Predictors of Inhospital Mortality in Patients With Acute Myocardial Infarction and Cardiogenic Shock

Thesis submitted for partial fulfillment of Doctorate Degree in Critical Care Medicine

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2010

Acknowledgement

*For **ALLAH** the merciful, the compassionate, I need to express my gratitude for all the countless gifts I have been offered, including those who gave their hands to enable me to fulfill this work.*

*No words are sufficient to express my deep appreciation and profound gratitude to **Prof. Dr. Sherif Mokhtar**, Professor of Critical Care Medicine for his abundant encouragement and endless giving.*

*With my whole sincere, I want to thank **Prof. Dr. Hossam Mowafi**, Professor of Critical Care Medicine for his kind guidance and continuous support, not only in the medical field but also in our steps in life. He is the teacher and the father to us.*

*I with great honor express my sincere gratitude to **Prof. Dr. Hassan Khalid**, Professor of Critical Care Medicine and Chief of Critical Care Medicine Department, Cairo university .I truly thank him for his great encouragement and unlimited support.*

*I am truly grateful to **Prof. Dr. Waheed Radwan**, Professor of Critical Care Medicine and Chief of the third unit of Critical Care Medicine, the one who do his best to support our department.*

*I must thank **Prof. Dr. Allia Abd el-Fattah,** Professor of Critical Care Medicine for her great support and active participation. She kindly offered her remarkable experience during practicing this work and during revising every part of this thesis.*

*My true appreciation is due to **Dr. Ahmed Abd-Alaziz,** Professor of Critical Care Medicine for his meticulous supervision, generous help and valuable instructions.*

*Special thanks are due to **Dr. Amr El-Hadidy,** Professor of Critical Care Medicine for his sincere efforts, fruitful encouragement, authentic guidance and magnificent assistance.*

*I am deeply thankful to **Dr. Gert Richardt,** Professor of Cardiology, Bad Segeberg, Germany for his great help and outstanding support.*

*I am very thankful to **Dr. Ahmed Khattab,** Professor of Cardiology, Bern University, Switzerland for his great help, generous support and for his efforts in leading me in the way of interventional cardiology during his stay with us in Segeberger Kliniken.*

*I would like as well to thank my professors and colleagues in the critical care department, Cairo university hospitals. As well, the catheterization laboratory and the study nurse staff specially Frau **Schürmann-kuchenbrandt** in Heart-Center, Bad Segeberg for their efforts in this work.*

Finally I am so thankful and honored to belong to the critical care medicine department, the land of imagination, innovation and fruitful research.

Mohammed Abu-Elnour Saad

Abstract

Background: Acute myocardial infarction complicated by cardiogenic shock is associated with an exceedingly high mortality, even if patients are treated with early reperfusion therapy. The aim of this study was to evaluate predictors of in-hospital mortality of patients with cardiogenic shock treated with primary percutaneous coronary intervention (PCI).

Methods: Twenty-five patients with acute myocardial infarction complicated by cardiogenic shock within 24 h after symptom treated with percutaneous coronary intervention from October 2007 to April 2009 in the heart centre, Segeberger Kliniken, Germany were considered for this analysis.

Results: 17 patients survived till discharge (group S) and 8 patients suffered in-hospital mortality (group D). Total in-hospital mortality was 32%. In univariate analysis, plasma concentrations of LDH, level of CRP, Noradrenalin, Adrenalin, aldosteron and creatinin were significantly higher in group D than in group S. (LDH: 1178 ± 705 U/L vs 563±369 U/L, P = 0.012; CRP: 22.5±10.5 mg/dl vs 12.5±10.9 mg/dl, P = 0.027; Noradrenalin: 2693±2215 ng/l vs 789±659 ng/l, P = 0.002; Adrenalin: 231.6±173 ng/l vs 130±354 ng/l, P = 0.007; Aldosteron: 282±124 pg/ml vs 48±50 pg/ml, P $\leq$ 0.001; Creatinin: 2.43±1.0 mg/dl vs 1.23±0.86 mg/dl; P = 0.011). The occurrence of renal failure during in-hospital stay was associated with significantly increased mortality in our patient population (87% vs 12%, P = 0.001). Noradrenalin level > 1128 ng/l had a sensitivity of 87.5% and specificity of 88.2% and Adrenalin at level of > 96 ng/l had a sensitivity of 87.5% and specificity of 94.1% to predict mortality. However, Aldosteron had a specificity of 100% and sensitivity of 87.5% to predict mortality with a cut level > 228 ng/l. Creatinin level >1.5 mg/dl predicts mortality with a sensitivity of 87.5% and specificity of 88.2% while CRP >13.3 mg/dl had a sensitivity of 87.5% and specificity of 70.6%. The occurrence of renal failure during hospital stay was a significant predictor of mortality in the study group (OR 0.0190, 95% CI 0.0015-0.2471, P = 0.0025).

Conclusion: In patients with AMI complicated by CS successfully treated by primary PCI, total in-hospital mortality was 32%. From our data, it would appear that the acute-phase plasma concentration of catecholamine, aldosterone and CRP are reliable predictors of mortality in patients with AMI complicated by CS and successfully treated by primary PCI.

Noradrenalin level > 1128 ng/l, Adrenalin at level > 96 ng/l, Aldosteron level > 228 ng/l and CRP >13.3 mg/dl have high sensitivity and specificity to predict mortality. Creatinin level >1.5 mg/dl has as well high sensitivity and specificity to predict mortality. Logistic regression analysis showed that the occurrence of renal failure during hospital stay was a significant predictor of mortality in the study group. Identifying high risk of mortality patients would help us to modify our plane of management.

KEYWORDS: Cardiogenic shock; Acute myocardial infarction; Angioplasty; Stents, Peptides; Prognosis

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List of Abbreviations

ACC/AHA	:	American College of Cardiology/American Heart Association
ACS	:	Acute Coronary Syndrom
ADH	:	Antidiuretic Hormone
ALT	:	Alanine Aminotransferase
AMI	:	Acute Myocardial Infarction
ARDS	:	Adult Respiratory Distress Syndrome
ARQ	:	Aldosteron-Renin Quotient.
ASD	:	Atrial Septal Defect
AST	:	Aspartate Aminotransferase
ATP	:	Adinosin Triphosphate
BNP	:	Brain Natriuretic Peptide
BP	:	Blood Pressure
CABG	:	Coronary Artery Bypass Grafting
CAD	:	Coronary Artery Disease
CIN	:	Contrast Induced Nephropathy
CK	:	Creatin Phosphokinase
CK-MB	:	Creatin Phosphokinase MB
CRP	:	C-Reactive Protein
CS	:	Cardiogenic Shock
CVA	:	Cerebrovascular Accident
DIC	:	Disseminated Intravascular Coagulation
DM	:	Diabetes Mellitus
DPTI	:	Diastolic Pressure Time Index
EF	:	Ejection Fraction
EMF	:	Electromagnetic Force
ERV	:	Early Revascularisation
FDA	:	Food and Drug Administration
GISSI-I study	:	Gruppo Italiano per lo Studio della Streptochinasi nell' Infarto Miocardico study
GP	:	Glycoprotein

GUSTO-III trial	:	Global Use of Strategies to open occluded coronary arteries trial
HF	:	Heart Failure
IABP	:	Intra-Aortic Balloon Counterpulsation
IDE	:	Investigator Device Exemption
IRA	:	Infarct-Related Artery
LAD	:	Left Anterior Descending
LCX	:	Left Circumflex
LDH	:	Lactate Dehydrogenase
LV	:	Left Ventricle
LVADs	:	Left Ventricular Assist Devices
LVEF	:	Left Ventricular Ejection Fraction
MACE	:	Major Adverse Cardiac Events
MEXIS-Study	:	The Metoprolol and Xamoterol Infarction Study
MI	:	Myocardial Infarction
mRNA	:	messenger RNA
NSTEMI	:	Non-ST-Elevation Myocardial Infarction
Nt-pro-BNP	:	N-terminal pro-Brain Natriuretic Peptide
PCI	:	Percutaneous Coronary Intervention
Pro BNP	:	Pro-Beta Natriuretic Peptide
PTCA	:	Percutaneous Transluminal Coronary Angioplasty
PURSUIT-Trial	:	Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin Therapy trial
RCA	:	Right Coronary Artery
SHOCK-Registry	:	Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock Registry
SMASH Trial	:	Swiss Multicenter Trial of Angioplasty for Shock
STEMI	:	ST-Elevation Myocardial Infarction
TT	:	Thrombolytic Therapy

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Review of literature

Definitions:

Regarding Cardiac Output:

Cardiogenic shock has been defined as a state of tissue hypoxia caused by reduced systemic cardiac output in the presence of adequate intravascular volume *(1)*. This broad definition accounts for the great variability in the diagnosis of shock among different clinicians and investigators. In several series, cardiac index measurements of 2.2 L/min/m2 or less were considered supportive of the diagnosis *(2–9)*. Others have considered measurements of only 1.8 L/min/m2 or less to be indicative of cardiogenic shock *(10)*.

In addition to the boundaries of specific index measurements used, there may be variability in measuring methods. Currently, cardiac output is measured primarily using pulmonary artery catheters. This technique demands some expertise and carries certain, albeit minimal, risks *(11)*. It is, therefore, not universally used in patients with cardiogenic shock *(1)*. In cases where pulmonary artery catheterization is not used, cardiac output can only be estimated.

Regarding Tissue Hypoxia:

Because there are no widespread bedside assays for tissue hypoxia, surrogate clinical and laboratory indices of tissue function that may reflect

tissue hypoxia are sought. However, these indices may not be sensitive enough to identify accurately the gravity of tissue hypoxia, which may range from mild to severe. This problem is underscored among patients with antecedent cardiac disease that has already caused reduced cardiac output and tissue hypoperfusion. In these patients, any additional compromise of cardiac function may result in a disproportionate deterioration of the hemodynamic status resulting in shock, even if the reduction in systemic cardiac output was minimal.

Regarding Blood Pressure:

Although systemic hypotension is essential to the diagnosis of the syndrome, the severity of hypotension defining shock varies. Commonly, the cut point for the systolic blood pressure is less than 90 mm Hg *(2–9)* or less than 80 mm Hg *(10,12,13)*. Some also consider the diagnosis of cardiogenic shock in patients with blood pressure measurements greater than 90 mmHg if they require medications and support devices to maintain normal hemodynamic parameters. A patient may initially have signs associated with the clinical state of cardiogenic shock in the presence of systolic blood pressure measurements greater than 90 mm Hg *(9)*. Therefore, hypotension alone should not be the basis for the diagnosis in the absence of signs of peripheral hypoperfusion, nor should blood pressure measurements within the lower end of the normal range negate the diagnosis of shock in the appropriate clinical scenario. The method used to measure blood pressure also deserves consideration. Brachial cuff pressure measurements are often inaccurate in states of shock. Arterial blood pressure is more accurately monitored using intra-arterial cannulas.

Clinical Definition:

The previous section underscored the difficulty of diagnosing cardiogenic shock based on numerical values alone; thus, cardiogenic shock is primarily diagnosed based on clinical findings. This diagnosis can be supported by measured hemodynamic values. Patients with long-standing heart failure frequently fall into the range of values that are used to define shock numerically, although they are clearly not in shock clinically.

As early as 1912, Herrick described the clinical features of cardiogenic shock in patients with severe coronary artery disease: a weak, rapid pulse; feeble cardiac tones; pulmonary rales; dyspnea; and cyanosis *(14)*. These signs are not always present, however. In the full-blown state of shock, some of the characteristic signs of shock are unequivocally evident. In the earlier phases of shock or in less severe circumstances, these signs may be more subtle. For example, a reduction in urine output or slight confusion may represent a state preceding shock. The signs of shock may also be affected by chronic or current medical therapy. For example, a patient taking oral β-blockers on a chronic basis may not be tachycardic during shock, although the heart rate may be much more rapid than in the basal state. Therefore, these signs should be evaluated in the context of the specific clinical setting.

For cardiogenic shock to be diagnosed, any reduction in cardiac output must be accompanied by signs of hypoperfusion. The systemic signs of hypoperfusion that may be detected in cardiogenic shock include an altered mental state; cold, clammy skin; and oliguria.

Additional systemic features may reflect the severity of shock. For example, prominent jugular venous distention in a patient with shock may indicate severely increased preload. Peripheral cyanosis may reflect reduced cardiac output and severely increased peripheral vascular resistance. These signs, however, are usually not specific to the various etiologies. For example, increased jugular venous distention may occur as a result of severe left ventricular dysfunction as well as right ventricular dysfunction.

Pathophysiology Of Cardiogenic Shock:

In cardiogenic shock due to myocardial infarction, the initiating event occurs in the heart. In addition to a decline in systolic function, there is also a substantial decrease in left ventricular compliance, increasing the filling pressure at a given end-diastolic volume *(15–18)*. The increased left ventricular end-diastolic pressure causes pulmonary congestion, leading to hypoxemia and ischemia, which further reduces coronary perfusion pressure. Myocyte swelling occurs *(19)* as a consequence of an intracellular accumulation of sodium and calcium resulting from anaerobic glycolysis, further decreasing left ventricular compliance *(20)*. The further reduction in compliance and the myocyte swelling lead to an increase in ventricular wall stress, elevating myocardial oxygen requirements. As the myocardium becomes less compliant, the pumping capacity of the heart becomes less efficient, increasing the imbalance between myocardial oxygen requirements and supply.

Soon after the onset of cardiogenic shock, compensatory mechanisms are activated. A primary objective of the regulatory system of the circulation is to maintain arterial pressure *(21–24)* to preserve perfusion to the vital

organs such as the brain and the heart. This is accomplished by activation of neurohumoral systems, not dissimilar from the responses observed during hemorrhagic shock and exercise. In particular, there are withdrawal of the parasympathetic system and activation of the sympathetic, renin–angiotensin–aldosterone and vasopressin systems, culminating in arterial and venous vasoconstriction, salt and fluid retention, positive chronotropy, and inotropy. Although beneficial in hemorrhagic shock and severe exercise, these compensatory mechanisms may be detrimental in cardiogenic shock. For instance, venoconstriction and salt and fluid retention would increase the preload and arterial vasoconstriction would increase the afterload, thereby overloading the already failing ventricles.

Increased heart rate and myocardial contractility would increase the demands in the face of limited supply of oxygenated blood to at-risk myocardial regions (ischemic territories and the subendocardium). The skill of immediate management is therefore to curb the excesses of the compensatory mechanisms without negating some of their potential beneficial effects.

As the shock state persists, hypoperfusion of both the myocardium and peripheral tissues will induce anaerobic metabolism in these tissues and may result in lactic acidosis. An earlier study has shown that the serum lactate level is an important prognostic factor in cardiogenic shock *(25)*. Uncorrected, the accumulation of lactic acid may cause mitochondrial swelling and degeneration, inducing glycogen depletion, which, in turn, impair myocardial function and inhibit glycolysis, leading to irreversible ischemic damage *(26)*. The shock state in patients with an acute myocardial infarction leads to a vicious cycle that causes a downward spiral of worsening ischemia: As cardiac output falls, arterial pressure falls and coronary

perfusion is lowered, thus exacerbating the low output state. This eventually leads to further ischemia and extension of necrosis in the left ventricle. Several compensatory mechanisms occur during this chain of events that, if left untreated, lead to cardiac pump failure and, ultimately, death.

Energetics and Metabolism of Hypoperfused Myocardium:

As a result of circulatory shock and hypoperfusion of the myocardium, aerobic cellular metabolism cannot be maintained. The regeneration of high-energy phosphate compounds is impaired and intracellular high-energy reserves therefore decline. When oxygen delivery to the cardiomyocytes is inadequate, oxidative metabolism ceases, cellular citrate and ATP levels fall, and the cell switches to glycolytic anaerobic metabolism to produce a limited amount of ATP. The rate of glucose uptake is accelerated and available glycogen is rapidly depleted *(27, 28),* resulting in lactate production instead of lactate uptake by the myocardium *(29-32)*. The energy made available from anaerobic glycolysis is only about 6% of that obtainable from oxidative metabolism *(33)*. Anaerobic glycolysis is therefore a poor means of compensating for inadequate supply of oxygen *(29)* albeit it may be sufficient to maintain viability of the jeopardized myocytes.

When ischemia is severe, the products of glycolysis accumulate. Anerobic glycolysis yields lactic acid, which results in cellular acidosis that, in turn, inhibits glycolysis and ATP generation ceases. The relative lack of ATP means failure of energy-dependent ion transport pumps, impairing cation transport, with an efflux of potassium and intracellular accumulation of sodium and calcium *(34)*. This causes myocyte swelling and decreasing ventricular compliance. As the ischemia becomes severe, myocardial cell injury becomes irreversible with necrosis; mitochondrial swelling;