INTRODUCTION

Cardiogenic shock is the major cause of death among patients with acute myocardial infarction. Although there is some improvement of acute myocardial infarction patients outcome recently, the morbidity rate of cardiogenic shock remained constant for 20 years. The study has demonstrated that early revascularization strategy has lowered the mortality rate in 6 and 12 months and it is more superior than initial aggressive medical therapy. Although the early percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG) have some advantage, once shock is diagnosed, the mortality rate remains high, despite intervention, and half of the deaths occurred within the first 48 hours. This may be caused by irreversible extensive myocardial and vital organ damage. The new evidence suggests that a systemic inflammation response, complement activation, release of inflammatory cytokines, inducible nitric oxide synthase (iNOS) expression and inappropriate vasodilatation may play an important role, not only in the genesis of shock but also in outcome after-shock.

DEFINITION OF CARDIOGENIC SHOCK

Cardiogenic shock is disorder caused by decreased of systemic cardiac output in the presence of adequate intra-vascular volume, resulting in tissue hypoxia. Shock may be the result of severe left ventricle dysfunction, but it may also occur in some condition with adequate left ventricle function. Systemic hypotension usually used as basic of diagnosis. The cut off point for systolic blood pressure, is less than 90 mmHg. The decreased systolic blood pressure will increase cathecolamine level that will cause constriction of systemic artery and vein. Clinical manifestations that can be found are the signs of systemic hypoperfusion including an alter mental state, cold skin and oliguria.

Cardiogenic shock is defined as systolic blood pressure < 90 mmHg for ≥ 1 hour, that is:
- No response only by fluid loading
- Secondary to cardiac dysfunction or,
- Associated with signs of hypoperfusion or cardiac index < 2.2 l/minute per m2 and pulmonary capillary wedge pressure > 18 mmHg.

Also considered in this definition are:
- Patients with increased systolic blood pressure > 90 mmHg within 1 hour after inotropic agents administration, and
- Patient who died within 1 hour of hypotension, but met other criteria for cardiogenic shock.

EPIDEMIOLOGY

There is some variation in incidence of cardiogenic shock complicating acute coronary syndrome. This is related to the definition of cardiogenic shock and criteria of acute coronary syndrome that have been used in various studies.

Cardiogenic shock occurs in 2.9% patient with unstable angina pectoris and 2.1% patient with non ST elevation of Acute Myocardial Infarction (AMI). The range of time establishment to shock in these patient are 76 hours and 94 hours, that most frequently is after 48 hours. Shock is more frequently found as complication of AMI with ST elevation than other type of acute coronary syndrome. In the three large international series of patients receiving thrombolytic therapy for AMI, the occurrence of cardiogenic shock are ranged from 4.2% to 7.2% quoted from.
ETIOLOGY

The availability of echocardiography has reduced invasive hemodynamic procedures, and cardiac index of <2.2 l/minute/m² is significant in the process of diagnosis decision making. Echocardiography could identify the shock mechanism and patient, which is useful in surgery action in internal or external miocardial rupture.

Picard MH et al, reported that structural and functional abnormality of heart in wide range were found in the patient of acute cardiogenic shock. Both short term and long term mortality appear to be associated with initial left ventricular systolic function and mitral regurgitation as assessed by echocardiography, and the advantage of early revascularization is noted regardless of baseline left ventricular ejection fraction or mitral regurgitation.

Systemic inflammatory response syndrome was occurs in the setting of a number of non infectious condition, i.e. trauma, cardiopulmonary bypass, pancreatitis and burn injury. Patient with large miocardial infarction (MI) often have elevation of body temperature, white blood cell, complement, interleukin, C-reactive protein and other inflammatory markers. NO which is synthesized at low level by endothelial nitric oxide (eNOS) of endothelial and miocardial cell, is a cardioprotective molecule.

The study shows that there are cytokine release after miocardial infarction. In post MI patient, we suggests that there is activation of inflammatory cytokines which cause elevation level of iNOS, NO and peroxynitrate. All of them have multiple deleterious effects, i.e.:
- Direct inhibiton of miocardial contractility
- Suppresion of mychondria respiration in non-ischamic miocardium
- Effects on glucose metabolism
- Pro-inflammatory effect
- Reduce of cathcolamine responsitivity
- Induction of systemic vasodilatation

PATOPHYSIOLOGY

The old paradigm patophysiology of cardiogenic shock is depression of myocardial contractility, resulting in a viscous cycle of reduced cardiac output, low blood pressure, further coronary insufficiency, and further reduction of contractility and cardiac output. The classic paradigm predicts that compensatory systemic vasoconstriction with high systemic vascular resistance should occur in response to the depression cardiac output, quoted from

FIGURE 1. Apical Four-chamber Echo View with Relative Incidence of The Mechanisms Responsible for Cardiogenic Shock. LV = Left Ventricle, RV = Right Ventricle, VSD = Ventricular Septil Defect, MR = Mitral Regurgitation

PREDICTOR

Recognising patients at highest risk for the development of shock could facilitate the early transfer of high risk patients before the onset of hemodynamic instability.

A number of scoring system that using predictive model for the development of the shock help the decision making strategy. In the GUSTO I study, age, systolic blood pressure and heart beat and Killip class

FIGURE 2. Classic and New Shock Paradigm
were giving more than 85% of the predictive information. The same four variable are significant in GUSTO III study and they give > 95% of the predictive information. The major predictor of shock in PURSUIT population include age, systolic blood pressure, ST depression, heart beat, height, enrolling miocardial infaction and rales on physical examination.

**MANAGEMENT**

The left ventricular filling volume should be optimized, and in the absence of pulmonary congestion a saline fluid challenge of at least 250 ml should be administered over 10 minutes. Adequate oxygenation is important and intubation or ventilation should be administered immediately if there is abnormality of oxygen diffusion. The ongoing hypotension could directly trigger the respiratory muscle failure and administering mechanical ventilation can prevent this situation.

The report of dramatic reduction of cardiogenic shock mortality by implementing early revascularization was begin to emerge in the late 1980s. Randomised clinical trials, which examined superiority and general nature of early revascularization strategy has been done in USA that is SHOCK trial. In SHOCK study, it reported an increase in 30 days survival from 46.7% to 56% by early revascularization strategy, but the 9% absolute difference is not significant (p=0.11). On follow up, the difference of survival in early revascularization strategy became larger and significant after 6 months (36.9% vs. 49.7%, p=0.027) and one year (33.6% vs. 46.7%) for an absolute reduction of 13.2% (95% CI 2.2% to 24.1%, p < 0.03). There is 10 sub-group that were examined, including sex, age, history of MI, hypertension, diabetes and anterior myocardial infarction, early or late shock and references or direct hospitalization status. The advantage of early revascularization was demonstrative for all of sub group except in the elderly. The advantage of early revascularization is higher in the age of < 75 years.

Figure 3. Algorithm on Management of Cardiogenic Shock Following ST Elevation Myocardial Infarction

AS, aortic stenosis; CABG, coronary artery bypass graft; CAD, coronary artery disease; IABP, intra-aortic ballon pump; LAD, left anterior descending; LBBB, left bundle branch block; LV, left ventricle; MR, mitral regurgitation; MS, mitral stenosis; PTCA, percutaneous transluminal coronary angioptasty; RV, right ventricle; VSR, ventricular septal rupture.
MANAGEMENT STEPS OF CARDIOGENIC SHOCK

**Step 1. Immediate Resuscitation Measures**

The aim is to prevent organ destruction when the patient is delivered to get definitive therapy. Maintaining adequate mean arterial pressure in order to prevent neurologic and renal sequelae is vital. Dopamine or nor-adrenaline (nor-epinephrine), depends on the degree of hypotension, should be administered immediately in order to increase the mean arterial pressure and to maintain it at minimal required dose. We could combine dobutamine and dopamine at moderate dose or using single dobutamine without any combination in low output condition without frank hypotension.

*Intra-aortic balloon counterpulsation (IABP)* should be initiated before transportation if that facilities are available. We should monitor the blood gas analysis and oxygen saturation by giving *continuous positive airway pressure* or mechanical ventilation as needed. The ECG must be continuously monitored and defibrillator device, anti-arrythmia drugs such as amiodarone and lidocaine must be available. (33% of patient at early revascularization of SHOCK trial undergoing cardiopulmonary resuscitation, persistent ventricular tachycardia, or ventricular fibrillation before randomisation).

Initial fibrinolytic therapy must be started on patient with ST elevation if we should anticipate the angiography delayed more than 2 hours. The 35 days mortality for patients with systolic blood pressure < 100 mmHg who have thrombolytic in the FTT meta-analysis was 28.9% compared to 35.1% with placebo (95% CI 26 up to 98, p<0.001). Increasing the blood pressure through IABP in this condition could facilitate thrombolysis by increasing the coronary perfusion pressure.

In cardiogenic shock because of ST non-elevation myocardial infarction that waiting for catheterization, a glycoprotein IIb/IIIa inhibitor should be initiated.

**Step 2. Early Determination of Coronary Anatomy**

This is an important step in cardiogenic shock management, that derived from pre-dominant ischemic pump failure. Patient in Community Hospital must be immediately referred to the experienced tertiary medical services. Hypotension must be handled by IABP. Shock has high characteristic of vascular disease, *left main* disease, and functional reduction of left ventricle. The dysfunction level of ventricle and hemodynamic instability have correlation to coronary anatomy. A *circumflex* lesion or right coronary lesion rarely could have shock manifestation in no right ventricle infarct, left ventricle underfilling, bradiarrythmia, or myocardial infarction or prior cardiomyopathy.

**Step 3. Implementing Early Revascularization**

After determining the coronary anatomy, it should be followed rapidly by selection of the modality of revascularisation. There was no randomised trial which compare PCI with CABG in cardiogenic shock. The SHOCK Trial recommended emergency CABG in *left main* patient or 3 severe vascular disease. The mortality rate in hospital with CABG at SHOCK study and registry is equal to the outcome of PCI, eventhough there was much more severe coronary arterial disease and diabetes that is 2 times in the patient who undergone CABG.

Therapeutic recomendation of early reperfusion in cardiogenic shock because of complication of acute myocardium infarct is showed in figure 5.

**The Role of Intra Aortic Baloon Pump**

In keeping with last *guidelines* of ACC/AHA, we recommend early IABP placement in the cardiogenic shock patient who is candidate of agressive strategy.

The combination of reducing *afterload*, increasing diastolic pressure for coronary perfusion and increasing cardiac output have made IABP become an attractive choice of cardiogenic shock.

**FUTURE DIRECTION**

The role of *NG-monomethyl-L-arginine* (L-NMMA), a selective inhibitor of nitrate-oxide is quite promising. Cotter et al18, in their study of 11 patient with persistent shock despite vasopressors, IABP and...
The inhibition cascade of complement at the C5 level causes reduction of excess iNOS response, to ischemia and reperfusion and theoretically it could inhibit shock development. Initial result of COMplement inhibition in Myocardial infarction treated with Angioplasty (COMMA) study shows that C5 inhibition is related to shock rate and lower mortality rate in the high risk patient who had undergoing primary PCI despite an absence of effect on infarct size quoted from 2.

Recently, there is study design of SHOCK-2 (Should we inhibit nitric Oxide synthase in patients with Cardiogenic shock?) to examine NO inhibitor, L-NMMA, by good randomised trial of patient with persistent shock despite a patent infarct related artery (IRA) patient quoted from 2.

CONCLUSION

Early recognition and transfer of high risk patients and adoption of early revascularisation strategy many decrease the incidence of cardiogenic shock. Establishing the activity of shock and early definition of coronary anatomy in the setting of pump failure are crucial in management of cardiogenic shock.
REFERENCES


