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Original Article

The Impact of Intra-Aortic Balloon Pump in Elderly with ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Cardiovascular Intervention: Benefits and Risks?

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SUMMARY

Objectives: To assess the outcomes of elderly (age ≥ 65 years) patients supported by intra-aortic balloon pumping (IABP) for ST-segment elevation myocardial infarction (STEMI) complicated by cardiogenic shock (CS).
Background: The effectiveness of IABP in patients with acute myocardial infarction complicated by CS is unclear, as few IABP trials have included elderly STEMI patients. Therefore, studies investigating the use of IABP for CS during primary percutaneous coronary intervention (PCI) and associated outcomes in patients aged ≥ 65 years with STEMI are needed.
Methods: We studied 169 STEMI patients with CS who received primary PCI between January 2012 and December 2015. Based on age and the presence of IABP, the patients were classified into three groups; those ≥ 65 years with or without IABP, and those < 65 years with IABP. The mortality rates and risk factors for mortality were analyzed.
Results: IABP supported 102 of the patients (60.4%) regardless of age. Of these patients, 49% were ≥ 65 years old, and they were more likely to have left main disease (26% vs. 6.9%, $p = 0.037$) and decompensated heart failure. There was no significant difference in in-hospital mortality between the two elderly groups (40% vs. 20.69%, $p = 0.97$). The in-hospital mortality rate in the elderly group was insignificantly higher than that in the younger group (40% vs. 26.92%, $p = 0.39$).
Conclusions: Regardless of age, the use of IABP did not affect the in-hospital mortality rate in the patients with STEMI and CS undergoing primary PCI. Systolic blood pressure and door to first balloon inflation time were independent predictors of in-hospital mortality.

1. Introduction

Cardiovascular heart disease represents the leading cause of death in both males and females older than 65 years of age.[1] As the elderly population increases globally, more elderly patients are presenting with acute coronary syndrome (ACS).[2] ACS is the cause of cardiogenic shock (CS) in 7% to 10% of patients, with short- to mid-term mortality rates approaching 40% and 60%.[3–6]

Several studies have shown that mortality after ST-segment elevation myocardial infarction (STEMI) increases exponentially with age.[7–11] How to optimize outcomes for older adults with CS is a challenging task. Intra-aortic balloon pumping (IABP) has been the most widely used mechanical circulatory support (MCS) device for ≈ five decades.[4] IABP can temporarily improve cardiovascular hemodynamics in the recovery phase of acute myocardial infarction (AMI) after reperfusion.[12] Experimental and registry trials have suggested that diastolic blood pressure can be augmented by IABP, thereby improving coronary perfusion with a small but significant effect on cardiac output.[13,14]

However, the IABP-SHOCK II trial did not show any beneficial effects on 30-day and 1-year mortality between patients who received IABP compared to controls.[15,16] In addition, both European and US guidelines have downgraded their recommendations on IABP for CS.[17–20]

There are currently no published data on the benefits and risks of the use of IABP in elderly Chinese patients with STEMI complicated by CS. Therefore, the aim of this study was to investigate this important issue and provide new insights into the management of this elderly population.

2. Materials and methods

2.1. Patient population

At our hospital, all patients with STEMI are considered eligible for primary PCI. Between January 2012 and December 2015, 777 consecutive patients of all ages presenting with STEMI of < 12 hours duration underwent primary PCI. Patients were excluded if they were resuscitated due to cardiac arrest for more than 30 minutes, had a mechanical cause of CS (e.g., ventricular septal defect or papillary muscle rupture), had a massive pulmonary embolism, or

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were in shock as a result of a condition other than AMI. Of these 777 patients, 169 were complicated by CS. We excluded 38 patients aged < 65 years who did not receive IABP support, and the remaining patients were then categorized into three groups. Of the 79 patients aged ≥ 65 years old; 29 treated with conventional therapy were classified as group B, and 50 with IABP support as group A. The remaining 52 patients aged < 65 years old supported by IABP were categorized as the younger group (group C). Figure 1 shows the detailed schematic presentation of the enrollment process of the patients. The relationships between in-hospital prognosis and IABP were then compared between group A and B and group A and C, as shown in Figure 2.

2.2. Study definitions

STEMI was diagnosed according to: (1) a history of typical chest discomfort consistent with myocardial ischemia; (2) an electrocardiogram demonstrating ST-segment elevation ≥ 1 mm or new Q waves (or both) in 2 consecutive leads; (3) new onset of complete left bundle branch block; and (4) elevation of serum creatine kinase (CK) level and its MB fraction (CK-MB) to at least twice the upper limit of the normal range.

A patient was categorized as having CS[15] if he or she had a systolic blood pressure (SBP) of less than 90 mm Hg for more than 30 minutes or required the use of catecholamines to maintain a systolic pressure above 90 mm Hg, had peripheral circulatory disturbances such as cold extremities, change in mental state, or persistent oliguria.

2.3. Procedures and protocol

This observational study was approved by the Institutional Review Committee on Human Research at our institution.

At our hospital, a transradial artery approach is used for STEMI patients receiving primary PCI unless Allen's test is positive bilaterally or transradial vascular access fails. The timing of IABP insertion (before PCI, during the procedure of PCI, or following PCI) was at the physician's discretion. A multiple regression analysis was performed with IABP placement as the dependent variable due to the study's retrospective nature. As covariates, we included clinical and angiographic variables that could potentially influence the operator's decision as follows: brain natriuretic peptide (BNP) and CK level, the presence of pulmonary edema, the number of diseased vessels, and left ventricular ejection fraction less than 35% (measured using Simpson's biplane method).

The counterpulsation pump rate was 1:1 immediately after the placement of the IABP. The IABP pump rate was gradually reduced to 4:1 and removed when the patient's hemodynamic status had stabilized, defined as SBP higher than 90 mm Hg for more than 30 minutes without the need for catecholamines.[15]

All patients who were scheduled for primary PCI received dual antiplatelet therapy (aspirin with clopidogrel or ticagrelor) in the emergency room. Other commonly prescribed medications included low molecular weight heparin, statins, and diuretics. Guideline-recommended drugs such as angiotensin converting enzyme inhibitors and β-blockers were often deferred because of CS.

2.4. Data collection

Detailed in-hospital and follow-up data were collected as follow: 1) patients' baseline clinical characteristics, including the presence or absence of pre-existing chronic diseases; 2) laboratory data including peak serum CK, CK-MB, and BNP values; 3) imaging studies such as chest X-ray and transthoracic echocardiography; 4) coronary angiographic findings (number of diseased vessels) and door to first balloon inflation time (D2B); and 5) in-hospital mortality, defined as death at any time after the start of IABP. Repeat angioplasty findings were also recorded, which was performed for the following reasons: recurrent ischemia defined as angina of at least 20 minutes' duration with new electrocardiogram changes followed by significant (> 50%) residual stenosis in the infarct-related artery. In addition, severe or life-threatening bleeding and moderate bleeding events during the hospital stay, as assessed according to the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) criteria were also recorded.[21]

2.5. Statistical analysis

Continuous and categorical variables were presented as means (± standard deviations) or numbers (percentages), respectively. Comparisons were performed using the unpaired Student t-test or Wilcoxon rank-sum test for continuous variables and the chi-square or Fisher's exact test for categorical variables as appropriate. The baseline characteristics of the patients in different groups were compared. Multivariate logistic regression analysis was used to deter-

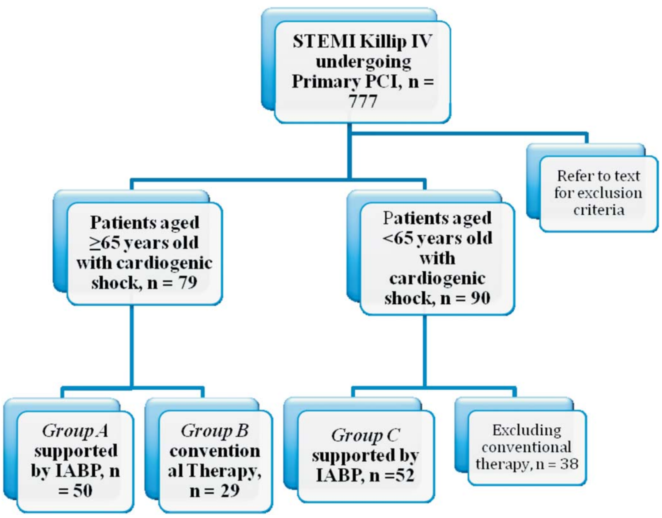

Figure 1. Detailed schematic presentation of the enrollment process.

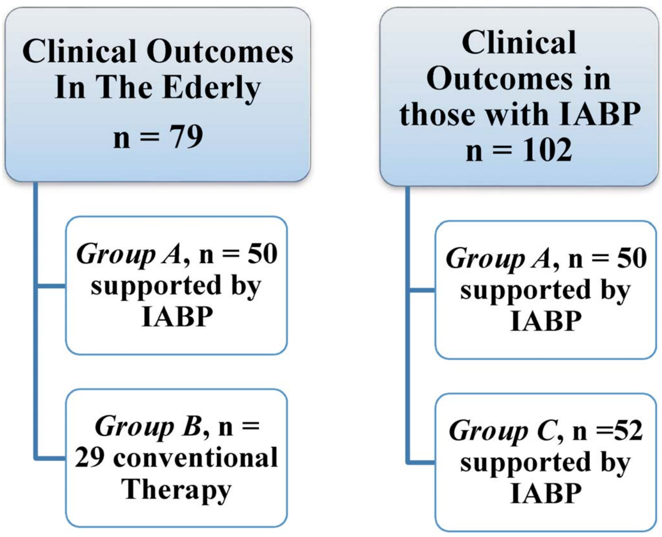

Figure 2. The in-hospital prognosis between the three groups.

mine the effect of age or IABP on the risk of in-hospital death among the patients. Significance was set at $p < 0.05$ (2-tailed). SAS statistical software (version 9.2 for Windows; SAS Institute, Cary, NC, USA) was used for all analyses.

3. Results

3.1. Characteristics of the elderly groups

Between January 2012 and December 2015, a total of 777 patients with STEMI of < 12 hours duration underwent primary PCI at our hospital. Of these patients, 169 (21.8%) who were complicated by CS were enrolled and retrospectively analyzed. Among the patients with CS, 102 (60.4%) were supported by IABP, including 50 who were ≥ 65 years of age (group A) and 52 who were < 65 years of age (group C). The mean age of group A was 75.4 ± 7.3 years, and the mean age of the elderly without IABP support (group B) was 77.8 ± 9.4 years. The study population was predominantly male (> 70%). The baseline characteristics were well balanced between the two elderly groups, as shown in Table 1.

3.2. Hemodynamic status of the elderly groups

The mean SBP was < 90 mmHg in all three groups before receiving IABP. Group A had a higher incidence of decompensated heart failure than group B, including (1) lower SBP with compensatory tachycardia, (2) higher BNP (880.1 ± 139.8 vs. 399.8 ± 74.4, *p* = 0.0034), (3) pulmonary edema (40% vs. 13.79%, *p* = 0.014), and (4) lower left ventricular ejection fraction (46.7 ± 11.5 vs. 53.9 ± 11.4, *p* = 0.0091) as estimated by transthoracic echocardiography (Table 1). Multiple regression analysis showed that elevated BNP level was the only variable independently associated with IABP placement (odds ratio [OR] 1.00, 95% confidence interval [CI] 1.00–1.01; *p* = 0.04). This finding suggested that IABP support played a key role in maintaining hemodynamic stability to achieve final procedural success.

Table 1
Baseline characteristics of the three groups who underwent PCI for STEMI complicated by CS.

Characteristic	Group B (N = 29)	Group A (N = 50)	*p*-value[#]	Group C (N = 52)	*p*-value[##]
Age, years old	77.8 ± 9.4	75.4 ± 7.3	0.22	53.5 ± 8.0	< 0.0001*
Gender, number (%)			0.72		0.024*
Male	21 (72)	38 (76)		48 (92)	
Female	8 (28)	12 (24)		4 (8)	
Cardiovascular risk factors, number (%)					
Current smoker	11 (38)	20 (40)	0.86	35 (67)	0.005*
Hypertension	19 (66)	35 (70)	0.68	29 (56)	0.14
Hyperlipidemia	5 (17)	9 (18)	0.93	16 (31)	0.13
Diabetes mellitus	13 (45)	20 (40)	0.68	21 (40)	0.97
Prior CAD, number (%)	4 (14)	12 (24)	0.28	12 (23)	0.91
Prior stroke, number (%)	5 (17)	4 (8)	0.21	4 (8)	0.95
Prior myocardial infarction, number (%)	3 (10)	9 (18)	0.36	1 (2)	0.006*
Prior PCI, number (%)	2 (7)	9 (18)	0.15	7 (14)	0.53
CKD/ESRD, number (%)	3 (10)	7 (14)	0.55	7 (14)	1.00
Systolic blood pressure, mmHg	88.2 ± 8.6	83.5 ± 10.4	0.04*	85.3 ± 14.9	0.48
Heart rate, beats per minute	74.5 ± 14.5	89 ± 25.3	0.001*	87.7 ± 25.3	0.80
Af, number (%)	3 (10)	4 (8)	0.72	12 (23)	0.04*
BNP, pg/mL	399.8 ± 74.4	880.1 ± 139.8	0.0034*	601.5 ± 663.8	0.10
Peak CK, IU/L	2460.1 ± 2166.7	4147.6 ± 3572.3	0.01*	6956.96 ± 6888.8	0.011*
Peak CK-MB, ng/mL	180 ± 140.8	199.2 ± 114.8	0.51	118.87 ± 105.3	0.005*
LVEF, %	53.9 ± 11.4	46.7 ± 11.5	0.0091*	44.8 ± 13.4	0.43
Pulmonary edema, number (%)	4 (14)	20 (40)	0.01*	19 (37)	0.99
Vessel disease			0.75		0.26
SVD, number (%)	6 (21)	14 (28)		9 (17)	
DVD, number (%)	9 (31)	13 (26)		11 (21)	
TVD, number (%)	14 (48)	23 (46)		32 (62)	
LMD, number (%)	2 (7)	13 (26)	0.037*	8 (15)	0.19
Achieve D2B in 90 minutes	16 (55)	14 (28)	0.017*	20 (38)	0.26
D2B, minutes	134.22 ± 196.2	114.82 ± 55.4	0.62	106.19 ± 72.3	0.55
$P2Y_{12}$-receptor antagonist, number (%)			0.72		0.23
Ticagrelor	8 (28)	12 (24)		18 (35)	
Clopidogrel	21 (72)	38 (76)		34 (65)	
Timing of IABP, number (%)			NA		0.98
Before PCI	NA	24 (48)	NA	23 (44)	
During PCI	NA	26 (52)	NA	26 (50)	
Following PCI	NA	3 (6)	NA	3 (6)	
IABP duration (days)	NA	3.66 ± 3.2	NA	3.9 ± 2.3	0.66
Hospitalization (days)	8.41 ± 7.3	16.56 ± 22.6	0.022*	16.42 ± 20.9	0.98

Data are n (%) or mean ± SD unless otherwise stated.
* *p*-value < 0.05; [#] *p*-value between group A and group B; [##] *p*-value between group A and group C.
NA – not applicable; Af – pre-existing atrial fibrillation; BNP – brain natriuretic peptide; CAD – coronary artery disease; CKD – chronic kidney disease; CK – creatine kinase; CK-MB – creatine kinase-MB isoenzyme; Clopidogrel – 300 mg loading dose followed by a maintenance dose of 75 mg once daily; D2B – door to first balloon inflation time; DVD – double vessel disease; ESRD – end-stage renal disease; LMD – left main disease; LVEF – left ventricle ejection fraction; PCI – percutaneous coronary intervention; STEMI – ST-segment elevation myocardial infarction; SVD – single vessel disease; Ticagrelor – 180 mg loading dose followed by a maintenance dose of 90 mg twice daily; TVD – triple vessel disease.

3.3. Angiographic findings and procedural results of the elderly group

All patients underwent revascularization. The incidences of angiographic findings of obstructive coronary artery disease, multiple vessel disease was similar between group A and B. However, group A had a higher incidence of left main disease than group B (26% vs. 6.9%, $p = 0.037$). The percentage of elderly patients achieving D2B time < 90 minutes was notably lower in group A than in group B. The patients in both group A and B received a similar proportion of $P2Y_{12}$ receptor antagonists (Table 1). With the successful placement of IABP, the mean duration of IABP support was 3.66 ± 3.2 days in group A.

3.4. Comparison between the elderly (group A) and younger (group C) patients with IABP

The mean age of group C was 53.50 ± 7.99 years. Group A were more likely to have previous MI, while there were more current smokers and patients with pre-existing atrial fibrillation in group C. However, multivariate regression analysis showed that pre-existing atrial fibrillation, was not associated with in-hospital mortality (OR 0.079, 95% CI 0.005–1.189; $p = 0.067$). The severity of coronary artery disease, hemodynamic status, and the proportion of patients achieving a D2B time within 90 minutes were not significantly different between the two age groups.

3.5. Clinical outcomes of the three groups

Tables 2 and 3 show the in-hospital outcomes of all three groups. The in-hospital mortality rate of group B was 20.69% compared to 40% in group A ($p = 0\ .97$). Upon discharge, the mortality rate of those who received IABP was similar (40% in group A and 26.92% in group C; $p = 0.39$). Group A had fewer repeat angioplasties, implying less recurrent ischemia compared to group B (0% vs. 21%, $p = 0.003$). Although there was a trend toward a higher rate of hemorrhagic complications, the overall bleeding complication rate was low (4–6%) in the patients who received IABP.

3.6. Predictors of outcome

Multivariate analysis revealed that SBP on presentation (OR 0.88, 95% CI 0.80 to 0.97; $p = 0.008$) and D2B time (OR 1.02, 95% CI 1.01 to 1.04; $p = 0.003$) were the two significant predictors of in-hospital mortality (Table 4).

4. Discussion

CS remains a "devastating complication" for elderly patients with STEMI, and is associated with a high risk of mortality due to hemodynamic instability after subsequent left ventricular dysfunction. Such patients have been excluded from clinical trials because of their higher risk profiles, and hence the role of MCS after CS in elderly patients is unclear.

In our study, the in-hospital mortality rate showed a higher trend in the elderly patients supported by IABP (group A), however subsequent statistical analysis revealed no significant difference in mortality between these patients and those who received medical therapy (group B). In addition, age contributed very little to in-hospital mortality when we compared the elderly and younger patients who received IABP.

The effects of IABP counterpulsation in patients with AMI complicated by CS on cardiac output, left ventricular stroke work index, and systemic vascular resistance are modest and may not reduce mortality.[14,22] Thiele et al.[16] reported that the in-hospital mortality rate of patients with AMI complicated by CS may be associated with hemodynamic deterioration, the occurrence of multi-organ dysfunction, and the development of systemic inflammatory response syndrome.[23,24] The GUSTO-I trial was conducted in 1997 and included 68 CS of 310 (22%) patients. The results showed no significant difference in 30-day mortality rate between the early IABP and no IABP groups.[25] The IABP-SHOCK II trial, which randomized 600 patients with CS after AMI and early revascularization to IABP or conventional treatment, also found no difference in 30-day mortality between the treatment groups.[16] In addition, analyzing data from 17 studies, Romeo et al. reported no overall differences in short- or long-term mortality in patients receiving IABP therapy.[26]

However, Ohman et al. reported that the use of IABP during emergency PCI significantly improved in-hospital infarct-related artery patency and reduced recurrent ischemic events, thereby reducing the need for repeat interventions.[27] Our results are consistent with those of the previous studies, and suggest that the use of IABP may be a plausible method to increase the sustained patency

Table 2
Secondary and safety outcomes of the three groups.

Outcomes	Group B (N = 29)	Group A (N = 50)	*p* value
Bleeding, number (%)	0 (0)	2 (4)	0.28
Repeat angioplasty, number (%)	6 (21)	0	0.003*
	Group A (N = 50)	Group C (N = 52)	
Bleeding, number (%)	2 (4)	3 (6)	0.68
Repeat angioplasty, number (%)	0	3 (6)	0.12

Bleeding during the hospital stay was assessed according to the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) criteria.[21]
Analyzed using the chi-square or Fisher's exact test; * p value < 0.05.

Table 4
Multivariate logistic regression for mortality in group A and B.

Variables	Odds ratio	95% confidence interval	*p* value
Gender	0.25	0.96–1.20	0.09
Door-to-balloon time (minutes)	1.02	1.01–1.04	0.003*
Systolic blood pressure (mm Hg)	0.88	0.80–0.97	0.008*
Hypertension	1.44	0.31–6.57	0.64
Diabetes	1.72	0.31–9.72	0.54
Coronary artery disease	1.01	0.16–6.50	0.99
IABP use or not	2.88	0.57–14.63	0.20

IABP – intra-aortic balloon pump.
* p value < 0.05.

Table 3
Primary outcomes: in-hospital mortality between the three study groups.

Outcomes	Group B (N = 29)	Group A (N = 50)	Odds ratio (95% CI)	*p* value
Primary endpoint: In-hospital all-cause mortality, number (%)	6 (20.69)	20 (40)	0.92 (0.02–48.03)	0.97
	Group A (N = 50)	Group C (N = 52)		
Primary endpoint: In-hospital all-cause mortality, number (%)	20 (40)	14 (26.92)	2.01 (0.41–10.0)	0.39

Analyzed using multivariate logistic regression.

rate in elderly patients undergoing primary PCI.

In the elderly patients who received IABP in this study, the D2B time was independently associated with a significantly reduced risk of in-hospital all-cause mortality compared to the elderly patients who were treated conventionally. Previous observational studies have shown a strong association between promptly undergoing a primary PCI, assessed in terms of the D2B time, and reduced mortality.[28,29]

A recent analysis of nearly 8,000 patients older than 65 years presenting with AMI undergoing early revascularization confirmed a low in-hospital mortality rate. In addition, several studies have reported a positive correlation between shorter D2B time and lower risk of mortality.[30,31] Data from the KAMIR (Korea Acute Myocardial Infarction Registry)–National Institutes of Health (NIH) also demonstrated consistent survival benefits with a shorter D2B time, even in less than 60 minutes.[32]

The utilization and timing of IABP in our study were at the physician's discretion. The elderly patients selected for IABP support tended to be at a higher risk regarding left main disease and they had more pronounced signs of heart failure. When most physicians encounter an adult aged over 65 years, they assume that early MCS support will be more hazardous due to geriatric syndromes. Our findings support that interventional cardiologists should proceed with early MCS support in their STEMI patients, regardless of age. It is possible that quality of life, rather than survival, may be the outcome of interest in older adults. Further studies are necessary to answer this question.

4.1. Limitations

Several limitations of the present study require consideration. This research was a nonrandomized, observational study with a relatively small number of patients, an issue common to all CS studies. This may explain why some characteristics identified to be significant in previous studies were insignificant in the present study. A larger sample size would improve the likelihood of determining whether there were substantial differences in outcomes between the prespecified subgroups. Second, we did not provide additional hemodynamic parameters or laboratory inflammatory markers other than blood pressure, heart rate, BNP, and peak CK level, which are often available in other trials. Finally, there was no definitive indication regarding conventional therapy or IABP as the first choice for these patients. Thus the outcomes could have been influenced by physician selection bias.

5. Conclusions

We conducted a retrospective trial of IABP in elderly patients with STEMI complicated by CS for whom early revascularization was planned. The use of IABP, as compared with conventional therapy, did not reduce in-hospital mortality, although it may have prevented repeat angioplasty in the elderly patients. The most important factor determining survival after MI was the immediate provision of coronary blood flow. Despite these findings, physicians should not deny treatment to elderly individuals based on their age; instead, they should have a thorough discussion detailing the potential pros and cons with the patient and their family.

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