronary syndrome (ACS), and is the most important cause of OHCA [10]. Clinical and pathological analysis suggest that CAD, cardiac dysrhythmia, cardiomyopathy, or hypertensive heart disease increase the risk of ACS [11]. Risk factors such as smoking, elevated lipids, inactivity, diabetes mellitus, and obesity also contribute to CAD [12] [13].

The 2013 American College of Cardiology Foundation and American Heart Association (ACCF/AHA) guidelines recommend immediate angiography and percutaneous coronary intervention (PCI) in resuscitated OHCA patients whose initial electrocardiogram (ECG) show ST-segment elevation myocardial infarction (STEMI) [14]. There is increasing evidence that PCI should be considered in all OHCA patients for whom a cardiac etiology cannot be clinically excluded, regardless of electrocardiogram (ECG) findings. Dumas *et al.* studied 435 patients with return of spontaneous circulation (ROSC) and found at least one significant coronary artery lesion in nearly all patients with ST-elevation [1]. Furthermore, coronary artery lesions were also present in over 50% of patients without ST-segment elevation [1]. Successful PCI was associated with a significant survival advantage for both ST-elevation (51% vs. 31%, $p < 0.001$) and the non-ST elevation patients (47% vs. 31%, $p < 0.001$), compared to patients not receiving PCI [1]. Given the high incidence of ACS in patients with OHCA, guidelines recommend immediate angiography in all resuscitated OHCA patients suspected of ACS regardless of ECG finding [1] [8]. Despite these current recommendations, the real world use of PCI in this setting remains low.

Currently there are few cohort studies examining the utilization of PCI after OHCA and its effect on survival. The Kunadian *et al.* study and the Dumas *et al.* studies are both retrospective studies examining the utilization of PCI for OHCA in United Kingdom and Parisian population respectively [1] [3]. The current study examined a large cohort of OHCA patients from the Nationwide Inpatient Service (NIS) database to compare demographic and clinical differences between those who received PCI and those who did not, and the impact of PCI on survival.

2. Methods

Data for the current study was extracted from the Nationwide Inpatient Sample (NIS) database, a part of the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality (AHRQ) database, between 2001 and 2011. The NIS is the largest all-payer inpatient care database in the US, containing data on more than eight million hospital stays from over 1000 hospitals. All patients identified to have had OHCA were identified and exported to IBM SPSS®v20.2. ICD-0-CM code 427.5 was utilized. Demographic and clinical data extracted included age, gender, race, admission source, primary expected payer, and preexisting comorbidities. Endpoints examined included length of stay (LOS), and overall inpatient mortality. Patients who received primary percutaneous coronary intervention (PCI), as a primary procedure, was identified using ICD-9 code 00.66, 00.40 - 00.48. Data was compared across the two subgroups: patients who received primary percutaneous coronary intervention and those who did not. Categorical variables were compared using the *Chi*-square test, and continuous variables were compared using student t-test and analysis of variance (ANOVA). Multivariate analysis using the "backward Wald" method was performed to calculate odds ratios (OR) and determine independent factors which increased the risk of mortality following cardiac arrest. All reported data was included in the calculations and analysis, including frequencies and multivariate analysis. The total number of patients included in the analysis for each variable has been reported in the corresponding tables. Statistical significance was accepted at the level of $p < 0.05$.

3. Results

There were 247,456 patients who had OHCA reported in the NIS database over the 11-year period (2001-2011) (Table 1). There were 11,111 (4.5%) patients who received PCI and 236,345 (95.5%) patients who did not receive PCI.

3.1. Demographic Characteristics

The mean age for all OHCA patients was 66 ± 19 years (Table 1). Patients who received PCI were younger than those who did not receive PCI (mean age of 64 ± 13 years vs. 66 ± 19 years). A greater proportion of patients who received PCI were between the age of 50 and 64 years old (38.0% vs. 23.4%), while a lower percentage of patients receiving PCI were <50 years (14.1% vs. 16.6%) and >65 years (47.9% vs. 60.0%), $p < 0.001$. The majority of patients who developed OHCA were males (54.2%) with a male to female (M:F) ratio of 1.18:1. More males underwent PCI than females (66.5% vs. 33.5%, $p < 0.001$). Among those who received PCI, 79.6% (N = 6931) were Caucasian, 7.7% (N = 675) were African American, 6.5% (N = 563) were Hispanic, and 6.2% (N = 541) were designated as "other". A significantly greater proportion of patients who received PCI were Caucasians (79.6% vs. 68.3%) while fewer patients who received PCI were African Americans (7.7% vs. 16.3%) and Hispanics (6.5% vs. 9.2%), $p < 0.001$.

Overall, most patients who developed OHCA were admitted from the emergency room (ER) (67.5%), or transferred from home (21.9%) or another hospital (7.7%). A smaller proportion of patients who received PCI were admitted from the ER (62.7% vs. 67.6%, $p < 0.001$), and a greater percentage of them were admitted through another

Table 1. Demographic profile 247,456 patients with out of hospital cardiac arrest from the nationwide inpatient sample database (2001 to 2011).

Variables	Overall	PCI	No PCI
N (%)	247,456	11,111 (4.5%)	236,345 (95.5%)
Age, (Mean ± SD)	66 ± 19	64 ± 13	66 ± 19
Under 50	40,813 (16.5%)	1567 (14.1%)	39,246 (16.6%)
Age 50 to 64	59,426 (24.0%)	4220 (38.0%)	55,206 (23.4%)
Age 65 and older	147,144 (59.5%)	5323 (47.9%)	141,821 (60.0%)
Gender			
Male	134,100 (54.2%)	7391 (66.5%)	126,709 (53.6%)
Female	113,311 (45.8%)	3719 (33.5%)	109,592 (46.4%)
Race, N (%)			
Caucasian	133,492 (68.8%)	6931 (79.6%)	126,561 (68.3%)
African American	30,948 (16.0%)	675 (7.7%)	30,273 (16.3%)
Hispanic	17,639 (9.1%)	563 (6.5%)	17,076 (9.2%)
Other	11,908 (6.1%)	541 (6.2%)	11,367 (6.1%)
Admission source, N (%)			
ER	122,290 (67.5%)	3559 (62.7%)	118,731 (67.6%)
Another hospital source	14,009 (7.7%)	799 (14.1%)	13,210 (7.5%)
Other health facility, including long-term care	5079 (2.8%)	108 (1.9%)	4971 (2.8%)
Court/Law enforcement	61 (0.0%)	1 (0.0%)	60 (0.0%)
Routine admission from home	39,750 (21.9%)	1209 (21.3%)	38,541 (22.0%)
Primary expected payer, N (%)			
Medicare	152,445 (61.7%)	5259 (47.4%)	147,186 (62.4%)
Medicaid	24,589 (10.0%)	710 (6.4%)	23,879 (10.1%)
Private insurance	50,978 (20.6%)	3933 (35.5%)	47,045 (19.9%)
Self-pay	11,518 (4.7%)	761 (6.9%)	10,757 (4.6%)
No charge	1027 (0.4%)	65 (0.6%)	962 (0.4%)
Other	6490 (2.6%)	363 (3.3%)	6127 (2.6%)

Abbreviations: ER = emergency room; N = number; PCI = primary percutaneous coronary intervention; SD = standard deviation.

hospital source (14.1% vs. 7.5%, $p < 0.001$).

The majority of patients who developed cardiac arrest had Medicare insurance (61.7%), followed by private insurance (20.6%), Medicaid (10.0%), self-pay (4.7%), other (2.6%), or no charge (0.4%). A significantly greater proportion of patients who received PCI had private insurance (35.5% vs. 19.9%, $p < 0.001$), compared to those who did not receive PCI.

3.2. Clinical Characteristics

A smaller percentage of patients undergoing PCI after cardiac arrest had preexisting

comorbidities (Table 2). Specifically, fewer PCI patients had a history of alcohol abuse (4.4% vs. 4.9%), deficiency anemia (14.1% vs. 15.6%), congestive heart failure (4.1% vs. 18.4%), coagulopathy (7.1% vs. 10.2%), depression (3.9% vs. 4.5%), diabetes with chronic complications (3.9% vs. 5.9%), hypothyroidism (5.7% vs. 7.1%), liver disease (1.0% vs. 3.1%), fluid and electrolyte disorder (32.7% vs. 42.0%), other neurological disorder (7.1% vs 13.9%), renal failure (13.1% vs 19.1%), and valvular disease (1.0% vs 4.8%). In contrast, a greater percentage of PCI patients suffered from uncomplicated diabetes mellitus (20.8% vs. 19.7%), hypertension (52.1% vs. 43.3%), obesity (9.0% vs. 5.9%), and peripheral vascular disease (8.8% vs. 7.5%).

3.3. Clinical Outcomes

Patients who received PCI had an equivalent LOS to those who did not (9 ± 10 days vs. 9 ± 15 days) (Table 3). The overall in-hospital mortality rate for patients who developed cardiac arrest was 63.7%, however, it was significantly lower in PCI patients compared to those not receiving PCI (28.3% vs. 65.4%, $p < 0.001$).

3.4. Multivariate Analysis

Multivariate analysis identified age > 65 (OR 1.6), female gender (OR 1.1), African

Table 2. Clinical profile 247,456 patients with out of hospital cardiac arrest from the nationwide inpatient sample database (2001 to 2011).

Variables	Overall	PCI	No PCI
N (%)	247,456	11,111 (4.5%)	236,345 (95.5%)
Comorbidity, N (%)			
Alcohol abuse	11,847 (4.8%)	488 (4.4%)	11,359 (4.9%)
Deficiency anemias	38,052 (15.5%)	1567 (14.1%)	36,485 (15.6%)
Congestive Heart Failure	43,448 (17.7%)	460 (4.1%)	42,988 (18.4%)
Chronic Pulmonary Disease	56,465 (23.0%0)	2020 (18.2%)	54,445 (23.3%)
Coagulopathy	24,750 (10.1%)	788 (7.1%)	23,962 (10.2%)
Depression	10,903 (4.5%)	434 (3.9%)	10,469 (4.5%)
Diabetes, uncomplicated	48,320 (19.7%)	2311 (20.8%)	46,009 (19.7%)
Diabetes, with chronic complications	14,249 (5.8%)	433 (3.9%)	13,816 (5.9%)
Hypertension	107,159 (43.7%)	5789 (52.1%)	101,370 (43.3%)
Hypothyroidism	17,252 (7.0%)	634 (5.7%)	16,618 (7.1%)
Liver Disease	7,469 (3.0%)	113 (1.0%)	7356 (3.1%)
Fluid and electrolyte disorder	101,967 (41.6%)	3631 (32.7%)	98,336 (42.0%)
Other neurological disorder	33,302 (13.6%)	788 (7.1%)	32,514 (13.9%)
Obesity	14,746 (6.0%)	1004 (9.0%)	13,742 (5.9%)
Peripheral Vascular Disease	18,469 (7.5%)	977 (8.8%)	17,492 (7.5%)
Renal failure	46,179 (18.8%)	1457 (13.1%)	44,722 (19.1%)
Valvular Disease	11,362 (4.6%)	109 (1.0%)	11,253 (4.8%)

Abbreviations: N = number; PCI = primary percutaneous coronary intervention.

Table 3. Clinical outcomes profile 247,456 patients with out of hospital cardiac arrest from the nationwide inpatient sample database (2001 to 2011).

Variables	Overall	PCI	No PCI
N (%)	247,456	11,111 (4.5%)	236,345 (95.5%)
Length of stay (mean days ± SD)	9 ± 15	9 ± 10	9 ± 15
Outcome of hospitalization, N (%)			
Alive	89,749 (36.3%)	7958 (71.7%)	81,791 (34.6%)
Dead	157,429 (63.7%)	3146 (28.3%)	154,283 (65.4%)

Abbreviations: N = number; PCI = primary percutaneous coronary intervention; SD = standard deviation.

American (OR 1.2), advanced cancer (OR 2.3), and liver dysfunction (OR 1.8) as independent risk factors for mortality, while PCI (OR 0.2) conferred a survival advantage in patients with cardiac arrest, $p < 0.001$. Insurance status was not found to be independently associated with mortality, $p > 0.05$.

4. Discussion

Coronary artery disease is a leading cause of morbidity and mortality in both men and women in industrialized countries [15]. In the US, there are over 350,000 cases of OHCA and over 200,000 cases of IHCA each year [5]. According to the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines, PCI is a Class I-A recommendation following cardiac arrest secondary to ischemic-mediated events, including acute coronary syndrome (ACS) [16]. CAD has been the leading cause of OHCA, and the AHA 2010 Cardiopulmonary Resuscitation and Emergency Cardiovascular Care guidelines recommend emergent activation of coronary reperfusion protocols when there is high suspicion of acute myocardial infarction, regardless of EKG findings [17]. The two absolute contraindications to PCI are single vessel disease without proximal left anterior descending (LAD) artery involvement and when there are no anatomical or physiological indications for revascularization [16]. This study showed that overall mortality was significantly lower in OHCA patients who undergo PCI (28.3% vs. 65.4%, $p < 0.001$). Despite guideline recommendations, improved survival, and few contraindications to PCI use, there continues to be disparities in race, sex, age, and insurance coverage which limit access to this life saving therapy.

In the current study, 79.6% of PCI patients were Caucasian, while only 7.7% were African American and 6.5% were Hispanic. The discrepancy between ethnicities for healthcare access has been longstanding and is well documented. Bradley *et al.* conducted a retrospective observational study of over 37,000 patients from 434 unique hospitals, concluding that Caucasians accounted for 85.3% of those who received PCI, while 5.0% were African Americans, and 3.5% were Hispanic [18]. Not only were African Americans and Hispanics significantly less likely to receive PCI compared to Caucasians, but the time in which they received treatment was also significantly increased. The mean door-to-balloon (D2B) time across all hospitals was 122.3 minutes for African Americans, 114.8 minutes for Hispanics, and 103.4 minutes for Caucasians [18]. The current recommendations are that PCI should be performed in OHCA patients

within 90 minutes of first medical contact at a hospital with PCI capability and within 120 minutes at a hospital without PCI capability [16]. After adjusting the model to take into account age, sex, insurance providers, hospital characteristics, and time of presentation, the model was attenuated, but D2B times still remained 8.7 minutes longer (95% CI, 6.7 - 10.8) for African Americans and 3.7 minutes longer (95% CI, 1.3 - 6.1) for Hispanics when compared to Caucasians [18].

In addition to race, gender disparities are also present in access to PCI after OHCA. This study showed that 66.5% of the patients who received PCI were male while only 33.5% were female. Males are more likely than females to have an OHCA (54.2% vs. 45.8%). Although males had a greater incidence of OHCA, there is a large discrepancy between the percentage of females having an OHCA and the percentage receiving PCI. Jackson *et al.* studied over 8000 similar patients from 34 hospitals and reported that only 28.9% of the cohort receiving PCI was female. There was no significant difference in the study between men and women having a cardiac arrest (7.3% vs. 7.8%, $p = 0.41$). Further, the mean D2B time was significantly longer for females compared to males (94 vs. 85 minutes, $p < 0.001$) [19]. The authors found that women tend to be undertreated and are less likely to receive aspirin before PCI, even in the presence of multiple comorbidities [19]. Similarly, Jneid *et al.* studied over 78,000 similar patients in 420 US hospitals, in which 38% of the cohort were women [20]. Compared to men, women were less likely to receive PCI (36.1% vs. 52.3%, $p < 0.0001$) and had prolonged D2B time (103 vs. 95 minutes, $p < 0.0001$) [20].

The current study documented that younger patients (64 ± 13 vs. 66 ± 19 years, $p < 0.001$) were more likely to receive PCI compared to the elderly, patients aged 65 and older. Patients between 50 - 64 years old received PCI more often than patients >65. A multicenter prospective observational study of over 11,000 patients conducted by Mylotte *et al.* demonstrated that the severity of coronary artery disease varied significantly by age. The mean age for patients presenting with single vessel disease was 56.1 ± 13.6 years compared to patients presenting with multi-vessel disease was 67.2 ± 12.1 years [21]. Community studies have also shown that elderly patients are less likely to undergo revascularization due to decreased efficacy and increased complications [22]. Furthermore, there has been a paucity of evidence to guide therapy in the elderly population, since most clinical trials excluded this advanced age group [22].

This current study clearly demonstrates that access to PCI may be biased depending on patient insurance status, though this is difficult to determine precisely since the mean age of the patient cohort is over the Medicare qualifying age. The majority of patients who received PCI had either Medicare (47.4%) or private insurance (35.5%), whereas only 6.4% of Medicaid and 6.9% had no insurance or were self-paying. Bradley *et al.* demonstrated the same discrepancies in provider coverage, noting that PCI was performed more often in patients with either Medicare (18.5%) or private insurance (45.9%) compared to those with Medicaid (2%) or self-paying (7.6%) [18]. Treatment related to insurance provider is simple to correlate; however, the association between the two may mask a more important aspect of healthcare disparity—socioeconomic status. Chang *et al.* conducted a study in Canada where all residents are fully insured, and stratified patients into 4 socioeconomic groups based on median income for the

neighborhood they resided. The study showed that despite having the same insurance coverage, the use of PCI varied significantly between the lowest and highest socioeconomic groups (12.4% vs 21.8%, $p < 0.1$) [23].

Trends from this study show those patients < 65 years old, Caucasians, males, and those with Medicare or private insurance are the most likely to receive PCI. An explanation for these trends may be elucidated from center specific variations. Hypotheses, such as limited access to PCI-capable facilities, delays in treatment due to atypical disease presentations, lack of treatment due to clinical judgement, and delays in seeking treatment due to high out-of-pocket cost have been considered as possible explanations for these disparities. For example, African Americans and Hispanics present more frequently to community hospitals requiring transfer to a PCI-capable facility, thus increasing D2B time. Hsia *et al.* studied the distance between zip codes and PCI capable facilities, concluding untimely access (≥60 minutes) from a zip code to a PCI capable facility was more common in low-income communities (OR 3.00; 95% CI, 2.39 - 3.77) and Hispanic communities (OR 2.55; 95% CI, 1.86 - 3.49) [24]. Furthermore, ACS typically presents as NSTEMI and unstable angina in females compared to STEMI in males which can account for differences in immediate PCI use [15]. Despite these guidelines, placement of PCI is primarily based on clinical judgement, and in some scenarios the risks of the procedure may outweigh the benefits when evaluating overall health and comorbidities in the elderly. Finally, data has emerged that patients with Medicaid and self-pay insurance present later to the emergency room than patients with Medicare, delaying treatment and increasing the risk of morbidity and mortality [25].

The limitations of the current study include those inherent to large administrative databases, such as errors in coding and sampling. Immediate post-operative complications were apparent in the NIS database; however, readmissions for a complication of undergoing PCI were not identifiable, likely resulting in an underestimation of the actual complication rates. Of note however, this limitation would apply to all groups, and should not have altered the overall findings of this report. This limitation to in-hospital information without follow-up data could lead to long-term complications and mortality after hospital discharge not being captured in this study. Another potential limitation of this study design is the presence of comorbidities, which were based on the presence of administrative codes within the NIS database and were not clinically confirmed. Participation in the NIS database is voluntary, and only selected centers participate in the registry. Further, timing of treatment relative to the qualifying event and the management or medications given to the patients is unknown. Despite these limitations however, the NIS includes data from 1000 different hospitals in the US and more than 700,000 patient records were obtained for this study, and is likely a diverse enough sample to be able to generalize across most US hospitals in terms of delivery of care.

5. Conclusion

OHCA is associated with high mortality and morbidity. Specialized cardiac arrest centers and updated post-OHCA management protocols allow for better risk stratification and have led to significantly reduced mortality in patients suffering CA. PCI provides

significant survival advantage, and is performed most often in Caucasian males age >50 with private insurance, and less often in AA and Hispanics. Significant cultural, ethnic and socioeconomic barriers to PCI have been discussed in this study which warrants additional studies and resources to assure equity in access to this potentially life-saving therapy.

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