International Journal of Cardiology 168 (2013) 3758–3763

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

# Impact of intra-aortic balloon pump support initiated before versus after primary percutaneous coronary intervention in patients with cardiogenic shock from acute myocardial infarction ☆

Jin M. Cheng *, Maarten A.H. van Leeuwen, Sanneke P.M. de Boer, Marisa C.G. Tjong Joe Wai, Corstiaan A. den Uil, Lucia S.D. Jewbali, Robert-Jan van Geuns, Isabella Kardys, Ron T. van Domburg, Eric Boersma, Felix Zijlstra, K. Martijn Akkerhuis

*Erasmus University Medical Center, Thoraxcenter, Department of Cardiology, Rotterdam, The Netherlands*

ARTICLE INFO

*Article history:*
Received 15 August 2012
Received in revised form 24 April 2013
Accepted 15 June 2013
Available online 3 July 2013

*Keywords:*
Cardiogenic shock
ST-segment elevation myocardial infarction
Intra-aortic balloon pump
Primary percutaneous coronary intervention
Prognosis

ABSTRACT

*Background:* Little evidence is available on the optimal sequence of intra-aortic balloon pump (IABP) support initiation and primary percutaneous coronary intervention (PCI) in patients who present with cardiogenic shock from ST-elevation myocardial infarction (STEMI). The aim of this study was to evaluate the order of IABP insertion and primary PCI and its association with infarct size and mortality.
*Methods:* A series of 173 consecutive patients admitted with cardiogenic shock from STEMI and treated with primary PCI and IABP between 2000 and 2009 were included. The order of IABP insertion and primary PCI was left at the discretion of the interventional cardiologist.
*Results:* All baseline characteristics were similar in patients who first received IABP ($n = 87$) and patients who received IABP directly after PCI ($n = 86$). In these two groups, cumulative 30-day mortality was 44% and 37% respectively ($p = 0.39$). Median peak serum creatine kinase (CK) concentrations were 5692 U/l and 4034 U/l respectively ($p = 0.048$). In multivariable analysis, IABP insertion before PCI was independently associated with higher CK levels ($p = 0.046$). In patients who survived 30 days, IABP insertion before PCI was not associated with late mortality evaluated at five years of follow-up (HR1.5, 95% CI 0.7–3.3; $p = 0.34$).
*Conclusions:* Early IABP insertion before primary PCI might be associated with higher peak CK levels, indicating a larger infarct size. A possible explanation may be the increased reperfusion delay. Our study suggests that early reperfusion could have priority over routine early IABP insertion in STEMI patients with cardiogenic shock. Randomized studies are needed to determine the optimal timing of IABP insertion relative to primary PCI.



## 1. Introduction

Cardiogenic shock complicating ST-segment elevation myocardial infarction (STEMI) remains the leading cause of death in this patient population, despite improvements in therapy over the last decade including primary PCI [1,2]. The in-hospital mortality rate has been reported to be as high as 50% [1,2]. Intra-aortic balloon pump (IABP) counterpulsation is the most widely used method of mechanical support in cardiogenic shock [3–5]. Although the efficacy of IABP adjunctive to primary percutaneous coronary intervention (PCI) has been questioned, IABP remains the method of first choice for mechanical assistance in patients with cardiogenic shock who do not respond adequately to standard pharmacological treatment [6,7].

With regard to the sequence of both treatments, current guidelines recommend insertion of an IABP before primary PCI [3,4]. However, there is little evidence supporting this recommendation [8]. Hypothetically, IABP counterpulsation may provide additional hemodynamic support during the procedure when it is inserted prior to percutaneous coronary revascularization. On the other hand, each additional minute in delay to the actual reperfusion of the occluded coronary artery, including the time needed for IABP insertion, may result in decreased myocardial salvage from primary PCI, and thus increased myocardial infarct size [9,10]. Moreover, early revascularization is the only treatment proven to decrease mortality rates in patients with acute myocardial infarction complicated by cardiogenic shock [11,12]. Therefore, the aim of this study was to evaluate the order of IABP insertion and primary PCI and its association with infarct size, 30-day and late mortality in a series of 173 STEMI patients presenting with cardiogenic shock in our hospital.

☆ The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author at: Erasmus Medical Center, Department of Cardiology, Room Ba-559, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands. Tel.: +31 10 703 3004; fax: +31 10 704 4759.
*E-mail address:* j.cheng@erasmusmc.nl (J.M. Cheng).

0167-5273/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ijcard.2013.06.009

## 2. Methods

### 2.1. Study population

Between January 2000 and December 2009, all consecutive STEMI patients presenting with cardiogenic shock who were treated with IABP and primary PCI at the Erasmus MC in Rotterdam, the Netherlands, were included. In order to evaluate the effects associated with the relative timing of IABP insertion and primary PCI, we only included patients who presented with cardiogenic shock at time of admission to our hospital and excluded those who developed cardiogenic shock during primary PCI or during hospital stay.

Our center is a tertiary referral center for primary PCI, mechanical support for cardiogenic shock (e.g. IABP counterpulsation) and heart transplantation. During the inclusion period, about 450 STEMI patients were admitted to our center annually. STEMI was defined as acute myocardial infarction with clinical symptoms of ischemia, persistent (>20 min) ST-segment elevation in at least 2 contiguous precordial leads or at least 2 adjacent limb leads by ECG, and a diagnostic rise in cardiac markers during the hospitalization period [4]. Cardiogenic shock was defined as systolic blood pressure < 90 mm Hg due to cardiac insufficiency with clinical signs of hypoperfusion (cold extremities, oliguria, altered mental state etc.), not responsive to fluid resuscitation [4]. In our center, IABP counterpulsation was the method of first choice for mechanical assistance in the patients with cardiogenic shock who did not adequately respond to standard pharmacologic treatment including inotropics. In our hospital, consensus was reached that IABP insertion should be withheld only when insertion was technically not feasible (e.g. because of severe atherosclerotic peripheral artery disease, aortic disease or aortic insufficiency), as well as in patients judged to have a definite fatal short-term prognosis because of concomitant disease. Ethics committee approval or informed consent was not required for this study according to Dutch Ethical Review Board regulations.

### 2.2. Patient management

Patient management was in accordance with the STEMI guidelines of the European Society of Cardiology (ESC) [3,4,13]. As an exception, consensus was reached in our hospital that there was no clear evidence on the optimal timing of IABP insertion relative to primary PCI. Therefore, the order of IABP insertion and primary PCI was left at the discretion of the interventional cardiologist. When the operator decided to insert the IABP first, this was done in the catheterization laboratory before angiography and PCI. When the operator decided to perform primary PCI first, the IABP was inserted directly following the PCI procedure in the catheterization laboratory. In all study patients, Arrow (Arrow Corp., Reading, PA, USA) 8 French IABP catheters were used.

Inotropic agents used in our hospital were catecholamines (dobutamine, dopamine, and/or norepinephrine) and phosphodiesterase inhibitors (enoximone). During the study period, primary PCI was the standard treatment of STEMI. Patients received an aspirin and clopidogrel (300 to 600 mg) loading dose prior to primary PCI. Primary PCI was performed using bare metal stents from January 2000 until April 2002, sirolimus eluting stents from April 2002 until March 2003, paclitaxel eluting stents from March 2003 until March 2007 and everolimus eluting stents from March 2007 to December 2009. After the procedure, all patients were advised to remain on aspirin (>80 mg/day) indefinitely. Patients were treated with clopidogrel (75 mg/day) for at least one month for those treated with bare metal stents, at least 3 months for patients treated with sirolimus eluting stents, at least 6 months for patients treated with paclitaxel eluting stents and at least 12 months for patients treated with everolimus eluting stents. Use of periprocedural glycoprotein IIb/IIIa antagonists was left at the discretion of the interventional cardiologist.

### 2.3. Study endpoints

Primary study endpoints were enzymatic infarct size measured by peak serum creatine kinase (CK) concentration and 30-day all-cause mortality. Serum CK was measured every 6 h after hospital admission until a clear peak of CK concentration had been reached. Other serum biomarkers of myocardial injury were not routinely measured during the whole inclusion period. Secondary study endpoints included peak serum CK-MB activity level, CK-MB mass concentration, troponin-T concentration and residual changes on the first 12-lead electrocardiogram (ECG) that was required after PCI (<24 h). Serum CK-MB activity levels were available in patients admitted before April 2006 (n =99), while CK-MB mass measurements were available in patients admitted after April 2006 (n = 74). Serum troponin-T concentrations were available in patients admitted after January 2001 (n = 160). Infarct related pathologic Q-wave formation and cumulative residual ST-deviation in all ECG leads were analyzed according to the universal ESC/American College of Cardiology (ACC)/American Heart Association (AHA) definitions [14]. Furthermore, we performed a landmark analysis in patients who survived the first 30 days after primary PCI (30-day survivors) to evaluate late all-cause mortality at 5 years of follow-up.

### 2.4. Data collection and follow-up

Baseline, clinical and procedural characteristics were prospectively entered into digital patient records. These data were retrospectively retrieved and recorded in a dedicated database. The reported blood pressures were measured at arrival in the catheterization laboratory, thus before IABP insertion and primary PCI. For patients admitted from January 2000 until June 2005, the order of IABP insertion and primary PCI was acquired retrospectively from patient medical records and primary PCI reports. After July 2005, the order of IABP insertion and primary PCI was entered prospectively in a dedicated database. In March 2012, vital status of all patients was acquired from municipal civil registries.

### 2.5. Statistical analysis

All data were analyzed with SPSS software (SPSS 17.0, SPSS Inc., Chicago, IL, USA). All statistical tests were two-tailed and p-values < 0.05 were considered statistically significant. Normally distributed continuous variables were compared by Student *t* test and are presented as mean ± standard deviation. Non-parametric continuous variables were compared by Mann–Whitney U test and are presented as median and interquartile range (IQR). Categorical variables were compared by chi-square test or Fisher's exact test, when appropriate, and are presented in percentages. Univariable and multivariable linear regression analyses were performed to evaluate the relationship between timing of IABP insertion with peak CK concentration. In multivariable analyses, the covariates age, sex, history of myocardial infarction, out-of-hospital cardiac arrest, mechanical ventilation, systolic blood pressure, location of myocardial infarction and left main culprit lesion were a priori chosen for inclusion in the model, since these clinical characteristics are well known to be associated with infarct size and/or clinical outcome. The final results are presented as unadjusted and adjusted beta (β) ± standard error (SE).

Patients lost to follow-up were considered at risk until the date of last contact, at which time-point they were censored. Cumulative mortality was estimated according to the Kaplan–Meier method. Kaplan–Meier survival curves were compared by log-rank test. Univariable and multivariable logistic regression analyses were performed to evaluate the relationship between timing of IABP insertion with 30-day mortality. In patients who survived the first 30 days, multivariate Cox proportional hazards regression analyses were performed to evaluate the relationship between timing of IABP and long-term all-cause mortality. The final results are presented as unadjusted and adjusted odds ratios (OR), and respectively as unadjusted and adjusted hazard ratios (HR), both with the associated 95% confidence intervals (95% CI).

## 3. Results

### 3.1. Patient characteristics

During the inclusion period, 4352 STEMI patients underwent primary PCI in our center (Fig. 1). In our center, the median symptom-to-balloon time for STEMI patients in that time period was 166 min [IQR 110–275]. A total of 291 patients were treated with IABP counterpulsation because of cardiogenic shock. After exclusion of patients who did not present with cardiogenic shock at the time of admission to our hospital, 173 patients were included in this study. The baseline and procedural characteristics of patients who received

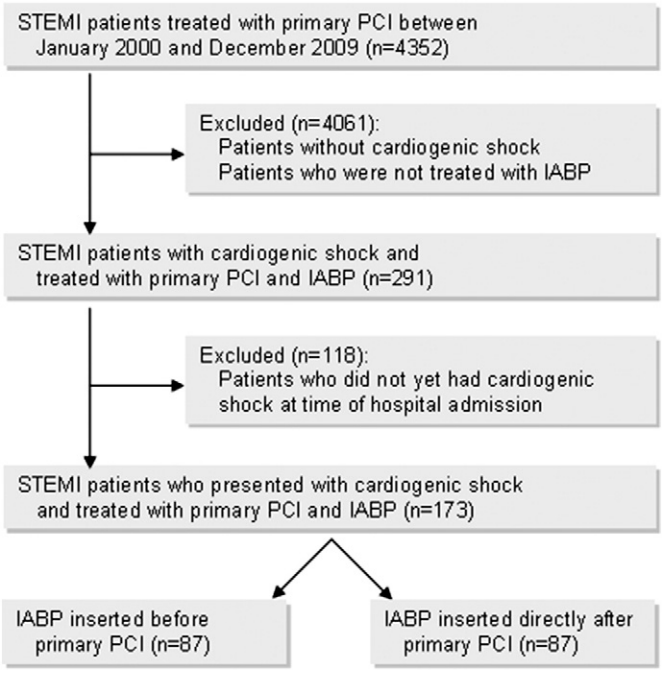


**Fig. 1.** Patient inclusion.