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Temporal Trends and Outcomes of Patients Undergoing Percutaneous Coronary Interventions for Cardiogenic Shock in the Setting of Acute Myocardial Infarction

A Report From the CathPCI Registry

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ABSTRACT

OBJECTIVES The purpose of this study was to examine the temporal trends in demographics, clinical characteristics, management strategies, and in-hospital outcomes in patients with acute myocardial infarction complicated by cardiogenic shock (CS-AMI) who underwent percutaneous coronary intervention (PCI) from the Cath-PCI Registry (2005 to 2013).

BACKGROUND The authors examined contemporary use and outcomes of PCI in patients with CS-AMI.

METHODS The authors used the Cath-PCI Registry to evaluate 56,497 patients (January 2005 to December 2013) undergoing PCI for CS-AMI. Temporal trends in clinical variables and outcomes were assessed.

RESULTS Compared with cases performed from 2005 to 2006, CS-AMI patients receiving PCI from 2011 to 2013 were more likely to have diabetes, hypertension, dyslipidemia, previous PCI, dialysis, but less likely to have chronic lung disease, peripheral vascular disease, or heart failure within 2 weeks ($p < 0.01$). Between 2005 and 2006 to 2011 and 2013, intra-aortic balloon pump use decreased (49.5% to 44.9%; $p < 0.01$), drug-eluting stent use declined (65% to 46%; $p < 0.01$), and the use of bivalirudin increased (12.6% to 45.6%). Adjusted in-hospital mortality; increased (27.6% in 2005 to 2006 vs. 30.6% in 2011 to 2013, adjusted odds ratio: 1.09, 95% confidence interval: 1.005 to .173; $p = 0.04$) for patients who were managed with an early invasive strategy (<24 h from symptoms).

CONCLUSIONS Our study shows that despite the evolution of medical technology and use of contemporary therapeutic measures, in-hospital mortality in CS-AMI patients who are managed invasively continues to rise. Additional research and targeted efforts are indicated to improve outcomes in this high-risk cohort. (J Am Coll Cardiol Intv 2016;9:341–51) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

BMI = body mass index

CS-AMI = cardiogenic shock in the setting of acute myocardial infarction

IABP = intra-aortic balloon pump

LAD = left anterior descending

MI = myocardial infarction

NSTEMI = non-ST-segment elevation myocardial infarction

NYHA = New York Heart Association

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

Cardiogenic shock (CS) is a leading cause of in-hospital mortality associated with acute myocardial infarction (AMI) with prevalence between 5% and 15% (1,2). Data regarding temporal trends in incidence, clinical characteristics, management strategy, and outcomes of patients with cardiogenic shock after myocardial infarction (CS-AMI) are limited (3,4). In the past decade, there has been an increased emphasis on timely revascularization, mechanical hemodynamic support, and optimal medical therapy in patients with CS-AMI. These interventions are being aggressively used in hopes of favorably affecting high morbidity and mortality rates associated with CS-AMI. Studies have shown that an early revascularization strategy (coronary artery bypass graft surgery or percutaneous coronary intervention [PCI]) is beneficial in such patients (5). Based on these findings, the American College of Cardiology (ACC) and the American Heart Association (AHA) have recommended early revascularization for cardiogenic shock with ST-segment elevation or new left bundle-branch block AMI as a Class I indication for patients younger than 75 years (Class IIA for age >75 years) in their revised guidelines for the management of AMI (6).

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Recently, a study derived from three nationwide registries in France (1999 to 2005) has demonstrated that although early mortality in such patients has been reduced concomitant with broader use of revascularization and medical treatment, the 1-year survival rate has not changed (7). Data for the United States thus far has been limited to few studies that allude to similar favorable results with respect to mortality with an invasive strategy (8-10). However, none of these studies dealt exclusively with data on CS-AMI patients treated with PCI. With the dynamic changes in the management of cardiogenic shock, there is a need to obtain a real-world perspective regarding this high-risk subset of CS-AMI patients with the help of a nationwide registry in the United States. Additionally, results of the IABOP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock II) trials have raised questions regarding the benefit of using devices such as the intra-aortic balloon pump (IABP) in this high-risk subset of patients (11). Hence, it would be interesting to evaluate whether trials such as these have impacted operator practice in the contemporary era.

Hence, this study has examined the temporal trends from the Cath-PCI registry (2005 to 2013) in demographics, clinical characteristics, management strategies, and in-hospital outcomes in patients with CS-AMI who underwent PCI. We hypothesized that in-hospital mortality from cardiogenic shock in myocardial infarction (MI) patients who are managed invasively is decreasing with improved use of timely revascularization, mechanical ventricular support, and advanced medical treatment.

METHODS

REGISTRY. The National Cardiovascular Database Registry (NCDR) Cath-PCI registry, co-sponsored by the American College of Cardiology (ACC) and the Society for Cardiovascular Angiography and Interventions (SCAI), has been previously described elsewhere (12,13). The registry catalogs data on patient and hospital characteristics, clinical presentation, treatments, and outcomes associated with PCI from >1,000 sites across the United States. The data are entered into ACC-certified software at participating institutions. There is a comprehensive data quality program, including both data quality report specifications for data capture and transmission and an auditing program (14). The data collected are exported in a standard format to the ACC Heart House (Washington, DC).

PATIENTS. Men and women age ≥18 years who underwent PCI between January 2005 and December 2013 for cardiogenic shock after AMI (CS-AMI-ST-segment elevation myocardial infarction [STEMI] and non-ST-segment elevation myocardial infarction [NSTEMI]) were included (n = 105,171, sites = 1463). To assess the temporal trends in demographic,

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clinical, and outcome variables, we chose four consecutive 2-year blocks: 2005 to 2006, 2007 to 2008, 2009 to 2010, and post-2010 (2011 to 2013). The exclusion criteria included patients presenting >24 h since symptom onset (n = 17, 791, sites = 7), transfer patients (n = 30, 882, sites = 12), and patients with missing in-hospital mortality data (n = 1, sites = 1).

Delayed and transfer patients tend to have several complicating variables that are not assessed within a national registry such as the NCDR. Incorporating these patients within the final analysis would skew the results, so these patients were excluded to maintain a cleaner database. The final cohort accounted for 56,497 patients from 1,444 sites across the nation.

DEFINITIONS. All study definitions were derived from the Cath-PCI Registry data dictionary (elements and definitions v1.08). Complete definitions of all variables were prospectively defined by an ACC committee and are available at the ACC NCDR Web site (http://cvquality.acc.org/en/NCDR-Home/Data-Collection.aspx). Cardiogenic shock was defined as a sustained (>30 min) episode of systolic blood pressure <90 mm Hg, and/or cardiac index <2.2 l/min/m^2 determined to be secondary to cardiac dysfunction, and/or the requirement for parenteral inotropic or vasopressor agents or mechanical support (e.g., IABP, extracorporeal circulation, ventricular assist devices) to maintain blood pressure and cardiac index above those specified levels.

OUTCOMES. The primary outcome was to evaluate temporal trends of demographics, clinical characteristics, management strategies, and in-hospital outcomes in patients undergoing PCI for cardiogenic shock (2005 to 2011). The secondary outcome of the study was to analyze adjusted associations between clinical variables and in-hospital mortality in this subgroup of patients.

STATISTICAL ANALYSIS. Categorical variables were presented as frequencies (percentages), and differences between the calendar time groups were assessed using the chi-square test when the sample size was sufficient; otherwise, a Fisher exact test was used. Continuous variables were presented as median (Q1, Q3) and were compared using the Wilcoxon rank-sum test. To assess trends in risk-adjusted outcomes and adjusted associations with in-hospital mortality, we used logistic regression with generalized estimating equations (GEE) to account for within-hospital clustering. For the GEE analysis we assumed the exchangeable correlation structure. We adjusted for clinical variables and hospital characteristics. Hospital characteristics included the number of Centers for Medicare and Medicaid Services-certified beds, location/community type, profit type, region, and a teaching program. Patient characteristics included age, gender, race, body mass index (BMI), STEMI, cardiogenic shock, prior congestive heart failure, prior valve surgery/procedure, cerebral vascular disease, peripheral vascular disease, chronic lung disease, prior PCI, diabetes, PCI status, IABP, ejection fraction, glomerular filtration rate, dialysis, pre-procedural Thrombolysis In Myocardial Infarction (TIMI) flow, New York Heart Association (NYHA) functional class, highest risk lesion segment category, Society of Cardiovascular Angiography and Interventions (SCAI) lesion class. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

The demographic and clinical characteristics of the study population are presented in Table 1. Of the total 56,497 patients within the study, around one-half were below the age of 65 years, and two-thirds were males, with female fraction decreasing from 35.1% in 2005 to 2006 to 31.8% in 2011 to 2013. Within the CathPCI database as a whole, an increasing number of patients have been undergoing PCI for the indication of CS-MI (n = 5,658 in 2005 to 2006 vs. n = 26,940 in 2011 to 2013). This trend was noted across all racial groups. Compared with 2005 to 2006, patients in 2011 to 2013 were more likely to have diabetes, hypertension, dyslipidemia, previous PCI, dialysis, and less likely to have tobacco abuse, chronic lung disease, renal dysfunction, peripheral vascular disease, heart failure within 2 weeks, and a family history of premature coronary artery disease ($p < 0.01$ for trend).

HOSPITAL SETTING. The exposure to such complex cases has significantly declined within teaching institutions from 49.4% in 2005, to 2006 to 42.3% in 2011 to 2013 (Table 1). A little less than one-half of the national volume (43%) was directed to centers with an annual PCI volume <500/year (low-volume center) compared with 22% in centers with an annual PCI volume >1,000/year (Table 1). Further, an increasing trend in such procedures is noted in the low-volume centers (30.7% in 2005 to 2006 to 48.1% in 2011 to 2013) compared with the higher volume centers (28.9% in 2005 to 2006, to 18.4% in 2011 to 2013). Geographical trends are shown in Table 1.

TRIAGE AND DIAGNOSTIC ANGIOGRAPHY. Compared with 2005 to 2006, the proportion of patients with a symptom onset to time of admission <6 h

TABLE 1 Demographic and Clinical Characteristics in Cardiogenic Shock in the Setting of Acute Myocardial Infarction Patients Undergoing Percutaneous Coronary Intervention

	2005–2006 (n = 5,658)	2006–2008 (n = 10,337)	2009–2010 (n = 13,562)	2011–2013 (n = 26,940)	p Value
Age, yrs	64.7 ± 13	64.9 ± 13	64.9 ± 13	65.0 ± 13	0.70
Male	65	65.9	67.4	68.2	<0.001
Ethnicity					
Caucasians	83.6	79.4	85.2	85.7	<0.001
African Americans	5.9	7.1	8.0	8.7	<0.001
Asians	2.2	2.5	3.0	4.0	<0.001
Hispanic	3.4	4.8	6.1	7.1	<0.001
BMI, kg/m^2	28.1 ± 6.2	28.2 ± 6.1	28.4 ± 6.3	28.6 ± 6.4	<0.001
Uninsured	10.2	11.1	13.1	14.5	<0.001
Length of stay					<0.001
1–2 days	9.8	9.5	10.8	12.7	
2–4 days	15.7	17.4	18.1	20.0	
>4 days	74.5	73.1	71.1	67.3	
Smoker (current/recent)	39.4	37.4	38.1	37.0	0.003
Hypertension	61.5	63.6	67.3	68.7	<0.001
Dyslipidemia	51.8	55.3	58.6	57.2	<0.001
PAD	11.7	10	10.4	10.0	0.003
Diabetes mellitus	27.2	27.3	29.0	30.5	<0.001
Dialysis	2.2	2.6	2.7	2.9	<0.001
Previous MI	23.2	21.2	22.8	23.1	0.001
Previous CHF	12.2	11.0	11.4	12.0	0.03
Cerebrovascular disease	11.4	10.3	10.7	11.0	0.15
Chronic lung disease	18.5	17.4	14.8	15.0	<0.001
Family history of CAD	18.5	16.3	16.0	15.6	<0.001
Previous PCI	19.6	21.3	22.5	23.0	<0.001
Previous CABG	9.1	9.1	8.8	8.4	0.11
Chronic kidney disease	7.9	8.8	4.1	2.9	<0.001
Location type					<0.001
Rural	13.5	12.2	11.5	13.4	
Suburban	30.7	30.3	34.4	35.6	
Urban	55.9	57.5	54.2	51.1	
Hospital type					<0.001
Private/community	91.6	90.2	90.4	89.6	
Government/university	8.4	9.8	9.6	10.4	
Residency/fellowship	49.4	46.0	44.2	42.3	<0.001
Geographical region					<0.001
West	24.1	24.1	22.2	21.3	
Northeast	10.6	11.8	13.2	13.7	
Midwest	33.8	28.3	27.7	26.5	
South	31.3	35.6	36.9	38.4	
Average annual PCI volume					<0.001
<500	30.7	34.6	43.7	48.1	
500–1,000	40.4	37.3	35.9	33.5	
1,000–1,500	16.9	16.2	13.9	12.6	
1,500–2,000	7.3	7.3	3.8	3.4	
>2,000	4.7	4.6	2.6	2.3	

Values are mean ± SD or %.

BMI = body mass index; CABG = coronary artery bypass surgery; CAD = coronary artery disease; CHF = congestive heart failure; MI = myocardial Infarction; PAD = peripheral arterial disease; PCI = percutaneous coronary intervention.

significantly decreased in 2011 to 2013 for NSTEMI (75% to 58%; $p < 0.01$) and STEMI (88% to 77%; $p < 0.01$). Use of thrombolytics has significantly decreased (4% to 1.2%; $p < 0.01$) within the STEMI patients group (Table 2). IABP use has significantly decreased from 49.5% in 2005 to 2006 to 44.9% in 2011 to 2013 with a trend toward insertion after the PCI has begun. In 2005 to 2006, 31.5% of patients had >1 lesion treated during the index catheter laboratory visit. This number decreased to 25.8 in 2011 to 2013 ($p < 0.01$) (**Table 2**). The left main had significant disease (≥70%) in 8.3% of patients, proximal left anterior descending artery in 45.3%, mid-distal left anterior descending artery in 42.7%, left circumflex artery in 45.2%, right coronary artery in 64.2%, and ramus intermedius in 4.2%. This indicates that majority of the patients within the study cohort presented with multivessel disease.

PROCEDURAL (PCI) CHARACTERISTICS. Among STEMI patients with delayed PCI, 35% were due to cardiac arrest or failure to intubate. Vascular access issues and delay in crossing the lesion accounted for 1.3% and 2.5%, respectively. This remained stable across the study period. Drug-eluting stent use declined significantly from 65% in 2005 to 2006 to 46% in 2011 to 2013, whereas the use of bare metal stents increased from 21% to 39% during the same time period ($p < 0.01$). Multi-lesion PCI (during index procedure) in the CS-AMI setting has shown a significant decline from 31.5% to 25.7% ($p < 0.01$). Trends in other procedural characteristics are shown in **Table 2**.

IN-HOSPITAL OUTCOMES. Post-procedure TIMI flow grade 3 was observed in 86% of the patients, with an overall dissection rate of 1.8%, and perforation rate of 0.5%. Although the rates of "any complication" have decreased significantly over the study period, they still occurred in about one-third of the procedures. Renal failure (5.3% to 3.1%), bleeding events within 72 h (11.5% to 8.7%), and rates of red cell transfusion (23.1% to 15.2%) decreased significantly during the same time period (**Table 3**). The rates of successful PCI increased marginally, but plateaued at 85% of the cases. The rates of coronary artery bypass grafting declined from 6.7% in 2005 to 2006 to 4.8% in 2011 to 2013 ($p < 0.01$), out of which one-half were either emergent or salvage in nature. Finally, in-hospital mortality continued to rise from 27.6% in 2005 to 2006 to 30.6% in 2011 to 2013 ($p < 0.01$) (**Figure 1**). Out of these, deaths in the cardiac catheterization laboratory comprised around one-fifth, and showed a notable increase with 15.6% in 2005 to 2006 and 19.9% in 2011 to 2013. The most common cause of death was cardiac in 83%, neurologic in 6.7%, and pulmonary in 2.9% of deaths. Adjusted associations with in-hospital mortality presented in **Table 4**. After multivariate adjustment, mortality rates in 2011 to 2013 versus 2005 to 2006 continue to increase (OR: 1.09; 95% CI: 1.01 to 1.19; $p < 0.05$), whereas frequency of renal failure and bleeding decreased (**Table 5**).

TABLE 2 Catheterization Laboratory Characteristics in Cardiogenic Shock in the Setting of Acute Myocardial Infarction Patients Undergoing Percutaneous Coronary Intervention

	2005–2006 (n = 5,658)	2006–2008 (n = 10,337)	2009–2010 (n = 13,562)	2011–2013 (n = 26,940)	p Value
STEMI	80.6	81.1	82.1	82.1	0.01
Symptom to presentation (STEMI only)					<0.001
<6 h	88.1	89.6	79.5	77.2	
6–12 h	7.7	6.6	9.2	9.3	
>12 h	4.2	3.8	11.3	13.5	
Thrombolytics	4.0	2.0	1.7	1.2	<0.001
Radial access	0.4	0.6	1.1	4.2	<0.001
>70% stenosis					
Left main	7.1	7.7	8.4	8.9	<0.001
LAD	88.0	87.0	90.0	87.4	<0.001
LCX	44.0	45.0	45.5	45.5	0.004
RCA	66.7	63.6	64.3	63.7	0.02
RI	4.2	4.5	4.1	4.2	<0.001
Grafts	11.1	10.9	10.6	10.0	<0.001
Median fluoroscopy time (min)	14.0	13.0	13.0	12.8	<0.001
Median contrast volume (ml)	200.0	200.0	190.0	180.0	<0.001
High-risk lesion (type C)	69.6	66.2	71.2	72.4	<0.001
>1 lesion treated	31.5	30.7	29.0	25.8	<0.001
IABP	49.5	49.7	49.5	44.9	<0.001
Other LV support devices	NA	NA	5.5	7.2	0.60
Medications					
LMWH	11.8	10.1	7.5	5.2	
UFH	82.3	78.9	74.5	68.0	
Bivalirudin	12.6	18.7	28.5	45.6	
GPI	75.8	71.6	66.1	52.8	
Pre-PCI aspirin	83.6	84.1	81.1	82.0	
Second antiplatelet	55.0	59.0	61.3	60.5	<0.001
Previously treated lesion	7.6	9.1	9.7	9.4	<0.001
Timeframe					<0.001
<1 month	31.2	23.5	18.7	18.7	
1–6 months	14.4	12.4	11.8	9.7	
6 months–1 yr	12.3	8.2	5.5	7.1	
1–2 yr	12.1	10.4	10.1	9.3	
>2 yr	16.1	29.1	42.5	43.7	
Discharge medications					<0.001
Aspirin	93.2	94.5	88.4	86.1	
Statin	80.6	84.3	80.7	83.1	
Second antiplatelet	90.4	92.2	86.3	78.5	
Beta-blocker	87.8	89.9	84.4	83.3	

Values are %.

GPI = glycoprotein IIb/IIIa inhibitor; IABP = intra-aortic balloon pump; LAD = left anterior descending artery; LCX = left circumflex artery; LMWH = low-molecular-weight heparin; LV = left ventricular; NA = not applicable; PCI = percutaneous coronary intervention; RCA = right coronary artery; RI = ramus intermedius artery; STEMI = ST-segment elevation myocardial infarction; UFH = unfractionated heparin.

DISCUSSION

In this large, multicenter, national registry of cardiogenic shock patients who underwent coronary

TABLE 3 Unadjusted In-Hospital Outcomes for Cardiogenic Shock in the Setting of Acute Myocardial Infarction Patients Undergoing Percutaneous Coronary Intervention

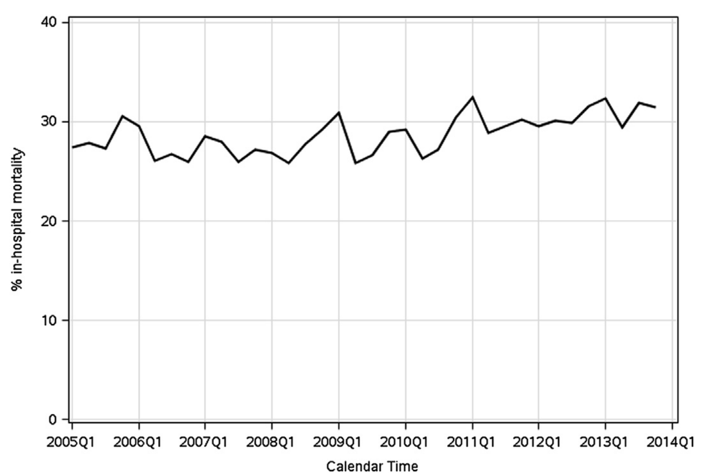
	2005-2006 (n = 5,658)	2006-2008 (n = 10,337)	2009-2010 (n = 13,562)	2011-2013 (n = 26,940)	p Value
Ischemic stroke	1.4	1.3	1.4	1.4	0.80
Renal failure	5.3	6.4	3.1	3.1	<0.01
Any vascular complications	1.6	1.3	1.4	1.2	0.06
RBC transfusion	23.1	23.5	18.7	15.3	<0.01
Bleeding event <72 h	11.5	12.3	10.0	8.7	<0.01
Mortality	27.6	27.4	28.2	30.6	<0.01

Values are %.

revascularization from 2005 to 2013, a distinct pattern of demographic and clinical variables is noted. While the use of IABP and drug-eluting stents significantly decreased, an increase in bivalirudin (12.6% to 45.6%) use was noted during this period. Despite the increased adoption of prompt revascularization, in-hospital mortality continues to rise significantly in patients who undergo PCI for CS-AMI.

DEMOGRAPHIC CHANGES. The lower mean age in such patients is consistent with previous studies. In a nationwide inpatient sample, Kolte et al. (15) demonstrated a decline of mean age from 69.3 to 67.7 years from 2003 to 2010. Our study too has shown a similar decline albeit with a minimal gradient (mean age: 64 years). Compared with previous studies on CS-AMI, our analysis exclusively deals with those who underwent percutaneous revascularization within 24 hours of symptom onset. Whether this had an impact on the lower mean age within our study needs to be explored further. Unlike trends of CS which are increasing in both genders (15), CS-AMI patients undergoing PCI show a proportional decline from 35% to 32% in women over this time period. All races showed an increase in patients undergoing PCI for CS-AMI. Inter-racial disparities as seen in different arena of interventional cardiology (16) were not evaluated.

FIGURE 1 Rate of In-Hospital Mortality Over Time



TRIAGE AND DIAGNOSTIC ANGIOGRAPHY. Across our study period, there was a decline in the proportion of STEMI patients who make it to the hospital within 6 h of symptom onset. This is despite the recent advances in medical technology, aggressive educational efforts (e.g., "time is muscle"), and revamping of several health care strategies to ensure prompt care for AMI patients. This is especially important for patients with CS-AMI, who are inherently at a higher risk for poor outcomes, particularly if therapeutic intervention is delayed.

IABP use has significantly decreased from 49.5% in 2005 to 2006 to 44.9% in 2011 to 2013 with a trend toward insertion after PCI has begun. This is probably suggestive of the fact that most operators do not prefer to use IABP pre-emptively to first stabilize the patient. This may be partially driven by the pressure to comply with the door-to-balloon time performance measures, and partially by the notion that treating the culprit vessel would eventually improve hemodynamics, obviating the need for additional support. Additionally, the IABP-SHOCK II trial suggested that IABP does not provide any 30-day mortality benefit in such patients (11).

A study similar to ours, based on a nationwide inpatient sample, showed a significant increase in the overall IABP use rates from 44.8% in 2003 to 54.5% in 2009, followed by a small decrease to 53.7% in 2010. However, this study encompassed all CS-AMI patients whereas our study was limited exclusively to those patients who underwent PCI. It is not surprising that despite the increase in adoption of radial access for elective PCI, the fraction of CS-AMI patients undergoing PCI via radial access is limited to <5%. This is understandable given the need for quick access and the necessity of using higher French guiding catheters to treat complex high-risk lesions. This is supported by the fact that about two-thirds of all lesions in patients presenting with cardiogenic shock were of the SCAI III/IV type.

Finally, our study showed that most of the patients undergoing PCI for CS-AMI had significant multivessel disease, the incidence of which has been increasing across the study period. However multilesion PCI (treating the nonculprit lesion in the same setting) has shown a significant decline. Though "culprit vessel only" PCI is considered appropriate in a routine STEMI, guidelines do provide options to consider multivessel stenting in conditions of hemodynamic instability. However, within the real-world setting, it seems that most operators are reluctant to do so and prefer the "culprit only" approach in CS-AMI patients. It is possible that treating the culprit vessels in these patients leads to improved hemodynamics, and thus the operator decided to stage the other lesions for a later date. The results of recent randomized control trials such as PRAMI (Preventive Angioplasty in Myocardial Infarction) (17) and the CvLPRIT (Complete versus Lesion only PRimary-PCI Trial) (18) suggest that immediate PCI of all angiographic nonculprit stenoses (>50% in PRAMI and >70% in CvLPRIT) is superior to culprit lesion only PCI. This benefit may be more pronounced in high-risk, unstable patients such as those with CS-AMI.

INTERVENTION DETAILS. Our study results indicate that the most common reason for delay in PCI in real-world practice is the occurrence of cardiac arrest (outside or in-hospital) or the need for intubation. These accounted for more than 70% of delays in PCIs. The latter problem may be better dealt with by streamlining the rapid response teams and educating the catheterization laboratory personnel to work synergistically with other ancillary staff so that multitasking can be achieved without significant delay. It is reassuring to know that vascular access issues and delay in crossing the lesion remained below 3% across the study period. Pre-loading of aspirin was >80% across the study period and of thienopyridine was around 55% to 60% (clopidogrel and prasugrel) (**Table 2**). These are concerning metrics because ~20% of the PCI in this high-risk subgroup may be occurring without any antiplatelet therapy on board (19,20). However, this finding may be alleviated by the fact that despite a decline in use of glycoprotein IIb/IIIa inhibitors across the study period, it still continues to be used in around 50% of the patients, probably supplementing some antiplatelet effect during the PCI until oral medications take effect.

These trends of anticoagulation mirror those of trends in acute coronary syndromes (ACS) and other interventional fields where rates of use of low-molecular-weight heparin and unfractionated heparin have gone down and that of bivalirudin have gone up (21,22). Apart from being compliant with the guidelines (with respect to bivalirudin use in STEMI patients), these trends also may be a reflection of bleeding favorable profile of bivalirudin when used with glycoprotein IIb/IIIa inhibitors. With the recent trials questioning the superiority of bivalirudin over unfractionated heparin, these trends may be subject to change in the future (23).

TABLE 4 Adjusted Association With In-Hospital Mortality

	Adjusted			
	OR	Lower 95% CI	Upper 95% CI	p Value
Year				
2007–2008 vs. 2005–2006	0.95	0.87	1.03	0.24
2009–2010 vs. 2005–2006	0.98	0.91	1.07	0.80
2011–2013 vs. 2005–2006	1.08	1.00	1.17	0.03
STEMI	1.01	0.95	1.08	0.55
Age >70 per 1 yr increase	1.03	1.03	1.04	<0.01
Prior CHF	0.98	0.92	1.05	0.73
Prior valve surgery/procedure	1.31	1.10	1.56	<0.01
CVD	1.10	1.03	1.17	<0.01
PVD	1.16	1.08	1.24	<0.01
Chronic lung disease	1.01	0.95	1.07	0.66
Prior PCI	0.78	0.74	0.82	<0.01
Pre-IABP	1.52	1.38	1.67	<0.01
Ejection fraction	0.98	0.98	0.98	<0.01
Coronary lesion ≥50% in a major artery	1.12	0.99	1.34	0.05
Pre-procedure TIMI flow: none vs. some	1.10	1.03	1.17	<0.01
No diabetes vs. insulin diabetes	0.72	0.67	0.78	<0.01
Non-insulin diabetes vs. insulin diabetes	0.92	0.86	1.00	0.06
SCAI lesion				
Class 2 or 3 vs. 1	1.01	0.94	1.10	0.65
Class 4 vs. 1	1.16	1.06	1.27	<0.01
BMI				
When BMI ≤30 kg/m^2	0.98	0.97	0.98	<0.01
When BMI >30 kg/m^2	1.01	1.01	1.02	<0.01
Dialysis	1.42	1.26	1.59	<0.01
NYHA functional class IV	1.01	0.95	1.06	0.73
pRCA/mLAD/pCIRC vs. other	1.01	0.96	1.06	0.59
pLAD vs. other	1.22	1.15	1.28	<0.01
Left main vs. other	2.56	2.33	2.81	<0.01
White race vs. other	0.92	0.87	0.98	0.01
Female	0.94	0.89	0.97	0.02
Average annual volume per 100 increase	0.99	0.99	1.00	0.55
Fellowship, internship, or residency program	1.04	0.97	1.11	0.25
No. of CMS beds per 100 increase	1.01	0.99	1.02	0.14
Region				
West vs. South	0.98	0.90	1.05	0.62
Northeast vs. South	0.87	0.79	0.96	0.005
Midwest vs. South	0.97	0.90	1.04	0.47
Hospital type				
Government/university vs. private/community	1.05	0.95	1.15	0.30
Rural vs. urban	0.90	0.82	0.99	0.03
Suburban vs. urban	0.91	0.85	0.98	0.01

BMI = body mass index; CHF = congestive heart failure; CI = confidence interval; CMS = Centers for Medicare and Medicaid Services; CVD = cerebral vascular disease; IABP = intra-aortic balloon pump; mLAD = middle left anterior descending artery; OR = odds ratio; PCI = percutaneous coronary intervention; pCIRC = proximal left circumflex artery; pLAD = proximal left anterior descending artery; pRCA = proximal right coronary artery; PVD = peripheral vascular disease; SCAI = Society for Cardiovascular Angiography and Interventions; STEMI = ST-segment elevation myocardial infarction; TIMI = Thrombolysis In Myocardial Infarction.

DISCHARGE MEDICATIONS. Apart from the increase in mortality, a further issue of concern is the worsening compliance with guideline-directed therapy for

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such high-risk patients. Regardless of the type of PCI, the use of aspirin and thienopyridines should not be declining—a trend that may have significant impact on short-term and long-term outcomes. Though it is encouraging to see statin adherence pickup, 17% of patients discharged are not receiving this coronary artery disease protective medication, which can lead to adverse long-term outcomes as well (Table 2).

HOSPITAL SETTING. It is surprising to see that 90% of CS-AMI patients undergo PCI in private/community hospitals whereas government/university hospitals comprise the rest (Table 1). This is important because there is a general belief that such patients should be referred to centers of excellence (usually university-based) for high-quality care; however, tertiary care is often not available in close proximity, and the preference for such institutions can cause significant delays that can be catastrophic in such patients (10). Hence, universal acceptance of CS-AMI patients is an encouraging sign. Although critics might argue that such a low proportion of CS-AMI cases routing to university hospitals (<10%) might dilute the training for future trainees; our analysis shows that regardless of the hospital setting around 43% of the hospitals have residency and fellowship training facilities. Geographical variation in proportional CS-AMI cases may be related to different times of enrollment of hospitals within the NCDR (Table 1). A little less than one-half of the national volume (43%) was directed to centers with annual PCI volume of <500/year (low-volume center). The ACC/AHA PCI guidelines define low-volume centers as PCI volumes of <400/year and provide Class IIa recommendations for urgent PCI (Level of Evidence: C) (6). Hence, though safety is a concern when it comes to high-risk procedures, it cannot be at the expense of immediate universal access to catheterization laboratories across the country. Hence, this trend may not be as ominous as it looks. In fact in-hospital mortality by center volume shows a mortality paradox. Low-volume centers have significantly lower mortality rates compared with the high-volume centers and comparable with those of ultra-volume centers (<500, 28.5%; 500 to 1,000, 29.5%; 1,000 to 1,500, 29.7%; 1,500 to 2,000, 31.3%; >2,000, 29.6%; $p < 0.01$). This bell-shaped curve may not be reflective of the quality of care but merely represents the fact that sicker patients are probably referred to centers with higher volume.

OUTCOMES. Despite majority of lesions being SCAI III/IV, a post-procedure TIMI flow grade 3 in >85% of the patients with excellent technical complication rates (<0.5% perforation and <2% dissection, <3% emergent/salvage coronary artery bypass graft) are encouraging findings. However, our study does show a significant decline in renal failure and bleeding outcomes. The latter is a reflection of operators being cognizant about the impact of bleeding on procedural outcomes, and their keenness to incorporate bleeding avoidance strategies (radial access, bivalirudin use, access site management team) into routine practice. However, it is disconcerting to note that despite employing the state-of-art medicines and devices to treat these high-risk patients, in-hospital mortality continues to rise from 27.6% in 2005 to 2006 to 30.6% (Table 3, Figure 1) in 2011 to 2013 ($p < 0.01$). These outcome trends were maintained after adjusting the data for several variables based on the NCDR model v3 (Table 5).

In a nationwide inpatient sample analysis of all CS patients with STEMI from 2003 to 2010, a 29% decline in in-hospital mortality was noted after adjusting for all variables (adjusted OR: 0.71; 95% CI: 0.68 to 0.75; $p < 0.001$). However, the adjusted data analyses from our study show a worsening trend in mortality (OR: 1.09; 95% CI: 1.005 to 1.173; $p = 0.038$). The NIS study had attributed the decline to the increased use of early percutaneous revascularization (PCI constituting about 60% of study population). In contrast, our study, which exclusively included patients who underwent early PCI (defined as <24 hours) for CS-AMI, demonstrated a trend that is not only concerning but raises questions about the strategy to treat such high-risk patients. This is concerning from the public health standpoint because all previous studies on CS-AMI have shown a trend toward improvement that was generally attributed to early mechanical revascularization. Alternatively it is feasible that we are increasingly managing much sicker patients invasively (with greater experience and better support devices), many of whom would not have been considered for PCI referral a decade ago; these rates may represent the best that can be achieved in this high-risk subset of AMI patients.

Variables associated with in-hospital mortality in patients undergoing PCI for cardiogenic shock are shown in Table 4. Critical angiographic findings, such as left main or proximal left anterior descending lesion, presence of TIMI flow grade 0 pre-PCI, or SCAI type IV lesions inherently stratifies patients into higher risk strata that translate into poor outcomes. This is also the case for associated comorbidities such as peripheral arterial disease, cerebrovascular disease, diabetes mellitus, and dialysis-dependent renal failure. Non-insulin-dependent diabetes was associated with a more favorable mortality outcome compared with insulin-dependent diabetes. Interestingly, placement of the IABP before PCI was significantly associated with higher mortality (OR: 1.5; 95% CI: 1.4 to 1.7; $p < 0.01$). This may be related to the fact that pre-PCI IABP is preferred by operators in the extremely sick patients.

Our study is the first one to show female sex as a protective factor against mortality. Prior data on CS-AMI patients have shown worse outcomes with women (15,24). However, it seems that when CS-AMI patients undergo early revascularization, women seem to outscore men with respect to survival. BMI has been identified as a culprit for mortality associated with PCI, especially in a bimodal presentation (<18.5 kg/m^2 and >40 kg/m^2) (25). Studies on the effect of BMI in patients with PCI after ACS have been inconclusive (26). Our study results are the first of their kind that exclusively look into CS-AMI patients undergoing PCI, and they indicate that a BMI <30 kg/m^2 is a protective factor. This probably has to do with ease of access and vulnerability to peri-procedural bleeding. The obesity paradox (lower mortality in mild-moderate obesity) seen in few studies (27) was not observed in our study. This may be related to the acuity of CS-AMI, or may be related to the fact that our analysis is not designed to evaluate hazards ratio within stratified BMI (mild, moderate, or severe obesity).

Interestingly, patients with a history of PCI seemed to fare better compared with patients with no PCI history. It may be hypothesized that the former group of the patients were more likely to be on cardioprotective medications due to their PCI history and more tuned with healthcare access compared with the latter group, who probably entered the healthcare zone due to this index event and were naïve to any medications. The concept of ischemic pre-conditioning may have also benefited the former group.

STUDY LIMITATIONS. Despite employment of an adjusted model for outcome analysis, residual unmeasured confounding or uncontrolled selection bias are some of the significant issues related to registry studies. Participation in the CathPCI Registry is voluntary, so the results may not be representative of the entire U.S. population, although the number of participating sites is large. Lack of adjudicated outcomes and lack of an angiographic core laboratory data are significant limitations. Data on operator experience, which might influence both ischemic and hemorrhagic procedural risk, is unavailable in the Cath-PCI Registry. Another limitation is the variable time frame for participation of each hospital within CathPCI registry such that there were only a small number of hospitals that consistently submitted patients during the entire study time frame; as a result, the changes over time may reflect hospital differences more overtly. Also, data on the severity of cardiogenic shock is not available, but data on PCI status (urgent/emergent/salvage) may have ameliorated the impact of this deficiency. Finally, CathPCI Registry data are collected for in-hospital stay only; as such, differences in long-term outcomes of the CS-AMI patients who underwent PCI could not be assessed.

TABLE 5 **Association of Time Categories With In-Hospital Outcomes**

	Unadjusted				Adjusted			
Category Versus 2005-2006	OR	Lower (95% CI)	Upper (95% CI)	p Value	OR	Lower (95% CI)	Upper (95% CI)	p Value
Mortality								
2007-2008	0.994	0.920	1.074	0.882	0.950	0.872	1.035	0.242
2009-2010	1.037	0.961	1.120	0.350	0.990	0.910	1.076	0.805
2011-2013	1.160	1.080	1.246	<0.001	1.085	1.005	1.173	0.038
Renal failure								
2007-2008	1.200	1.025	1.406	0.024	1.221	1.045	1.426	0.012
2009-2010	0.539	0.450	0.645	<0.001	0.567	0.474	0.677	<0.001
2011-2013	0.508	0.433	0.596	<0.001	0.523	0.445	0.615	<0.001
Bleeding								
2007-2008	1.129	0.996	1.280	0.057	1.142	1.012	1.289	0.031
2009-2010	0.912	0.798	1.042	0.174	0.956	0.840	1.089	0.501
2011-2013	0.796	0.698	0.909	<0.001	0.829	0.727	0.946	0.005
Stroke								
2007-2008	0.893	0.663	1.202	0.455	0.919	0.684	1.234	0.573
2009-2010	0.986	0.741	1.312	0.922	1.057	0.797	1.403	0.699
2011-2013	0.945	0.733	1.219	0.665	1.007	0.778	1.302	0.959

CI = confidence interval; OR = odds ratio.

CONCLUSIONS

This is the first study to exclusively examine patients with CS-AMI undergoing PCI. Despite the absolute mortality rates being lower than historical data on CS, we observed a rise in mortality in CS-AMI patients who were managed invasively. Female sex, BMI <30 kg/m^2, and a history of PCI seem to be associated with favorable outcomes. Finally, bleeding outcomes seem to be improving although adherence with guideline-directed medical therapy needs to markedly improve. Additional research to better understand the pathophysiology and prospective evaluation of targeted pharmacological and mechanical efforts is indicated to improve outcomes in this particularly high-risk cohort.

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PERSPECTIVES

WHAT IS KNOWN? Cardiogenic shock is a leading cause of in-hospital mortality associated with acute myocardial infarction (CS-AMI). Studies have shown that an early revascularization strategy is beneficial in such patients. However, none of the prior studies have dealt exclusively with data on CS-AMI patients treated with PCI. With the dynamic changes in management of cardiogenic shock, there is a need to obtain a real-world perspective regarding this high-risk subset of CS-AMI patients.

WHAT IS NEW? This is the first study to exclusively examine patients with CS-AMI undergoing PCI. Despite absolute mortality rates being lower than historical data on CS, we observed a rise in mortality in CS-AMI patients who were managed invasively. Female sex, BMI <30 kg/mm^2, and a history of PCI seem to be associated with favorable outcomes. Finally, bleeding outcomes seem to be improving although adherence with guideline-directed medical therapy needs to markedly improve.

WHAT IS NEXT? Additional research to better understand the pathophysiology and prospective evaluation of targeted pharmacological and mechanical efforts is indicated to improve outcomes in this particularly high-risk cohort.

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