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Invasive therapeutic strategies in acute heart failure complicating coronary artery disease: *effectiveness and boundaries*

Tudor C. POERNER, MD
From the Clinic for Internal Medicine I
of Friedrich Schiller University of Jena, Germany

ABSTRACT

Acute heart failure and especially its most severe form, the cardiogenic shock, remains the final common pathway to death in a substantial number of patients with acute myocardial infarction(MI). Several studies demonstrated that mechanical reperfusion of occluded coronary arteries by percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery improves survival in patients with acute MI and cardiogenic shock. There is strong evidence that intra-aortic balloon pump (IABP) support and ventricular assist devices can stabilize hemodynamics in these patients so that revascularization procedures can be safely performed. This article provides an overview of the therapeutic strategies for acute MI with cardiogenic shock, with focus on the role and particularities of different devices used as mechanic circulatory support in these patients.

Key words: cardiogenic shock, myocardial infarction, mechanical circulatory support

Abbreviations

ACC = American College of Cardiology
AHA = American Heart Association
AMI = acute myocardial infarction
CABG = coronary artery bypass graft
CS = cardiogenic shock
IABP = intraaortic counterpulsation balloon pump
LV = left ventricle
NSTEMI = non-ST-elevation myocardial infarction
PCI = percutaneous coronary intervention
STEMI = ST-elevation myocardial infarction
pCPS = percutaneous implantable cardiopulmonary support
RV = right ventricle
VA = left ventricular assist device

INTRODUCTION

Data from the Federal Statistics Center indicate that cardiovascular diseases represented – with 54.5% of the annual deaths in 2003 – the most frequent cause of mortality in Germany. While the total cardiovascular mortality is dominated by the irreversible end stage of chronic heart failure, 20% of deaths are caused by acute coronary syndromes. The acute heart failure and its most severe clinical form, the cardiogenic shock (CS) occurs especially as an early complication of acute myocardial infarction (AMI).

Although heart failure symptoms can show up during atherosclerotic coronary heart disease without being caused by a MI, for example due to cardiac arrhythmias, we will mainly discuss in this review the specific invasive therapeutic strategies in CS caused by AMI.

Address for correspondence:
Tudor C. Poerner, MD, Clinic for Internal Medicine I, Friedrich Schiller University, 101 Erlanger Street, D-07747, Jena, Germany
email address: tpoerner@googlemail.com

CARDIOGENIC SHOCK AFTER ACUTE MYOCARDIAL INFARCTION

Recent studies: advantages of early myocardial revascularization

Despite better therapeutic options in the acute phase of myocardial infarction, the incidence of cardiogenic shock remained at 7-10% almost the same during the last 25 years (1,2,3). Recent statistics show that the intra-hospital mortality has been reduced from 70% in the seventies to 50% in modern medical centers (4). Observational studies have underlined the prognostic improvement of patients with CS and mechanic reperfusion of the acute obstructed coronary artery through PCI or CABG. As a consequence to these positive conclusions, the multicenter randomized SHOCK study (*Should we emergently revascularize Occluded Coronaries for cardiogenic shock*) was initiated in the USA, to test the hypothesis whether urgent revascularization in CS caused by STEMI or recently installed LBBB could lower early mortality.

In this study, CS was defined as a combination of:

1. History of systemic low perfusion with systolic blood pressure < 90 mmHg more than 30 minutes, despite adequate fluid administration;
2. Cardiac index < 2.2 l/min/m^2 ;
3. Pulmonary capillary wedge pressure > 15 mm Hg.

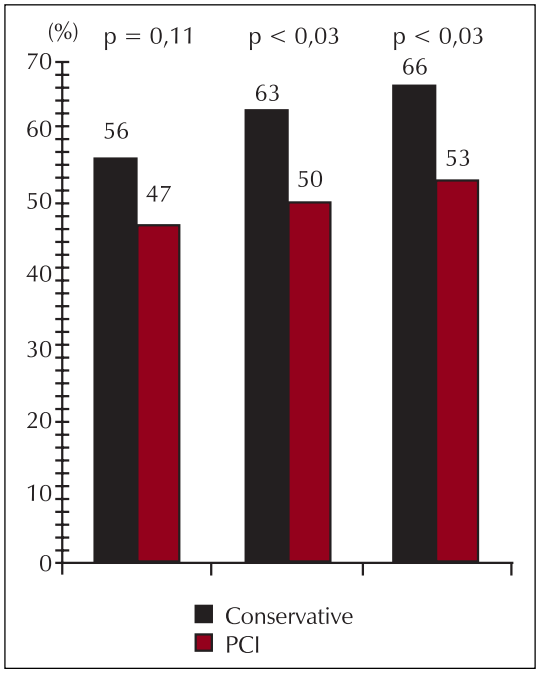

FIGURE 1. SHOCK Study: Mortality. Short- and long-term results of the SHOCK trial: significant survival benefit at 6- and 12-month follow-up for patients undergoing acute myocardial revascularization

The study population was randomized for acute revascularization (n = 152) or for initial medical therapy (n = 150). There was no statistically significant difference between the two subgroups with respect to the mortality rate at 30 days as primary end point, but the longtime mortality at 6 and 12 months was significantly lower in the group with acute myocardial revascularization **(Figure 1).** Therefore, these secondary endpoints showed that prompt myocardial revascularization represents the optimal therapeutic strategy in CS caused by AMI (5,6,7,8). Except that, the study has concluded that the survival rate at 12 months was higher in different subgroups: diabetes mellitus, women, AMI in young people. After the results of the SHOCK study, ACC and AHA guidelines stated that early revascularization in AMI and CS represent a class IA indication in patients < 75 years and, respectively a class IIA indication in patients > 75 years without prognostic limiting co-morbidity **(Table 1).**

In the TRACE European registry, carried out prospectively during 1990-1992, the incidence of CS in AMI was similar (6.7%) (9). Of the 440 included patients with CS, 59% developed the symptoms of CS within 48 hours, while 30% presented the symptoms only at day 5 after the AMI. The starting point of the shock symptoms showed a significant correlation with mortality: patients with early shock onset within the first two days had a mortality rate at 30 days of 45%, while patients with late onset of CS symptoms had a much higher lethality, reaching 80%. The European register has found a globally worse longtime prognosis in CS with conservative treatment, comparative to the randomized studies GUSTO-I and SHOCK.

Prognostic evaluation of CS

The GUSTO-I trial (*Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries*) has shown that the age of the patient, previous myocardial infarction and peripheral signs of low perfusion – such as diminished sensitive capacity, vasoconstriction and oliguria – are predictors for mortality in CS (10,11,12,13).

Class	Level of evidence	Therapy	Patients
I A	*A*	*PCI*	Age < 75 years
			STEMI or new LBBB
			CS developed < 36 hours after beginning of AMI
			Possibility of PCI < 18 hours after beginning of CS
			Absence of any formal contraindications
II A	*B*	*PCI*	Age > 75 years
			STEMI or new LBBB
			CS developed < 36 hours after beginning of AMI
			Possibility of PCI < 18 hours after beginning of CS
			Absence of any formal contraindications
			Good biological status

TABLE 1. AHA/ACC guidelines for primary PCI in cardiogenic shock

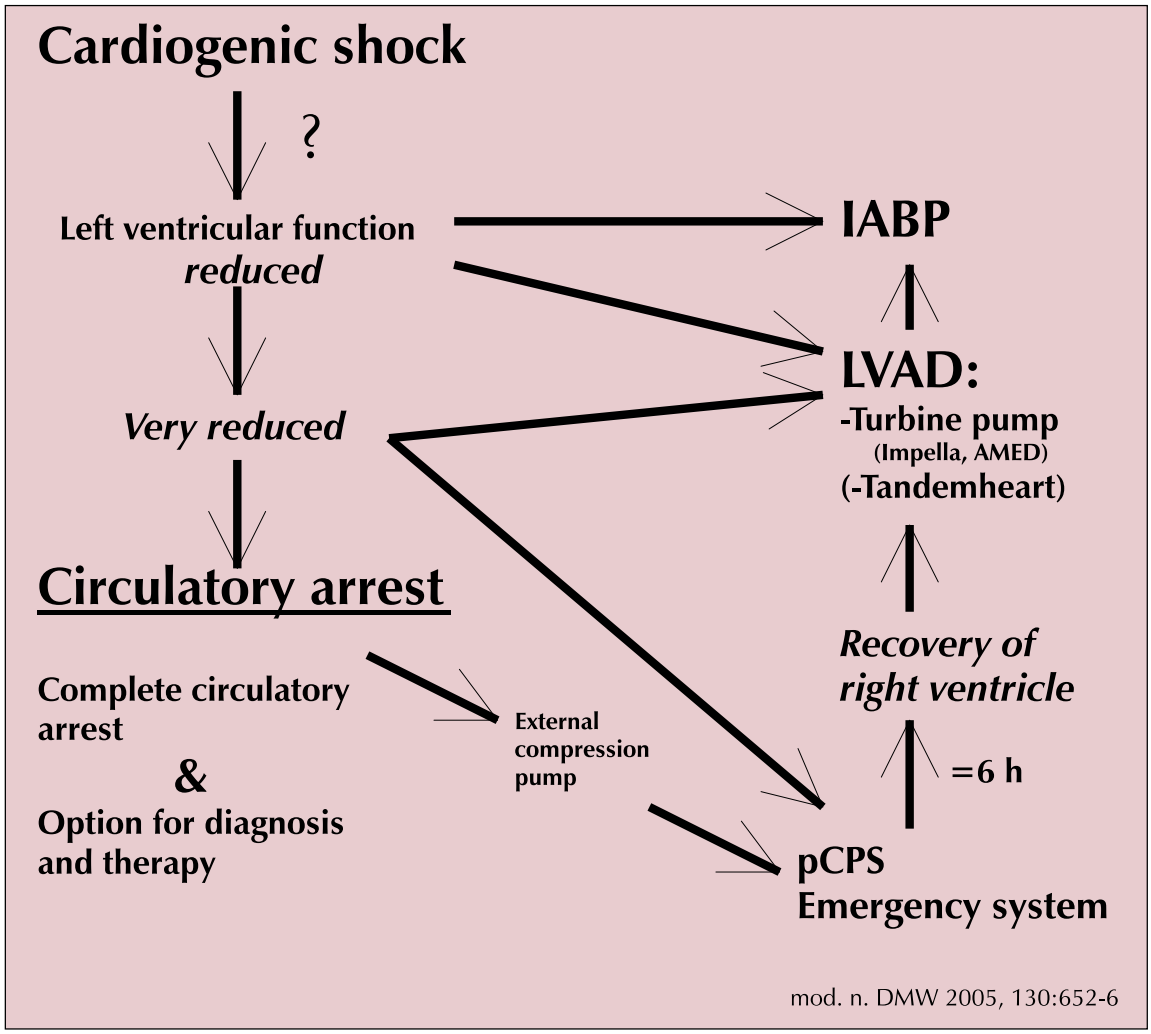

FIGURE 2. Flow-chart for acute management of cardiogenic shock. (IABP = intra-aortic counterpulsation balloon pump, LVAD = left ventricular assist device, pCPS = percutaneous cardio-pulmonary support)

Another conclusion of the SHOCK and GUSTO-I studies was that mortality in patients with CS due to STEMI or NSTEMI is not significantly different (14,15,16). Because the clinical signs characterize a rather late stage of CS, complex investigations are necessary for an early prognostic evaluation. The left ventricular ejection fraction (LVEF) and the existence of a significant mitral regurgitation are independent predictors for a high mortality. A LVEF of 28%

was associated with a survival rate of 24% at 12 months, compared to 56% for a LVEF > 28%. A moderate or severe mitral regurgitation indicates a survival rate at 1 year of only 31% vs. 58% in patients without mitral regurgitation (12).

Fibrinolysis

The thrombolytic therapy was successfully used in patients with acute STEMI, but its efficiency in patients with AMI complicated with CS was disappointing. The GISSI-2 study reported a 30-day mortality of 69.9% in the streptokinase group, compared to 70.1% in patients with placebo (17). The reason is probably a low reperfusion rate of the infarction-related coronary artery. The combination of fibrinolysis and intraaortic counterpulsation balloon has shown favorable effects on early mortality (18). Therefore, fibrinolysis remains indicated only in patients with CS and STEMI, in whom mechanical revascularization within 2 hours is impossible.

INTERVENTIONAL THERAPY

Particularities of coronary angioplasty in patients with cardiogenic shock

The particularity of CS compared to other etiologies of acute organ hypoperfusion is the presence of large areas of vital, but not functional myocardium (19). Myocardial stunning can be defined as postischemic dysfunction despite coronary reflow, having theoretically the capacity of "restitutio ad integrum". Essential is the rapid coronary reperfusion and adequate systemic pressure conditions with sufficient hemoglobin level. Particularly, this potentially reversible myocardial dysfunction represents the reason for a complete revascularization, including coronary lesions not associated to the AMI. While PCI in coronary arteries not associated with MI is not indicated in hemodynamic stable patients, it is of great help in CS, especially in stenotic arteries which irrigate a large myocardial area. This procedure implies a rapid transport of the patients in specialized centers, which are not very frequent. For example in the USA, the National Registry of Myocardial Infarction showed that only 60% of patients reach the hospital in due time for PCI or CABG (20). Data from the CRUSADE study indicate that only 49% of patients with NSTEMI were revascularized within the first 24 hours (21). We must underline the clearly favorable influence of intracoronary stents and antiplatelet therapy with glycoprotein IIB-IIIA receptor antagonists (22).

Concerning the bypass operation consequently to CS, we should consider review data from the SHOCK study. The mortality rate in patients with CS, who underwent CABG within 18 hours, was low (39.6%). Patients with acute heart failure had a lower mortality (27.9%) after CABG compared to 45,5% in the PCI group. Based on these data, ACC/AHA guidelines recommend urgent CABG in patients with CS and severe stenosis of the left main coronary artery or severe trivascular coronary artery disease, without infarction of the right ventricle and prognostic significant co-morbidity, like renal insufficiency or pulmonary disease (23). There was no difference between PCI with complete revascularization and CABG (GUSTO-I study: 29% mortality after CABG vs. 29% after PCI).

Intraaortic balloon pump (IABP)

Sanborn and al. (18) have monitorized 1,190 patients with STEMI, who underwent the following therapy: no fibrinolysis and no IABP (33%), IABP without fibrinolysis (33%), only fibrinolysis (15%) and fibrinolysis and IABP (19%). They showed that patients with CS with fibrinolytic therapy had similar mortality rates to patients without fibrinolysis (54% vs. 64%) and those patients who received additionally IABP had a significantly lower mortality (50% vs. 72%, $p<0.0001$) compared to patients without IABP. Also, a significant difference of intrahospital mortality in the 4 studied groups was demonstrated. Patients who received fibrinolysis and IABP had a significantly lower mortality (47%) compared to the other groups (IABP only 52%, fibrinolysis only 63%, no fibrinolysis, no IABP 77%, $p < 0.0001$). Revascularization therapies lowered consistently the mortality (39% with PCI or CABG vs. 78% without revascularization, $p= 0.0001$). The use of IABP diminishes the afterload of the left ventricle and augments the diastolic blood pressure and therefore the stroke volume and the coronary flow increase (24,25). IABP doesn't represent a definitive therapy, but creates a time gap for continuing the diagnostic procedures and initiation of the revascularization therapy. We already mentioned that IABP is very useful in

combination with fibrinolysis in the initial stabilization and transfer of the patient to a PCI center. Complications were mentioned in less than 30% of the cases, and are mainly local (at the puncture site). In very rare cases infections or hemolysis may occur. The time point of IABP introduction is essential: an early introduction could lead to a rapid hemodynamic improvement, while the late introduction doesn't bring any clinical advantages, mainly when hypoxic organ damage has already occurred (26).

Ventricular assist devices (VAD)

VAD are mechanical systems which can be implanted percutaneously or through sternotomy. They substitute totally or partially the systolic ventricular function and were initially used as bridge therapy to cardiac transplantation (27,28), or as weaning from extracorporeal circulation after cardiac surgery (29,30). The accelerated technical development offered percutaneous VAD (pVAD) to interventional cardiologists, which can be implanted in minutes through femoural approach. Besides CS in AMI, VAD are used in PCI with high risk as transitory therapy, when the target coronary artery irrigates more than one half of the vital myocardium and the LV function is severely depressed (31-34).

In a single-center study in patients with primary PCI in AMI, Thiele and al. have compared the efficiency of IABP and pVAD (35). 41 patients with CS after AMI were randomized to receive IABP (n=20) or pVAD (n=21) (Tandem Heart, Cardiac Assist, Pittsburgh, USA). The complications of the procedure occurred more frequent in the pVAD group (19 bleedings and 7 cases of ischemia of the lower limb vs. 8 bleedings in the IABP group). The 30 day mortality was almost equal in the two groups (45% in IABP vs. 43% in pVAD). Recent guidelines recommend therefore IABP or VAD as useful procedure for hemodynamic stabilization in patients who need revascularization therapy for CS. The specific indications for pVAD in primary PCI for AMI with CS are: severely reduced systolic function and an irrigation area of the target vessel > 50%, electric instability and unstable hemodynamics under IABP. The axial turbines are mostly used for percutaneous implantation (Hemopump®, Impella®, AMED®) because they can reduce the afterload of the left ventricle independent of arrhythmias.

In case of cardio-circulatory arrest in AMI with running reanimation procedures, the single available option is the percutaneous implantable cardio-pulmonary bypass (pCPS=percutaneous cardiopulmonary support, Medtronic®), which bridges completely the heart and the lung function. pCPS can be implanted without fluoroscopy, but needs time for priming. The new generation of such devices (for example Lifebridge™) is smaller and more easy to handle, the sheath dimension is 18 F. Evidently, the implantation time of these devices is limited (pCPS: hours, pVAD: days) and serves as time gap for diagnosis and revascularization therapy ("bridge to recovery"). If during this time the LV function doesn't recover, surgical implantable intrathoracic VAD or the total artificial heart (TAH) can be used, with the latter supporting also the right ventricle and therefore offering a longer bridge to cardiac transplantation (36-39).

Mechanical complications of myocardial infarction

The feared mechanical complications of AMI are: right ventricle infarction, acute mitral regurgitation, rupture of the interventricular septum or the free wall of the left ventricle, which are associated with a high mortality.

The right ventricle infarction complicates in about 30% of patients an AMI of the posterior wall and leads in 10 % of these cases to hemodynamic instability. The diagnostic can be established electrocardiographically through ST segment elevation in the right precordial derivations and echocardiographically in typical cases. The function of the right ventricle can be recovered through intense administration of fluids after a successful revascularization therapy (40). Percutaneous implantable mechanical circulatory support devices are not used yet for this indication.

Acute mitral regurgitation appears typically 2 to 7 days after myocardial infarction with an incidence of 1%, mainly affecting the posterior medial papillary muscle. The lowering of afterload is the primary therapy goal, which can be achieved by vasodilators or IABP. A meta-analysis of the SHOCK study showed that even a moderate mitral regurgitation complicating AMI determines a worse prognosis and is an independent predictor for mortality at 12 months (11). In hemodynamic unstable patients, surgical correction of significant mitral regurgitation becomes mandatory.

The postischemic ventricular septal defect occurs in about 0.3% of cases mainly in the first week post infarction. The clinical signs are represented by acute heart failure with renewed CS and a typical heart murmur. The diagnosis is confirmed by a difference between the blood oxygen saturation in the right atrium and the right ventricle. IABP and pharmacological circulatory support with catecholamine must be urgently started. There is no consensus yet concerning the optimal time for surgery, but most of the authors indicate the first 48 hours for surgery. Thus, the historical early mortality of these patients could be decreased from over 90% to 46-75%. Further prognostic improvement can be achieved through interventional catheter procedures (closing of the ischemic septal defect with a specially conceived occluder). In a monocentric study, Holzer and al. monitored 18 patients with implantation of such an occluder (Amplatzer PIMVSD®, AGA Corp.), whose 30 days mortality decreased to 28%. This procedure can be also used as bridge to surgery.

The rupture of the free wall of the ventricle is lethal in most cases due to acute heart tamponade (42).

CONCLUSION

The cardiogenic shock after acute myocardial infarction has an unfavorable natural course, which can be influenced only by prompt invasive management. The most important goal is the complete myocardial revascularization within shortest time, which can be presently accomplished only in experienced centers. In case of STEMI, if the transport of the patient to such a center takes longer than 2 hours and the onset of the infarction is estimated to lie in the past 3 hours, fibrinolysis and the implantation of IABP are indicated. The results of acute interventions are optimized by stent implantation and by the use of glycoprotein IIbIIIa inhibitors. There are no safety concerns regarding the implantation of drug-eluting stents, but no clinical advantages in cases of CS were noticed. If hemodynamics cannot be improved with IABP, catecholamine and adequate infusion of fluids and electrolytes, a mechanical circulatory support should be considered. An orienting algorithm is presented in **Figure 2**. The implantation of such devices takes place in the cardiac catheterism laboratory (axial venticulo-aortic turbines type Impella Recover LP® or the TandemHeart® pVAD as left atrium-femoural artery system). The decision to install a pVAD must be made before PCI, if the target vessel irrigates more than 50% of the estimated vital myocardium and the left ventricular systolic function is poor. Every hemodynamic worsening should raise the suspicion of mechanical complications post infarction. If cardio-circulatory arrest or uncontrolled arrhythmias occurred, the cardiopulmonary bypass system is indicated, as ultimate solution offering a time bridge for diagnosis including the neurological evaluation of the patient and further therapy.

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