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Outcome of Patients Presenting with ST Elevation Myocardial Infarct and Cardiogenic Shock: A Contemporary Single Center's Experience

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Key Words
Cardiogenic shock · ST elevation myocardial infarction · Renal failure · Diabetes · Prognosis

Abstract
Objectives: Acute ST elevation myocardial infarction (STEMI) presenting with cardiogenic shock (CS) is associated with dismal prognosis. In the last years, significant advances have been made in reperfusion techniques and pharmacological treatment. Therefore, we aimed to assess the outcome of these patients during the past decade and identify major factors that impact their prognosis. ***Methods:*** We identified 170 patients who presented with STEMI, CS, and underwent primary percutaneous coronary intervention (PCI) between 2001 and 2011. Patients were allocated into two groups based on period of presentation: 2001–2005 (n = 70) and 2006–2011 (n = 100). Clinical outcomes up to 6 months were evaluated. ***Results:*** Patients in the latter period were younger, and had lower rates of renal failure and higher rates of stent use. Despite these differences, mortality did not differ and remained high in both periods (52–59% at 6 months). Time frames from onset of symptoms to arrival to the emergency department and to performance of coronary intervention were similar in both periods. Intra-aortic balloon pump use was similar in both periods. In multivariate analysis, factors associated with 1-month mortality were: diabetes (OR = 3.6, 1.4–9.4, p = 0.007), LVEF <40% (OR = 1.8, 1.3–2.6, p = 0.001), GFR <60 ml/min/m^2 (OR = 1.8, 1.3–2.4, p < 0.009) and glycoprotein IIb/IIIa inhibitor use (OR = 0.5, 0.2–1.1, p = 0.08). The combination of diabetes and renal failure was associated with particularly high mortality. ***Conclusions:*** Prognosis of patients presenting with STEMI, CS, and treated with primary PCI during the past decade, remains poor. Better risk-stratification may help improve their grave outcome.

Cardiogenic shock (CS) complicating acute ST elevation myocardial infarction (STEMI) is associated with a high mortality rate, but is potentially treatable if approached urgently and aggressively [1]. The incidence of CS has fallen dramatically in the past 30 years from an average of 7.5% in 1975 to a nadir of 4.1% in 2003, and in accordance in-hospital mortality decreased from 76.1% to a nadir of 45.4%, respectively [2]. This is probably related to the adoption of early revascularization strategy, accompanied by increasing rates of primary percutaneous coronary interventions (PCI) [3]. In addition, significant advances in both catheter-based reperfusion tech-

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niques and adjunctive pharmacological agents used may have contributed to these trends. Nevertheless, mortality remains alarmingly high.

A number of studies have identified risk factors for mortality in patients presenting with CS complicating myocardial infarction (MI). The GUSTO-I database analysis identified predictors of 30-day mortality including age, prior MI, signs of shock during physical examination, and oliguria [4]. The more recent TRIUMPH database analysis identified systolic blood pressure on vasopressor support and creatinine clearance as significant predictors of 30-day mortality [5]. Irrespective of mortality risk factors on admission, patients who survive hospitalization have excellent long-term prognosis with good quality of life [3].

There is limited information whether the advances in both catheter-based reperfusion techniques and adjunctive pharmacological agents have altered the risk factors for poor outcome in patients with STEMI and CS treated with primary PCI. Our aim was to examine the clinical outcome of patients presenting to our center with STEMI and CS who were treated with primary PCI during the past decade, and to identify risk factors or risk factor combinations associated with worse outcome. We hypothesized that a history of both diabetes and renal failure was associated with particularly poor outcome.

Methods

From January 2001 to December 2011, a total of 1,725 consecutive patients with chest pain and STEMI undergoing emergency PCI at the Rabin Medical Center, Tel Aviv, Israel, were prospectively observed and entered into a clinical database. Acute STEMI was defined as the presence of typical chest pain and accompanying symptoms for ≥30 min but <12 h in the presence of ST-segment elevation ≥1 mm in ≥2 contiguous leads or new or undetermined duration of left branch bundle block in association with ≥twofold increase in cardiac enzymes (troponin I or T). Of those patients, we identified 170 patients (10%) presenting with STEMI and CS, defined as blood pressure <90 mm Hg associated with signs of organ hypoperfusion despite fluid challenge, associated with left ventricular with or without right ventricular dysfunction by echocardiography. The cohort included demographic, clinical, angiographic, and procedural data. This registry was approved by the ethics committee of the Rabin Medical Center. Patients were excluded from the present analysis if they presented with CS and dominant valvular pathology, had mechanical complication, or had accompanying sepsis.

All patients were treated with aspirin 325 mg before PCI and clopidogrel 300–600 mg either before PCI (pretreatment) or immediately after the procedure. Unfractionated heparin (70 U/kg loading) was given before PCI and adjusted to achieve an activated clotting time of 200–250 s during the procedure. Glycoprotein IIb/IIIa inhibitors were used during the procedure and immediately following the PCI, at the discretion of the operator. Coronary angiography was performed through the femoral route. Intra-aortic ballon pump deployment at the beginning or end of coronary angiography and selection of stent type, predilatation with undersized balloons, and postdilatation with larger balloons were left to the operator's discretion as well. All stents were implanted with moderate-to-high deployment pressure (12–16 atm). All patients were prescribed lifelong aspirin and clopidogrel (75 mg/day) for 3–12 months, depending on stent type. Baseline clinical characteristics, angiographic details, and clinical outcomes up to 6 months were collected. Coronary angiograms were recorded at baseline and after PCI. They were analyzed by experienced cardiologists at our angiography core laboratory using the MDView QA System (Medcon Telemedicine Technology, Tel Aviv, Israel). The cardiologists were blinded to the group allocation of the patients. Analysis was performed using automated edge-detection techniques. The contrast-filled guiding catheter (6 or 7 Fr) was used for calibration. Standard morphologic criteria were used to identify lesion location, lumen diameter, presence of thrombus, Thrombolysis In Myocardial Infarction (TIMI) flow grade, and no reflow. Based on these measurements, the percentage of diameter stenosis was determined before and after PCI. Patients with CS who did not undergo coronary catheterization were not included in our analysis.

Immediate and in-hospital events were recorded from hospital charts. For each patient, a standardized questionnaire was completed either by telephone or in the outpatient clinic at the 1- to 6-month follow-up visits. Mortality was confirmed by records of the Interior Ministry of Israel. Follow-up was completed for 100% of patients at 1 month. At 6 months, mortality data were available for 100% of the patients; revascularization and reinfarction data were available for 94% of patients.

Procedural success was defined as angiographic residual stenosis <20% by visual estimate or quantitative coronary angiography. The diagnosis of reinfarction was based on recurrent chest pain suggestive of acute MI accompanied by repeated increase in cardiac enzymes to ≥2 times the upper limit of normal ≥48 h after PCI and/or new ST elevation or pathologic Q waves. Target-vessel revascularization was defined as any revascularization that involved the target vessel. Stent thrombosis was defined according to the Academic Research Consortium definitions as definite in the context of ACS and/or reinfarction in the culprit coronary territory with angiographically proven thrombosis (thrombus or occlusion) of the previously implanted stent. Major adverse cardiac events at 1 and 6 months included cardiac death, nonfatal MI, and target-vessel revascularization (without repetition). All events were further adjudicated by an experienced cardiologist from our research team.

Several analyses were performed. First, our study group (patients with STEMI and CS who underwent primary PCI) was divided into two subgroups based on the period of presentation in order to identify possible changes in the treatment patterns or outcomes during the study period. The first subgroup included patients presenting with STEMI and CS between 2001 and 2005 (n = 70). The second subgroup included patients presenting with STEMI and CS between 2006 and 2011 (n = 100). Second, we performed multivariate logistic regression analysis in the whole group as well as subgroups to identify factors associated with poor prognosis – mainly mortality. Finally, after identifying dia-

Table 1. Clinical characteristics

Variables	1st period (n = 70)	2nd period (n = 100)	p value
Age, years	70 ± 12	66 ± 13	0.03
Male	64	76	0.1
Diabetes mellitus	31	25	0.4
Hypertension	49	62	0.2
Hyperlipidemia	44	51	0.3
Peripheral vascular disease	17	11	0.3
Previous stroke	15	6	0.07
GFR <60 ml/min/m^2	57	40	0.04
Smoking	25	37	0.1
Previous myocardial infarction	21	18	0.7
Anterior wall infarction	50	57	0.3
Right ventricular infarction	20	17	0.3
Previous coronary intervention	13	18	0.4
Previous coronary bypass grafting	7.4	8	0.9
Ejection fraction <40%	83	84	0.99
Hemoglobin, g/dl	12.4 ± 2	13.1 ± 2	0.03
White blood cell count, 1,000/μl	16.1 ± 7.1	17.3 ± 8.3	0.4

Values are percentages unless otherwise indicated.

Table 2. Medications prior to admission, time intervals, and management during PCI

Variables	1st period (n = 70)	2nd period (n = 100)	p value
Medications			
Aspirin	87	69	0.02
Clopidogrel	25	37	0.2
β-Blockers	15	5.5	0.05
ACE inhibitors/ARBs	12	5.0	0.2
Statins	46	39	0.4
Time intervals			
Symptom onset to ED, h	4.8 ± 5.5	4.5 ± 8.7	0.7
ED to coronary intervention, h	1.8 ± 1.5	1.4 ± 1.1	0.1
Shock management during PCI			
Glycoprotein IIb/IIIa inhibitor	57	43	0.07
Intra-aortic balloon pump	77	71	0.4

Values are percentages unless otherwise indicated. ED = Emergency department.

Table 3. Effects of timing of treatment on mortality

	Door-to-balloon <4 h (n = 62)	Door-to-balloon >4 h (n = 95)	p value
1-month mortality	32 (52%)	47 (49%)	0.8
6-month mortality	35 (56.5%)	51 (53.7%)	0.7
	Onset of pain till ER <6 h (n = 43)	Onset of pain till ER >6 h (n = 74)	
1-month mortality	20 (46.5%)	36 (48.7%)	0.9
6-month mortality	23 (53%)	39 (53%)	0.95

betes and renal insufficiency as important prognostic factors in our study, we performed an ancillary analysis in 147 patients (8.5%) who had a GFR measurement before PCI. These patients were allocated into four groups: group 1 = diabetes and renal failure (n = 25); group 2 = diabetes without renal failure (n = 18); group 3 = renal failure without diabetes (n = 42); group 4 = without diabetes or renal failure (n = 62). One-month mortality was assessed.

Continuous variables are presented as means ± SD and categorical variables as frequency (%). Comparisons were performed between the two study groups. Continuous variables were compared using unpaired Student's t tests. Categorical variables were compared using χ^2 statistics or Fischer's exact test, as appropriate. Multivariate logistic regression analysis was performed to determine the significance of variables related to 1-month and 6-month mortality among the two groups. The model included all clinical variables with $p < 0.1$ in the univariate analysis. Analyses were performed using Statisca software (StatSoft Inc., Tulsa, Okla., USA), and $p < 0.05$ was considered significant.

Results

Patients enrolled in the second period (2006–2011) were younger, less likely to have renal insufficiency, tended to have less strokes, and had higher mean hemoglobin values (table 1). There were no observed differences between the two time periods in the location of the infarct, left ventricular function, deployment of intra-aortic balloon pump, or use of glycoprotein IIb/IIIa inhibitors (tables 1, 2). Patients enrolled in the first period (2001–2005) were more likely to be treated with aspirin and β-blockers prior to their admission (table 2). Application of an intra-aortic balloon pump and frequency of use of glycoprotein IIb/IIIa inhibitors did not change over the decade (table 2). There was also no significant difference in the time frames from symptom onset to intervention (table 2). All patients had a door-to-balloon time <6 h. A door-to-balloon time <4 h did not improve the 1- and 6-month mortality when compared to a door-to-balloon time >4 h (table 3). Patients enrolled in the second period underwent more stenting procedures and more multiple vessel PCI

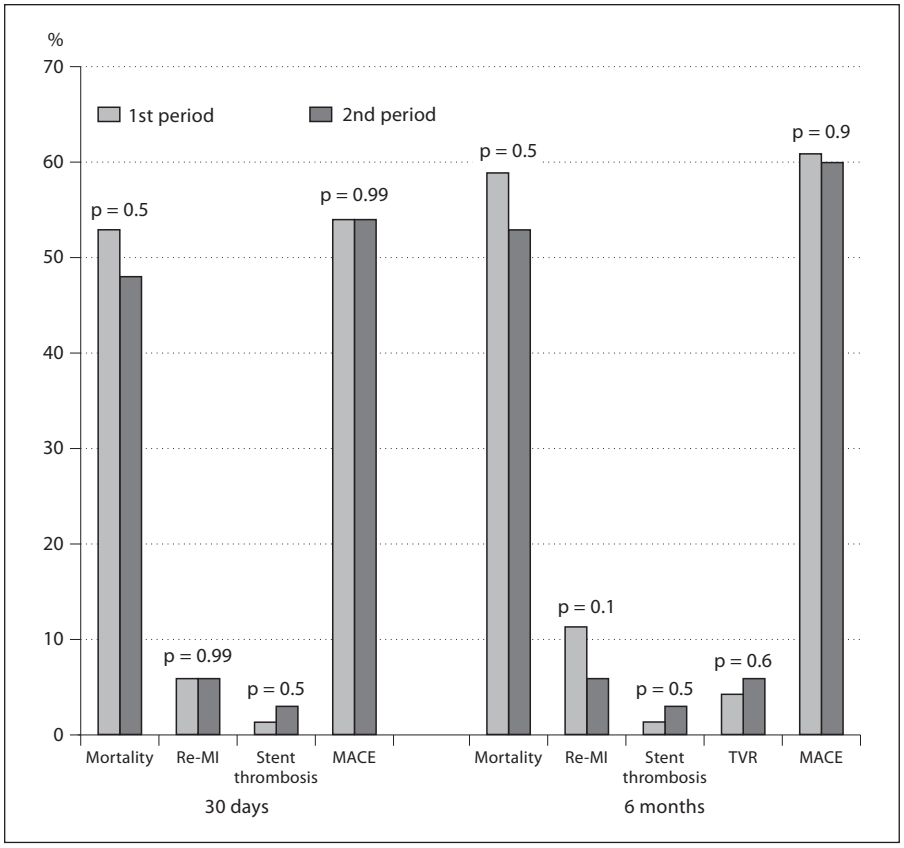

Fig. 1. Clinical outcomes. TVR = Target-vessel revascularization; MACE = major adverse cardiac events.

Table 4. Angiographic and procedural characteristics

Variables	1st period (n = 70)	2nd period (n = 100)	p value
Single vessel coronary intervention	23	34	0.4
Two/three vessel disease	77	81	0.7
Multivessel coronary intervention	57	75	0.01
Culprit artery			
Left main	3	8	0.6
LAD	47	51	0.6
Left circumflex	13	9	0.6
Right coronary	34	29	0.6
Saphenous vein graft	3	2	0.6
Stent deployment	89	97	0.06
Drug eluting stents/bare metal	2/60	8/89	0.2
Post-intervention TIMI flow 3	83	90	0.1
No reflow	17	9.2	0.3
Procedural success	83	90	0.1

Values are percentages unless otherwise indicated.

(table 4). The unadjusted outcomes of 1- and 6-month mortality, MI, stent thrombosis, and 1- and 6-month major adverse cardiac events did not differ significantly between the two time periods (fig. 1).

Only the variables that were statistically significant in the univariate analysis underwent adjustment applying multivariate analysis. The adjusted odds for 1-month mortality was 3.6 (CI: 1.4–9.4, p = 0.007) for diabetes, 1.8 (CI: 1.3–2.4, p = 0.009) for GFR <60 ml/min/m^2, 1.8 (CI: 1.3–2.6, p = 0.001) for ejection fraction <40%, and 0.5 (CI: 0.2–1.1, p = 0.08) for use of glycoprotein IIb/IIIa.

Diabetes and Renal Failure in Patients with STEMI and CS

Since diabetes and renal failure were factors that were strongly associated with statistically significant 1-month mortality, we compared patients with and without these factors. The 1-month mortality rate was 72% in patients with diabetes and renal failure, 28% in patients with diabetes without renal failure, 67% in patients without diabetes with renal failure, and 32% in patients without diabetes or renal failure (p = 0.02).

Discussion

Abundant research has been devoted to identify prognostic factors that affect outcome in patients presenting with STEMI and CS. In the last decade major advances have been made in both catheter-based reperfusion techniques and adjunctive pharmacological therapies, along with an increased effort to modify this population's poor prognosis. The main findings of our study are that the prognosis remains dismal despite these advances, with 1- and 6-month mortality ranging from approximately 50 to 55%, respectively.

A possible explanation for the poor prognosis in these patients is the extent of myocardium damage caused by the infarction, thrombotic load, and poor myocardial reserve, leading to inadequate compensation and pump function. Although not evident in our study, factors which may adversely affect these processes are inappropriate time frames from symptom onset to the achievement of adequate reperfusion and lack of optimal final results of the PCI (inadequate microvascular perfusion).

In the current study, the practice of using a intra-aortic balloon pump and glycoprotein IIb/IIIa inhibitors did not change over the decade. Prior reports have suggested that the high mortality rates of patients with CS may be partly related to underutilization of the intra-aortic balloon pump [6, 7]. This suggestion was strongly endorsed by the current European Society of Cardiology guidelines [8]. However, in a recently published meta-analysis of primary PCI studies, intra-aortic balloon pump therapy was associated with an absolute increase in 30-day mortality of 6% (95% CI: 3–10%, p = 0.0008) [9]. Nevertheless, these results should be interpreted cautiously as they may have been influenced by bias and confounders since the analysis was comprised of observational nonrandomized studies. In our center, intra-aortic balloon pumps were used in approximately 75% of cases of CS (table 2). Another surprising observation in our results is a tendency for better outcomes with the use of glycoprotein IIb/IIIa inhibitors (OR = 0.5, CI: 0.2–1.1, p = 0.08). There is a paucity of randomized controlled trials regarding the effects of glycoprotein IIb/IIIa inhibitors in patients with STEMI and CS. Most available data are derived from observational studies that display a beneficial effect of glycoprotein IIb/IIIa inhibitors in CS [10–12]. Recent studies had demonstrated the contrary effect [Widimsky P., et al: GP IIb/IIIa inhibitor of no benefit in AMI patients with cardiogenic shock. PRAGUE 7 study. ESC Congress, 2009; 13].

A principal finding of our analysis is that the presence of both diabetes mellitus and renal failure is associated with particularly high mortality. Their absence was associated with a much better outcome. Previous studies had reported risk factors associated with mortality risk in patients presenting with CS. Most included age and hemodynamic features [4, 5, 14]. Some included renal function and diabetes [15], but did not estimate the relative risk of both diabetes and renal failure. Consequently, the clinical implication is the added value for risk stratification by taking into consideration both diabetes and renal function.

The study has several limitations. First, the decade (2001–2011) was divided into two time periods arbitrarily; a division which was not based on a particular clinical turning point. Second, the study was based on a single-center registry with all the limitations inherent to a nonrandomized study. Third, the population studied was not homogenous; however, we did attempt to overcome this limitation by applying multivariate logistic regression analysis in order to minimize potential confounders. Fourth, there was a selection bias since patients had to have survived to be evaluated in the catheterization laboratory and to undergo PCI. Nevertheless, we do not believe there was significant referral bias since almost all hospitals in Israel have catheterization laboratories and therefore the distribution of STEMI patients relies primarily on the proximity of the patient's residence to the nearest hospital. Finally, this was a single-center study with a small sample size (as CS is fortunately not common), hence conclusions should be drawn cautiously.

Despite these limitations, our study, which is based on a large tertiary center experience, emphasizes that prognosis of patients presenting with STEMI and CS remains grave and has not changed significantly. The combination of both diabetes and renal failure is associated with particularly high mortality. Further research of catheter-based techniques and adjunctive pharmacological approaches, as well as ways to shorten treatment time and better risk-stratify the patients, may improve the poor outcomes of these patients.

Disclosure Statement

None declared.

References

1 Reynolds HR, Hochman JS: Cardiogenic shock: current concepts and improving outcomes. Circulation 2008;117:686.

2 Goldberg RJ, Spencer FA, Gore JM, Lessard D, Yarzebski J: Thirty year trends (1975–2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction: a population based perspective. Circulation 2009;119:1211–1219.

3 Hochman JS, Sleeper LA, Webb JG, Dzavik V, Buller CE, Aylward P, Col J, White HD: Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. SHOCK Investigators. JAMA 2006;295:2511–2515.

4 Hasdai D, Holmes DR, Califf RM, Thompson TD, Hochman JS, Pfisterer M, Topol EJ: Cardiogenic shock complicating acute myocardial infarction: predictors of death. GUSTO Investigators. Am Heart J 1999;138:21–23.

5 Katz JN, Stebbins AL, Alexander JH, Reynolds HR, Pieper KS, Ruzyllo W, Werdan K, Geppert A, Dzavik V, Van de Werf F, Hochman JS: Predictors of 30 day mortality in patients with refractory cardiogenic shock following acute myocardial infarction despite patent infarct artery. TRIUMPH Investigators. Am Heart J 2009;158:680–687.

6 Babaev A, Frederick PD, Pasta DJ, Every N, Sichrovsky T, Hochman JS: Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. JAMA 2005;294:448–454.

7 Goldberg RJ, Samad NA, Yarzebski J, Gurwitz J, Bigelow C, Gore JM: Temporal trends in cardiogenic shock complicating acute myocardial infarction. N Engl J Med 1999;340:1162–1168.

8 Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, Garg S, Huber K, James S, Knuuti J, Sendon JL, Marco J, Menicanti L, Ostojic M, Piepoli MF, Pirlet C, Pomar JL, Reinfart N, Ribichini FL, Schalij MJ, Sergeant P, Serruys PW, Silber S, Uva MS, Taggart D: Guidelines on myocardial revascularization. The task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardiothoracic Surgery (EACTS). Eur Heart J 2010;31:2501–2555.

9 Sjauw KD, Engstrom AE, Vis MM, van der Schaaf RJ, Baan J Jr, Koch KT, de Winter RJ, Piek JJ, Tijssen JGP, Henriques JPS: A systematic review and meta-analysis of intraaortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? Eur Heart J 2009;30:459–468.

10 Hasdai D, Harrington RA, Hochman JS, Califf RM, Battler A, Box JW, Simoons ML, Deckers J, Topol EJ, Holmes DR: Platelet glycoprotein IIb/IIIa blockade and outcome of cardiogenic shock complicating acute coronary syndrome without persistent ST-segment elevation. J Am Coll Cardiol 2000;36:685–692.

11 Assali AR, Iakobishvili Z, Zafrir N, Solodky A, Teplitsky I, Rechavia E, Butto N, Shor N, Hasdai D, Fuchs S, Battler A, Kornowsi R: Characteristics and clinical outcomes of patients with cardiogenic shock complicating acute myocardial infarction treated by emergent coronary angioplasty. Int J Cardiovas Interv 2005;7:193–198.

12 Bonello L, De Labriolle A, Roy P, Steinberg DH, Pinto Slottow TL, Xue Z, Smith K, Torguson R, Suddath WO, Satler LF, Kent KM, Pichard AD, Waksman R: Bivalirudin with provisional IIb/IIIa inhibitors in patients undergoing primary angioplasty in the setting of cardiogenic shock. Am J Cardiol 2008;102:287–291.

13 Ellis SG, Tendera M, de Belder MA, van Boven AJ, Widimsky P, Janssens L, Andersen HR, Betriu A, Savonitto S, Adamus J, Peruga JZ, Kosmider M, Katz O, Neunteufl T, Jorgova J, Dorobantu M, Grinfeld L, Armstrong P, Brodie BR, Herrmann HC, Montalescot G, Neumann FJ, Effron MB, Barnathan ES, Topol EJ, FINESSE Investigators: Facilitated PCI in patients with ST-elevation myocardial infarction. N Engl J Med 2008;358:2205–2217.

14 Jeger RV, Lowe AM, Buller CE, Pfisterer ME, Dzavik V, Webb JG, Hochman JS, Jorde UP, SHOCK Investigators: Hemodynamic parameters are prognostically important in cardiogenic shock but similar following early revascularization or initial medical stabilization: a report from the shock trial. Chest 2007;132:1794–1803.

15 Tedesco JV, Wright RS, Williams BA, Kopecky SL, Dvorak DL, Reeder GS, Miller WL, Mayo Coronary Care Unit Group: Effect of diabetes on the mortality risk of cardiogenic shock in a community-based population. Mayo Clin Proc 2003;78:561–566.