

CLINICAL RESEARCH

Primary Percutaneous Coronary Intervention in Patients With Acute Myocardial Infarction, Resuscitated Cardiac Arrest, and Cardiogenic Shock

CME

The Role of Primary Multivessel Revascularization

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CME Objective for This Article: At the completion of this article, the learner should be able to discuss the:

- The poor clinical outcomes in critically ill patients presenting with ST-segment elevation myocardial infarction (STEMI) complicated by cardiogenic shock and resuscitated cardiac arrest.
- The concept that the degree of myocardial ischemia impacts patient outcomes and may vary according to the number of significant coronary stenoses.
- That percutaneous coronary intervention of the only infarct related artery (IRA) is the treatment of choice for non-shock STEMI patients.
- And finally, that in patients with persistent cardiogenic shock following IRA-PCI, intervention to other significant coronary lesions supplying a large non-IRA territory may enhance survival.

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The Role of Primary Multivessel Revascularization

Objectives This study sought to assess the impact of multivessel (MV) primary percutaneous coronary intervention (PCI) on clinical outcomes in patients with ST-segment elevation myocardial infarction (STEMI) presenting with cardiogenic shock (CS) and resuscitated cardiac arrest (CA).

Background The safety and efficacy of MV primary PCI in patients with STEMI and refractory CS is unknown.

Methods We conducted a multicenter prospective observational study of consecutive STEMI patients presenting to 5 French centers. Patients were classified as having single-vessel (SVD) or multivessel (MVD) coronary disease, and underwent culprit-only or MV primary PCI. Baseline characteristics and 6-month survival were compared.

Results Among 11,530 STEMI patients, 266 had resuscitated CA and CS. Patients with SVD (36.5%) had increased 6-month survival compared to those with MVD (29.6% vs. 42.3%, $p = 0.032$). Baseline characteristics were similar in those with MVD undergoing culprit-only (60.9%) or MV (39.1%) primary PCI. However, 6-month survival was significantly greater in patients who underwent MV PCI (43.9% vs. 20.4%, $p = 0.0017$). This survival advantage was mediated by a reduction in the composite of recurrent CA and death due to shock ($p = 0.024$) in MV PCI patients. In those with MVD, culprit artery PCI success (hazard ratio [HR]: 0.63; 95% confidence interval [CI]: 0.41 to 0.96, $p = 0.030$) and MV primary PCI (HR: 0.57; 95% CI: 0.38 to 0.84, $p = 0.005$) were associated with increased 6-month survival.

Conclusions The results of this study suggest that in STEMI patients with MVD presenting with CS and CA, MV primary PCI may improve clinical outcome. Randomized trials are required to verify these results. (J Am Coll Cardiol Intv 2013;6:115-25) © 2013 by the American College of Cardiology Foundation

Increased availability of primary percutaneous coronary intervention (PCI) has reduced the incidence of cardiogenic shock (CS) in patients with ST-segment elevation myocardial infarction (STEMI) (1). In STEMI patients with established CS, prompt primary PCI of the infarct-related artery (IRA) improves survival (2); however, mortality remains unacceptably high (~50%), and is even worse in patients who have been resuscitated from cardiac arrest (3).

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The majority of patients with STEMI and CS have multivessel coronary artery disease (MVD). Multivessel disease is more likely to induce widespread myocardial ischemia and progressive left ventricular dysfunction, and has been associated with increased mortality (4). Not surprisingly, multivessel (MV) revascularization during pri-

mary PCI has been proposed as a strategy with the potential to improve outcomes in patients with MVD and persistent CS. Current societal guidelines concur (5,6); however, there is little evidence to support this strategy (7), which could conversely worsen outcomes by increasing the risk of non-IRA distal embolization, stent thrombosis, and contrast nephropathy (8).

To investigate the safety and efficacy of MV primary PCI, we conducted a multicenter study of patients with STEMI, CS, and resuscitated cardiac arrest, and compared clinical outcomes in patients treated with either culprit-only or MV primary PCI.

Methods

Patient population. Between 1998 and 2010, we prospectively collected data from consecutive unselected patients presenting with STEMI in 5 French centers. The study

population was derived from 11,530 patients admitted with STEMI, among whom 4.3% (n = 496) had resuscitated cardiac arrest, 9.8% (n = 1,130) had CS, and 2.4% (n = 272) presented with both resuscitated cardiac arrest and CS (Fig. 1).

Patients were selected for the current study if they had been resuscitated from cardiac arrest, met the criteria for STEMI and CS, and had a culprit lesion on coronary angiography, <24 h after the onset of ischemia. This patient population was specifically chosen as it represents the highest-risk patient group encountered by interventional cardiologists, and in light of the cardiac arrest, are the most likely to have ongoing global myocardial ischemia. Patients were excluded if further resuscitation was deemed futile on arrival at the catheterization laboratory, an alternative cause of shock was suspected, or if a mechanical complication of myocardial infarction (MI) was determined before PCI. The study complied with the Declaration of Helsinki.

Pre-hospital management. Pre-hospital medical care was performed by the emergency medical service (EMS) (Service d'Aide Médicale Urgence) as described previously (3). External defibrillation; administration of inotropic, paralytic, and antiarrhythmic drugs; and mechanical ventilation were routinely performed according to approved guidelines. According to the Utstein template (9), resuscitated patients with obvious extracardiac causes were investigated and treated according to standard critical care procedures. In the absence of an obvious extracardiac cause, survivors were transferred directly to cardiac catheterization laboratories under continuous electrocardiogram (ECG) monitoring. At least 1 pre-hospital 12-lead ECG was recorded in all patients.

In-hospital evaluation and treatment. All patients underwent a rapid clinical evaluation and immediate coronary angiography with a view to performing primary PCI. Hemodynamic status was cautiously evaluated on admission and during angiography. Our default strategy was to perform primary PCI in these high-risk, hemodynamically unstable patients unless, a mechanical complication, deemed coronary artery bypass graft (CABG) surgery to be more appropriate. All decisions regarding the PCI, including the number of vessels treated, were solely at the discretion of the treating physician. All patients were treated with intravenous heparin (1 mg/kg body weight) and aspirin (250 to 500 mg) before PCI. Further doses of heparin were given as required to maintain an activated clotting time of 300 to 350 s. A loading dose of 300 to 600 mg of clopidogrel was given before PCI, or immediately after the procedure through a nasogastric tube in unconscious patients.

Intensive medical care was provided in dedicated cardiac intensive care units for all patients following PCI. Mild therapeutic hypothermia, renal replacement therapy, and left ventricular assist devices were used where appropriate.

Data collection and follow-up. Data were prospectively collected using the Utstein-style guidelines for cardiac arrest

(9). Adverse cardiac events, including recurrent cardiac arrest, reinfarction, and early urgent revascularization were recorded. Cerebral Performance Categories Scale scores of outcome, graded 1 to 4, were calculated at hospital discharge for all survivors as follows: 1 = conscious and alert with good cerebral performance; 2 = conscious with moderate cerebral disability; 3 = conscious with severe disability and dependent on others for activities of daily living; and 4 = comatose or persistent vegetative state (10). Clinical follow-up was performed by hospital visit or patient/next-of-kin telephone interview at 6 months.

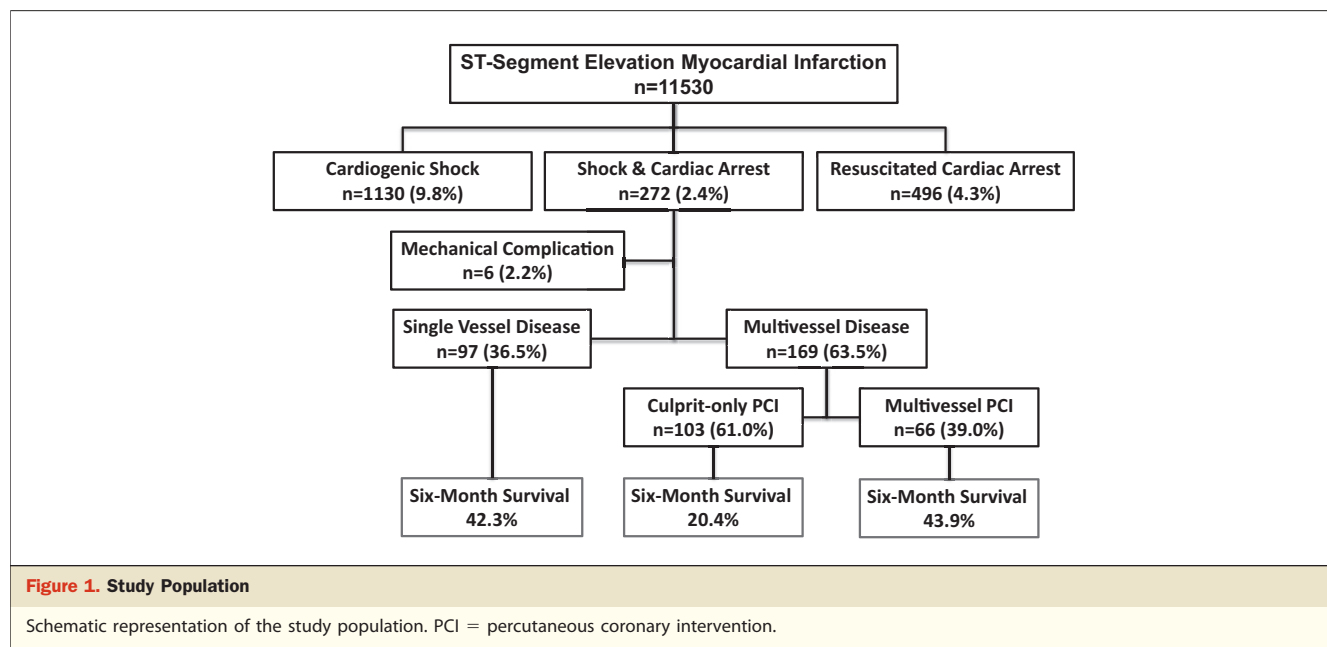
Study definitions. Cardiogenic shock was defined on admission according to the clinical criteria described in the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial (2): systolic blood pressure <90 mm Hg for >30 min or the requirement for supportive measures to maintain blood pressure \geq 90 mm Hg, and evidence of end-organ hypoperfusion (cool extremities, urine output <30 ml/h, and a heart rate \geq 60 beats/min). The diagnosis of CS was verified by the assessment of the original EMS patient encounter forms by an independent physician.

Acute MI was defined as ECG evidence of >2-mm ST-segment elevation in \geq 2 contiguous leads or a left bundle branch block or a posterior infarction with anterior ST-segment depression, and at least 1 culprit lesion on angiography. Cardiac arrest was defined as the cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation (9). A cardiac arrest in medical care indicated an arrest occurring either in-hospital or in the presence of the EMS.

Multivessel coronary disease was defined as the presence of an additional significant stenosis (\geq 70%) in a major (\geq 2.5-mm diameter) non-IRA, or as a distal left main lesion with significant stenosis of the ostia of both the daughter arteries. Immediate PCI of a stenosis \geq 70% in a non-IRA during the index procedure, not including branches of the IRA, and PCI of both branches of the distal left main defined MV primary PCI. Intervention to a non-IRA remote from the index procedure was not consid-

Abbreviations and Acronyms

CA	= cardiac arrest
CABG	= coronary artery bypass grafting
CI	= confidence interval
CK	= creatinine kinase
CS	= cardiogenic shock
ECG	= electrocardiogram
EMS	= emergency medical service
HR	= hazard ratio
IRA	= infarct-related artery
MI	= myocardial infarction
MV	= multivessel
MVD	= multivessel coronary disease
PCI	= percutaneous coronary intervention
ROSC	= resumption of spontaneous circulation
STEMI	= ST-segment elevation myocardial infarction
SVD	= single-vessel coronary disease
TIMI	= Thrombolysis In Myocardial Infarction
ULN	= upper limit of normal



ered as MV primary PCI. Angiographic success in the IRA was defined as residual stenosis $\leq 30\%$ and a final Thrombolysis in Myocardial Infarction (TIMI) flow grade >2 .

Reinfarction was defined as follows: 1) if the peak creatinine kinase (CK)-MB fraction (or CK) from the index infarction had not yet been reached: recurrent ischemic symptoms ≥ 20 min in duration or new ECG changes consistent with MI, and the peak CK-MB (or CK in the absence of CK-MB) level measured within 24 h after the event was elevated by at least 50% above the previous level; 2) if the elevated CK-MB (or CK) level from the index infarction was falling or had returned to normal: recurrent ischemic symptoms lasting ≥ 20 min in duration, or new ECG changes consistent with MI, and a new elevation of CK-MB (or CK) greater than the upper limit of normal (ULN) if the patient was being treated medically, or CK-MB/CK $>3 \times$ ULN within 24 h post-PCI if the CK-MB (or CK) level has returned to $<ULN$, or a rise by $>50\%$ above the previous nadir level (and $>3 \times$ ULN if post-PCI) if the CK-MB (or CK) level has not returned to $<ULN$ (11). The cause of death was defined as follows: CS, death due to persistent hypotension, refractory heart failure, or multiorgan failure; anoxia death due to a persistent vegetative state; arrhythmia death due to recurrent intractable cardiac arrest; sepsis death, death due to overwhelming systemic infection. All clinical events, including the cause of death, were adjudicated by 2 independent physicians blinded to the patient's initial treatment strategy.

Outcome variables. The primary outcome measure of the study was 6-month survival. Secondary endpoints included death due to CS, recurrent cardiac arrest, and a composite of these endpoints.

Statistical analysis. Continuous variables are presented as mean \pm SD or median and (interquartile range), and were compared with the Student *t* test or Mann-Whitney test, according to distribution. Categorical variables are presented as numbers and percentages, and were compared using the chi-square test or Fisher exact test. Survival at 6 months was calculated and analyzed by the Kaplan-Meier method, and differences between Kaplan-Meier curves were analyzed with the log-rank test. A multiple Cox regression analysis was performed to assess predictors of 6-month survival, including all baseline and treatment characteristics associated with 6-month survival in the univariate analysis ($p < 0.10$), and had availability in the database $>85\%$. The effect of MV primary PCI on 6-month survival in patients with MVD was assessed by a separate multiple Cox regression analysis. A 2-tailed *p* value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 17.0 (SPSS, Chicago, Illinois).

Results

Baseline demographic and clinical characteristics. A total of 272 STEMI patients met the criteria for resuscitated cardiac arrest and CS. Six patients with mechanical complications were referred for urgent CABG and were excluded from the analysis. The baseline demographics of the remaining 266 patients are presented in Table 1. Cardiac arrests occurred most commonly at home (35.4%), and the median no-flow, arrest to defibrillation, and resumption of spontaneous circulation (ROSC) intervals were (median [interquartile range]) 5.0 [2.0 to 14.0], 15.0 [6.0 to 24.5], and 25.0 [11.5 to 35.0] min, respectively. Ventricular fibrillation was the

Table 1. Baseline Characteristics of the Study Population

	All Patients (N = 266)	SVD (n = 97)	MVD (n = 169)	p Value	MVD		p Value
					Culprit-Only Primary PCI (n = 103)	MV Primary PCI (n = 66)	
Age, yrs	63.1 ± 13.0	56.1 ± 13.6	67.2 ± 12.1	p<0.001	68.5 ± 11.8	65.0 ± 12.4	0.088
Male	195 (73.3)	71 (73.2)	124 (73.4)	0.999	74 (71.8)	50 (66.0)	0.598
Body mass index, kg/m ²	25.3 [23.0–28.4]	25.8 [21.9–28.6]	25.1 [23.2–28.4]	0.796	26.0 [23.0–33.1]	25 [23.3–27.0]	0.288
Cardiac risk factors, %							
Hypertension	115 (43.2)	30 (30.9)	85 (50.3)	0.003	50 (48.5)	35 (53.0)	0.637
Hyperlipidemia	105 (39.5)	33 (34.0)	72 (42.6)	0.193	42 (40.8)	30 (45.5)	0.633
Current/past smoker	88 (33.1)	33 (34.0)	55 (32.5)	0.892	32 (31.1)	23 (34.8)	0.618
Diabetes mellitus	61 (22.9)	18 (18.6)	43 (25.4)	0.227	26 (25.2)	17 (25.8)	0.999
Family history of CAD	24 (9.0)	6 (6.2)	18 (10.7)	0.27	10 (9.7)	8 (12.1)	0.619
Prior MI	59 (22.2)	14 (14.4)	45 (26.6)	0.022	31 (30.1)	14 (21.2)	0.217
Prior PCI	49 (18.4)	15 (15.5)	34 (20.1)	0.412	23 (22.3)	11 (16.7)	0.434
Prior CABG	10 (3.8)	1 (1.0)	9 (5.3)	0.099	5 (4.9)	4 (6.1)	0.738
Location of cardiac arrest							
Home	94 (35.4)	36 (37.1)	58 (34.3)	0.69	35 (34.0)	23 (34.8)	0.999
Public place	86 (32.3)	34 (35.1)	53 (31.4)	0.588	34 (33.0)	19 (27.8)	0.613
In medical care	86 (32.3)	27 (27.8)	58 (34.3)	0.339	34 (34.0)	24 (36.4)	0.74
Cardiac arrest intervals, min*							
No-flow	5.0 [2.0–14.0]	5.0 [2.0–10.0]	6 [2.3–15.0]	0.412	10.0 [3.0–15.0]	5 [2.0–12.0]	0.186
Arrest to defibrillation	15.0 [6.0–24.5]	15.0 [8.0–25.0]	15.0 [5.3–23.0]	0.313	15.0 [6.0–25.0]	12 [5.0–20.0]	0.412
Arrest to ROSC	25.0 [11.5–35.0]	28.0 [15.0–45.0]	25.0 [10.0–30.0]	0.136	25.0 [15.0–30.0]	18.0 [10.0–31.3]	0.262
First monitored rhythm							
Ventricular tachycardia	26 (9.8)	6 (6.2)	20 (11.8)	0.197	13 (12.6)	7 (10.6)	0.809
Ventricular fibrillation	160 (60.2)	63 (65.0)	97 (57.4)	0.244	57 (55.3)	40 (60.6)	0.527
Asystole	61 (22.9)	19 (19.5)	42 (24.9)	0.365	28 (27.2)	14 (21.2)	0.467
Unknown/other	19 (7.1)	9 (9.3)	10 (5.9)	0.329	5 (4.9)	5 (7.6)	0.515
Defibrillation	222 (83.5)	86 (88.7)	136 (80.5)	0.089	86 (83.5)	50 (75.8)	0.237

Values are mean ± SD, n (%), or median [interquartile range]. *Based on 169 patients.
 CABG = coronary artery bypass grafting; CAD = coronary artery disease; MI = myocardial infarction; MV = multivessel; MVD = multivessel disease; PCI = percutaneous coronary revascularization; ROSC = resumption of spontaneous circulation; SVD = single vessel disease.

underlying arrhythmia in 60.2% of cases, and the initial ECG demonstrated ST-segment elevation in 86.5%. Pre-hospital thrombolysis was performed in 14.6% of patients. Mean admission systolic and diastolic blood pressures were 86.5 ± 18.0 mm Hg and 55.9 ± 13.8 mm Hg, respectively, despite inotropic support in 94.4% (Table 2).

Angiographic and treatment data. The culprit lesion was most commonly located in the left anterior descending coronary (51.9%), and was in the left main in 9.8% of cases (Table 3). The majority of patients had MVD (63.5%), and 18.8% had a non-IRA chronic total occlusion. Despite the high prevalence of MVD, most patients underwent culprit-only PCI (75.2%) (Table 4). Culprit-artery stenting was performed in 95.1%, glycoprotein IIb/IIIa inhibitors were used in 12.4%, and thromboaspiration in 41%. Angiographic success in the IRA was achieved in 80.5% of cases. The majority of patients required mechanical ventilation (77.4%) and intra-aortic balloon counterpulsation (76.3%). Mild therapeutic hypothermia was performed in

22.2%, and left ventricular assist devices were used in 8 (3%) patients.

Clinical outcomes. Death in the catheterization laboratory or within 24 h of hospital admission occurred in 7.9% and 29.3%, respectively (Table 5). A small proportion of patients had reinfarction (1.9%) or repeat emergent PCI (3.8%). Recurrent in-hospital cardiac arrest after primary PCI occurred in almost one-third of patients (32.7%). Six-month clinical follow-up was available in all patients. Overall 6-month survival was 34.6%. Refractory CS was the most common cause of death (60.2%). The median duration to death was 2.0 [1.0 to 9.0] days. Among survivors, the majority recovered good/moderate cerebral performance (89.5%), and 30.4% underwent further nonurgent revascularization.

Single-vessel and multivessel disease. Compared to those with SVD (36.5%), patients with MVD (63.5%) were more likely to have a history of hypertension (30.9% vs. 50.3%, p = 0.003), prior MI (14.4% vs. 26.6%, p = 0.022), and present

Table 2. Patient Characteristics on Hospital Admission

	All Patients (N = 266)	SVD (n = 97)	MVD (n = 169)	p Value	MVD		p Value
					Culprit-Only Primary PCI (n = 103)	MV Primary PCI (n = 66)	
Pre-arrest chest pain	172 (64.7)	66 (68.0)	107 (63.3)	0.505	67 (65.0)	40 (60.6)	0.625
Pre-infarct angina	84 (31.6)	31 (32.0)	53 (31.4)	0.999	36 (35.0)	17 (25.8)	0.237
Pre-hospital thrombolysis	39 (14.6)	18 (18.6)	21 (12.5)	0.208	15 (14.6)	6 (9.2)	0.251
Electrocardiographic findings							
ST-segment elevation	230 (86.5)	88 (90.7)	142 (84.1)	0.14	88 (85.4)	54 (81.8)	0.528
ST-segment depression	12 (4.5)	4 (4.1)	8 (4.7)	0.999	3 (2.9)	5 (7.6)	0.265
LBBB	24 (9.0)	5 (5.2)	19 (11.2)	0.12	12 (11.7)	7 (10.6)	0.999
Third-degree heart block	26 (9.8)	9 (9.3)	17 (10.1)	0.999	11 (10.7)	6 (9.1)	0.799
Ejection fraction, %*	31.0 ± 9.3	31.4 ± 9.4	30.6 ± 9.2	0.594	30.3 ± 9.0	31.0 ± 9.6	0.493
Hemodynamic parameters							
Systolic blood pressure, mm Hg	86.5 ± 18.0	94.8 ± 27.2	82.6 ± 19.2	0.001	83.0 ± 21.2	82.0 ± 15.7	0.742
Diastolic blood pressure, mm Hg	55.9 ± 13.8	58.3 ± 16.3	54.8 ± 14.8	0.17	55.0 ± 16.1	54.4 ± 12.7	0.798
Heart rate, beats/min	92.2 ± 24.0	97.9 ± 30.1	96.8 ± 20.8	0.103	98.0 ± 21.2	95.0 ± 20.0	0.36
Laboratory findings on admission							
pH†	7.2 ± 0.2	7.2 ± 0.2	7.2 ± 0.2	0.973	7.2 ± 0.2	7.2 ± 0.2	0.999
Lactate‡	8.2 ± 3.7	7.8 ± 3.5	8.3 ± 4.0	0.439	8.3 ± 4.3	8.1 ± 3.9	0.82
Glucose‡	8.3 ± 3.2	8.1 ± 2.9	8.4 ± 3.4	0.466	8.2 ± 3.1	8.2 ± 3.6	0.999
Estimated GFR, ml/min	75.1 ± 29.4	76.1 ± 33.0	73.7 ± 24.1	0.497	75.4 ± 37.5	72.9 ± 22.8	0.627
Peak creatinine kinase (>4 h), IU/L§	3,600 [2,220–6,000]	3,338 [2,075–5,147]	3,708 [2,221–6,509]	0.423	4,139 [2,427–6,500]	3,500 [2,055–7,485]	0.655

Values are mean ± SD, n (%), or median [interquartile range]. Based on *139, †142, ‡139, and §185 patients.

LBBB = left bundle branch block; GFR = glomerular filtration rate; other abbreviations as in Table 1.

with a lower systolic blood pressure (94.8 ± 27.2 mm Hg vs. 82.6 ± 19.2 mm Hg, $p = 0.001$). An average 2.5 ± 0.5 vessels were significantly diseased ($\geq 70\%$) in the MVD cohort. Six-month survival was significantly lower in patients with MVD (42.3% vs. 29.6%, $p = 0.032$) (Table 5, Fig. 2A).

Culprit-only or MV primary PCI in MVD. Of the 169 patients with MVD, 103 (60.9%) had culprit-only primary PCI, and 66 (39.1%) had MV primary PCI. There was a higher incidence of initial TIMI flow grade 0 (75.7% vs. 56.1%, $p = 0.011$) and a right coronary artery IRA (30.1% vs. 15.2%, $p = 0.029$) in the culprit-only primary PCI group. Distal left main lesions requiring intervention to both daughter branches were classified as MV PCI, and therefore, left main IRAs were more common in the MV primary PCI group (7.8% vs. 21.2%, $p = 0.018$). Intra-aortic counterpulsation was performed in 75.7% of culprit-only primary PCI patients and in 83.3% of MV primary PCI cases ($p = 0.256$). In the culprit-only primary PCI group, there were 2 cases where PCI of a non-IRA vessel was attempted and failed. In the MV primary PCI group, the mean number of non-IRA vessels attempted was 1.3 ± 0.5 , with 1.2 ± 0.4 vessels successfully treated, and complete coronary revascularization achieved in 63.6%. Predictably, less contrast media was used in the culprit-only primary PCI group (170.3 ± 67.4 ml vs. 221.7 ± 83.1 ml, $p < 0.0001$).

Six-month survival was significantly greater in those undergoing MV primary PCI compared with those who had culprit-only intervention (43.9% vs. 20.4%, $p = 0.0017$) (Table 5, Fig. 2B). This survival advantage was mediated by a significant reduction in the composite endpoint of recurrent cardiac arrest/shock death in the MV primary PCI group (50.0% vs. 68.0%, $p = 0.024$).

Association of baseline characteristics and treatment with 6-month mortality. Univariable analysis of the entire population revealed that 4 characteristics were associated with 6-month mortality ($p < 0.10$): 1) an asystolic cardiac arrest; 2) a right coronary IRA; 3) MV primary PCI; and 4) angiographic success in the IRA (Table 6). Following adjustment, an asystolic cardiac arrest (hazard ratio [HR]: 1.58; 95% confidence interval [CI]: 1.07 to 2.35, $p = 0.022$) remained a predictor of 6-month mortality and a right coronary IRA (HR: 0.65; 95% CI: 0.49 to 1.02, $p = 0.025$), and PCI success (HR: 0.49; 95% CI: 0.34 to 0.72, $p < 0.0001$) were associated with 6-month survival by multivariable analysis.

In patients with MVD, a right coronary IRA (HR: 0.54; 95% CI: 0.34 to 0.85, $p = 0.009$), MV primary PCI (HR: 0.57; 95% CI: 0.36 to 0.80, $p = 0.002$) and angiographic success in the IRA (HR: 0.65; 95% CI: 0.43 to 1.00, $p = 0.050$) were associated with 6-month survival following adjustment for other variables.

Table 3. Angiographic Characteristics

	All Patients (N = 266)	SVD (n = 97)	MVD (n = 169)	p Value	MVD		p Value
					Culprit-Only Primary PCI (n = 103)	MV Primary PCI (n = 66)	
Culprit lesion							
Left main	26 (9.8)	4 (4.1)	22 (13.0)	0.019	8 (7.8)	14 (21.2)	0.018
Left anterior descending	138 (51.9)	62 (63.9)	76 (45.0)	0.003	45 (43.7)	31 (47.0)	0.752
Circumflex	36 (13.5)	9 (9.3)	27 (16.0)	0.14	16 (15.5)	11 (16.7)	0.833
Right coronary	63 (23.7)	22 (22.7)	41 (24.2)	0.881	31 (30.1)	10 (15.2)	0.029
Bypass graft	3 (1.1)	0 (0.0)	3 (1.8)	0.556	3 (2.9)	0 (0.0)	0.282
Number of diseased vessels	1.9 ± 0.8	1.0 ± 0.0	2.5 ± 0.5		2.5 ± 0.5	2.5 ± 0.5	0.999
1	97 (36.5)	97 (100)					
2	86 (32.3)		86 (50.9)		54 (52.4)	32 (48.5)	0.639
3	83 (31.2)		83 (49.1)		49 (47.6)	34 (51.5)	0.639
Bifurcation lesion	67 (25.2)	25 (25.8)	42 (24.9)	0.884	20 (19.4)	22 (33.3)	0.046
Stenosis severity, %	94.4 ± 14.2	94.6 ± 17.7	94.4 ± 16.9	0.923	95.0 ± 16.6	93.4 ± 17.5	0.55
Pre-PCI TIMI flow grade							
0	188 (70.7)	73 (75.3)	115 (68.0)	0.263	78 (75.7)	37 (56.1)	0.011
1	14 (5.2)	4 (4.1)	10 (5.9)	0.776	5 (4.9)	5 (7.6)	0.515
2	22 (8.3)	3 (3.1)	19 (11.2)	0.021	10 (9.7)	9 (13.6)	0.461
3	42 (15.8)	17 (17.5)	25 (14.9)	0.602	10 (9.7)	15 (22.7)	0.026
Visible thrombus	232 (87.2)	87 (89.7)	145 (85.8)	0.447	92 (89.3)	53 (80.3)	0.117
Stent thrombosis	18 (6.8)	5 (5.2)	13 (7.7)	0.613	8 (7.7)	5 (7.6)	0.999
Drug-eluting stent	11 (61.1)	2 (40.0)	9 (69.2)	0.338	6 (75.0)	3 (60.0)	0.999
Bare-metal stent	7 (38.9)	3 (60.0)	4 (30.8)	0.708	2 (25.0)	2 (40.0)	0.644
Nonculprit CTO	50 (18.8)		50 (29.6)		33 (32.0)	17 (25.8)	0.49

Values are mean ± SD or n (%).
 CTO = chronic total occlusion; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

Discussion

In the present study, we found that STEMI patients with CS, resuscitated cardiac arrest, and MVD, had significantly greater survival following MV primary PCI compared with culprit-only primary PCI. The results of this study suggest that more complete upfront revascularization has the potential to improve outcomes in these critically ill patients.

The SHOCK trial confirmed that prompt revascularization improves survival in CS (2); however, the optimal revascularization strategy for shock patients with MVD is not clear. This is of particular relevance because MVD occurs in up to 87% of patients with CS (12) and is associated with increased mortality (4,13). Certainly, there is a rationale for more complete revascularization in MVD patients with CS refractory to IRA intervention. Mortality in CS is directly related to the degree of myocardial ischemia and the extent of acute left ventricular dysfunction (2). Therefore, treatment of significant non-IRA stenoses which supply a large area of myocardium has the potential to improve left ventricular function, by enhancing perfusion of the periinfarct area and minimizing non-IRA ischemia. Pathological studies have also demonstrated that those who die from MI frequently have

evidence of multiple separate thrombi in separate territories, despite a clear culprit lesion (14).

In the setting of nonshock STEMI, MV primary PCI is inappropriate (5,6), as several trials have illustrated the deleterious effects of this approach (15–18). By contrast, the safety and efficacy of MV primary PCI in STEMI with CS is unclear. Current societal guidelines support MV primary PCI as a possible treatment strategy for refractory CS (5,6), though supporting evidence is insufficient. Analysis of the PCI cohort in the SHOCK trial (n = 82) suggested that MV primary PCI was associated with increased 1-year mortality (19). However, PCI in the SHOCK trial does not reflect contemporary practice: 34% received a stent; and only 71% had angiographic success (final TIMI flow grade >2). In the current study, the IRA was stented in 95.1%, and angiographic success was achieved in 80.5%.

Previous retrospective analyses of large PCI databases have investigated the effect of multivessel PCI on clinical outcomes in patients with STEMI and CS, with somewhat conflicting results (20,21). Cavander et al. (20) found that multivessel PCI was associated with increased mortality at 1 year, whereas an analysis by Bauer et al. (21) did not find multivessel PCI to have any impact on in-hospital mortality.

Table 4. Percutaneous Coronary Intervention

	All Patients (N = 266)	SVD (n = 97)	MVD (n = 169)	p Value	MVD		p Value
					Culprit-Only Primary PCI (n = 103)	MV Primary PCI (n = 66)	
Thromboaspiration	109 (41.0)	42 (43.3)	67 (39.6)	0.605	41 (39.8)	26 (39.4)	0.999
GP IIb/IIIa receptor antagonists	33 (12.4)	15 (15.5)	18 (10.7)	0.254	10 (9.7)	8 (12.1)	0.619
Stent placement	253 (95.1)	90 (92.8)	163 (96.4)	0.238	96 (93.2)	65 (98.5)	0.151
Total stent length, mm	28.2 ± 17.8	24.1 ± 12.9	30.2 ± 18.9	0.004	26.2 ± 18.7	33.0 ± 17.1	0.018
Total number of stents	1.7 ± 1.1	1.2 ± 0.7	2.0 ± 1.1	<0.0001	1.6 ± 0.9	2.6 ± 1.1	<0.0001
Contrast volume, ml	178.8 ± 74.6	158.8 ± 64.1	190.3 ± 77.9	0.0008	170.3 ± 67.4	221.7 ± 83.1	<0.0001
Angiographic success in IRA	214 (85.5)	83 (85.6)	131 (77.5)	0.148	78 (75.7)	53 (80.3)	0.573
Post-PCI TIMI flow grade <3	47 (17.7)	12 (12.4)	35 (20.7)	0.097	23 (22.3)	12 (18.1)	0.564
Residual stenosis ≥30%	18 (6.8)	6 (6.2)	12 (7.1)	0.999	10 (9.7)	2 (3.0)	0.13
IRA no-reflow	29 (10.9)	8 (8.2)	21 (12.4)	0.316	17 (16.5)	4 (6.1)	0.056
IRA thrombus embolization	14 (5.3)	3 (3.1)	11 (6.5)	0.269	9 (8.7)	2 (3.0)	0.205
IRA side branch occlusion	3 (1.1)	1 (1.1)	2 (1.2)	0.999	1 (1.0)	1 (1.5)	0.999
Total number of vessels treated	1.3 ± 0.6		1.4 ± 0.6			2.2 ± 0.4	
Number of non-IRA vessels successfully treated	0.3 ± 0.6		0.45 ± 0.61			1.2 ± 0.4	

Values are mean ± SD or n (%).
GP = glycoprotein; IRA = infarct-related artery; other abbreviations as in Tables 1 and 3.

By contrast, the current study observed a considerable survival advantage associated with MV primary PCI. These disparate results must be viewed within the context of the patient population enrolled and the limitations of observational study design. The current study included the highest-risk cohort of patients studied to date, with both STEMI and resuscitated cardiac arrest, in an attempt to ensure the presence of shock and global myocardial ischemia. Previous studies have included lower-risk patient populations: intra-aortic balloon pump use (11.1% to 33.3%) and in-hospital mortality (36.5% to 48.8%). The inclusion of nonshock patients in these analyses may have mitigated any benefit associated with MV primary PCI. Furthermore, the prospective design of the current study afforded the availability of individual patient data, thus ensuring adherence to the patient selection criteria and the exclusion of patients with late presentations after symptom onset or those who underwent staged MV PCI.

The survival advantage observed in patients undergoing MV primary PCI was mediated by a reduction in events directly related to CS: recurrent cardiac arrest and death due to shock (68% vs. 50%, $p = 0.024$). A reduction in the overall myocardial ischemic burden in these critically ill patients is a possible explanation for these results. The equivalent 6-month survival in patients with MVD undergoing MV primary PCI (43.9%) and those with SVD (42.3%) are consistent with this hypothesis. Moreover, these data suggest that although complete revascularization results in a survival benefit in these unstable patients, there is a limit to what can be achieved with revascularization. However, among survivors, favorable neurological outcomes were

observed (89.5%), and thus, an initial aggressive treatment strategy is probably warranted.

Previous publications have identified early revascularization, left ventricular function, coronary stenting, patient age, and successful revascularization (TIMI flow grade >2) to be of critical importance when treating patients with CS (2,22,23). Angiographic success in the IRA was also an independent predictor of survival (HR: 0.54 95% CI: 0.37 to 0.78, $p = 0.001$) in the current study, as was MV primary PCI in those with MVD (HR: 0.57; 95% CI: 0.38 to 0.84, $p = 0.005$).

Urgent CABG is another possible strategy for treating patients with STEMI and CS (24). However, clinical practice reflects physician preference for PCI, as a more rapid, less invasive revascularization strategy: the rate of primary PCI for CS has increased (27.4% to 54.4%), whereas the rate of CABG remains stable (2.1% to 3.2%) (1).

Ultimately, the revascularization strategy for each patient with STEMI and CS should be individualized. In patients with MVD, the hemodynamic status should be reassessed following PCI of the IRA. If CS persists, MV primary PCI should be considered, depending on the complexity of the nonculprit lesions and their capacity to induce myocardial ischemia. We provide preliminary evidence that this strategy may improve clinical outcomes, supporting what is intuitively proposed by practice guidelines and practiced by physicians worldwide, and underscoring the need for adequately powered randomized trials to define the role of more complete revascularization in these critically ill patients.

	All Patients (N = 266)	SVD (n = 97)	MVD (n = 169)	p Value	MVD		p Value
					Culprit-Only Primary PCI (n = 103)	MV Primary PCI (n = 66)	
Death in catheterization laboratory	21 (7.9)	8 (7.2)	13 (7.7)	0.999	8 (7.8)	5 (7.6)	0.999
Death within 24 h	78 (29.3)	28 (28.9)	50 (29.6)	0.999	35 (34.0)	15 (22.7)	0.125
Reinfarction	5 (1.9)	2 (2.1)	3 (1.8)	0.999	1 (1.0)	2 (3.0)	0.561
Repeat emergent PCI	10 (3.8)	1 (1.0)	9 (5.3)	0.099	5 (4.9)	4 (6.1)	0.738
Recurrent cardiac arrest	87 (32.7)	33 (34.0)	54 (32.0)	0.786	36 (35.0)	18 (27.3)	0.316
6-month mortality*	174 (65.4)	55 (56.7)	119 (70.4)	0.032	82 (79.6)	37 (56.1)	0.0017
Shock death	102 (59.6)	26 (47.3)	76 (65.5)	0.03	54 (67.5)	22 (61.1)	0.532
Arrhythmic death	21 (12.3)	7 (12.7)	14 (12.1)	0.999	9 (11.3)	5 (13.9)	0.76
Anoxic death	45 (26.3)	21 (38.2)	24 (20.7)	0.017	16 (20.0)	8 (22.2)	0.807
Sepsis death	3 (1.8)	1 (1.8)	2 (1.7)	0.999	1 (1.3)	1 (2.8)	0.999
Composite of recurrent cardiac arrest and shock death	149 (56.0)	46 (47.4)	103 (60.9)	0.04	70 (68.0)	33 (50.0)	0.024
Time to in-hospital death, days	2.0 [1.0-9.0]	2.0 [1.0-7.0]	2.0 [1.0-9.5]	0.201	2.0 [1.0-8.8]	10.0 [2.0-20.0]	0.201
Scheduled nonurgent PCI†	22 (23.9)	3 (7.1)	19 (38.0)	0.0005	10 (47.6)	9 (31.0)	0.255
Scheduled nonurgent CABG†	6 (6.5)	0 (0.0)	6 (12.0)	0.029	3 (6.5)	3 (10.3)	0.686
Hospital discharge CPC score‡							
Favorable (1 or 2)	85 (89.5)	40 (95.2)	45 (84.9)	0.177	18 (78.3)	27 (90.0)	0.272
Not favorable (2 or 3)	10 (10.5)	2 (4.8)	8 (15.1)	0.177	5 (21.7)	3 (10.0)	0.272

Values are mean ± SD, median [interquartile range], or n (%). *Deceased patients; †survivors only.
 CPC = Cerebral Performance Categories; other abbreviations as in Table 1.

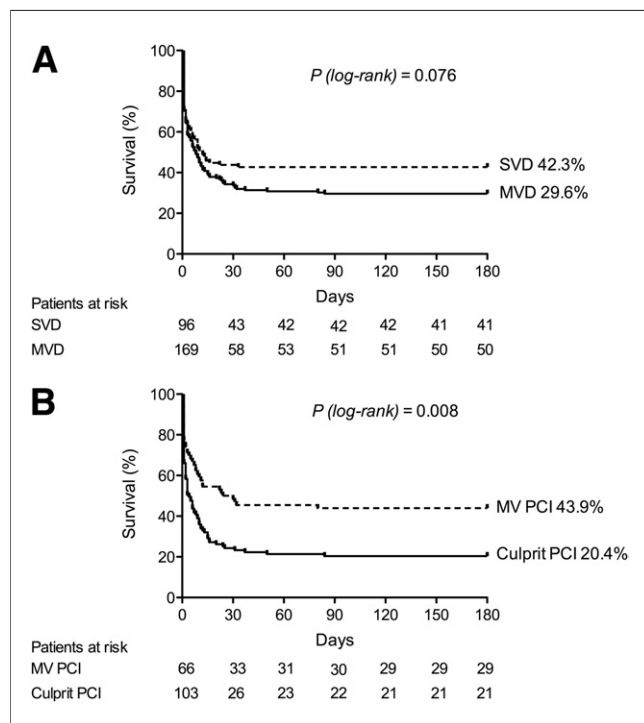


Figure 2. Primary Endpoint at 6 Months

Survival to 6 months in patients with (A) single-vessel (SVD) or multivessel (MVD) coronary disease, or (B) MVD undergoing culprit-only or MV primary PCI. MV = multivessel; PCI = percutaneous coronary intervention.

Study limitations. The present study is a nonrandomized, observational registry, and is thus limited by patient selection bias. The decision to perform primary culprit-only or MV primary PCI was based on operator preference. Although the baseline clinical and angiographic characteristics were well matched between patients undergoing culprit-only or MV primary PCI, the culprit-only group tended to be older; have longer no-flow, arrest to defibrillation, and ROSC intervals; and were more likely to have TIMI 0 flow grade on presentation. These factors could have resulted in inferior outcomes in the culprit-only cohort. Unrecognized confounding variables also have the potential to influence nonrandomized results. At the time of study conception, it was not recognized that intervals, such as the door to balloon and first medical contact to balloon were associated with improved survival in STEMI. These intervals would have provided useful additional information. Similarly, serum lactate levels and the resuscitation intervals were not tested in the multivariate analysis because the data were not available in >85% of cases. However, we have previously identified these factors as independent predictors of survival in STEMI patients with resuscitated cardiac arrest (3). Despite current recommendations, the use of therapeutic hypothermia worldwide remains poor (22). In the current study, therapeutic hypothermia was used in only 22.2% of cases, and more extensive implementation may have improved outcomes (25).

Table 6. Cox Regression Analysis for Predictors of 6-Month Mortality

	Simple Cox Regression			Multiple Cox Regression		
	Hazard Ratio	95% CI	p Value	Hazard Ratio	95% CI	p Value
All patients, N = 266						
Age	1.0	0.99–1.02	0.163			
Male	0.9	0.65–1.26	0.539			
Diabetes	1.3	0.93–1.84	0.13			
Asystole	1.55	1.05–2.30	0.028	1.58	1.07–2.35	0.022
Arrest in medical care	0.76	0.50–1.16	0.203			
Systolic blood pressure	1.01	0.99–1.01	0.186			
Pre-hospital thrombolysis	0.96	0.62–1.48	0.852			
Non-target CTO	1.29	0.95–1.91	0.123			
Right coronary IRA	0.71	0.49–1.03	0.067	0.65	0.44–0.95	0.025
Left main IRA	0.79	0.47–1.34	0.381			
MVD	1.26	0.92–1.73	0.156			
Pre-PCI TIMI grade 0	1.02	0.72–1.41	0.916			
Thrombus aspiration	0.94	0.65–1.34	0.723			
MV PCI	0.69	0.48–0.99	0.048	0.70	0.48–1.01	0.06
PCI success	0.6	0.42–0.86	0.006	0.49	0.34–0.72	<0.0001
Hypothermia	1.03	0.69–1.53	0.903			
MVD only, n = 169						
Age	1.0	0.99–1.02	0.969			
Male	0.9	0.60–1.34	0.595			
Diabetes	1.39	0.93–2.07	0.11			
Asystole	1.51	0.93–2.45	0.101			
Arrest in medical care	0.9	0.55–1.46	0.662			
Systolic blood pressure	1.01	0.99–1.02	0.337			
Pre-hospital thrombolysis	0.96	0.62–1.48	0.852			
Right coronary IRA	0.68	0.43–1.05	0.083	0.54	0.34–0.85	0.009
Left main IRA	0.59	0.33–1.08	0.085	0.55	0.30–1.01	0.054
Non-target CTO	1.29	0.95–1.91	0.123			
MVD	1.26	0.92–1.73	0.156			
Pre-PCI TIMI flow grade 0	1.19	0.80–1.77	0.396			
Thrombus aspiration	0.99	0.65–1.50	0.945			
MV PCI	0.55	0.37–0.81	0.003	0.53	0.36–0.80	0.002
PCI success	0.59	0.39–0.90	0.014	0.65	0.43–1.00	0.047
Hypothermia	0.79	0.47–1.35	0.391			

CI = confidence interval; other abbreviations as in Tables 1, 3, and 4.

Conclusions

The results of this study suggest that in STEMI patients with MVD presenting with CS and cardiac arrest, MV primary PCI may improve clinical outcome. Adequately powered prospective randomized clinical trials are required to verify these results.

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Key Words: cardiac arrest ■ cardiogenic shock ■ primary percutaneous coronary intervention ■ ST-segment elevation myocardial infarction.

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