Efficacy and timing of intra-aortic counterpulsation in patients with ST-elevation myocardial infarction complicated by cardiogenic shock

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Published online: 31 July 2012

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Abstract

Background Guidelines strongly recommend additional intra-aortic balloon pump (IABP) therapy in STEMI patients with cardiogenic shock (CS) treated by primary percutaneous coronary intervention (PCI). However, there is no randomised evidence suggesting survival benefit of IABP treatment in CS. It is suggested that timing of initiation of IABP therapy could be of great importance. Therefore, we compared mortality rates of IABP therapy versus no IABP therapy in the setting of STEMI complicated by CS. In addition, we investigated the effect of initiation of IABP therapy on mortality.

Methods From a cohort of 292 STEMI patients with CS treated by primary PCI, 199 patients received IABP therapy (IABP group) and 93 patients received no support (no IABP group). The IABP group was divided into two subgroups based on timing of initiation of support, i.e. ‘IABP pre PCI’ ($n=59$) and ‘IABP post PCI’ ($n=140$). Outcomes were assessed by propensity stratification and multivariate logistic regression.

Results All-cause 30-day mortality for the IABP versus the no IABP group was 47 % vs. 28 %, respectively, in univariate analysis resulting in an odds ratio (OR) of 1.67 (95%CI, 1.16 to 2.39). However, analyses adjusting outcomes by propensity stratification and logistic regression, respectively, neutralised this OR. In the IABP pre-PCI group vs. the post-PCI group 30-day mortality was 64 % vs. 40 %, resulting in an OR of 1.56 (95 % CI, 1.18 to 2.08). However, after

propensity stratification analysis and multivariate logistic regression analysis, there were no significant differences in odds of 30-day mortality.

Conclusion In our cohort of patients with STEMI complicated by CS treated with primary PCI we observed a difference in mortality between those treated with IABP and those treated without IABP in favour of the ‘no IABP’ group. The mortality difference was eliminated after adjustment for differences in case mix by propensity stratification or by logistic regression analysis. Neither did we observe any difference in mortality between patients whose IABP treatment was initiated before or immediately after PCI.

Keywords ST-elevation myocardial infarction · Cardiogenic shock · Intra-aortic balloon pump · Timing · Efficacy

Introduction

Studies investigating temporal trends in outcomes and management of ST-elevation myocardial infarction (STEMI) patients with cardiogenic shock (CS) show that mortality has only minimally improved during the last decades [1, 2]. Despite increasing adherence to an aggressive reperfusion strategy (primary PCI and CABG) and the use of intra-aortic balloon pump (IABP) therapy, as advocated by the guidelines, in-hospital mortality for CS patients is still exceedingly high. Appreciation of the role of the systemic inflammatory response syndrome that seems to develop with progressive CS also did not lead to interventions, i.e. (nitric oxide synthase inhibitors), which lowered mortality [3, 4]. With the development of new, perhaps more potent, mechanical cardiac assist devices, the role of IABP therapy in the management of CS in recent studies has again been of major interest [5–9]. Routine use of IABP therapy in the setting of high-risk STEMI is not supported by evidence

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from randomised trials, as shown in our recently published meta-analysis [10]. In the absence of large randomised clinical studies in the setting of STEMI complicated by CS, an ongoing debate remains whether there is sufficient scientific evidence for the use of IABP therapy in addition to primary PCI and whether IABP-assisted primary PCI would lead to better outcomes opposed to start of IABP therapy after PCI or no use of IABP therapy at all.

The present study had two main objectives. The first objective was to determine if IABP therapy in addition to primary PCI in the setting of CS results in an improved outcome. The second objective was to study the relation between timing of initiation of IABP therapy and short- and long-term mortality in patients with STEMI complicated by CS.

Methods

Study population

From January 1997 to March 2005 all consecutive STEMI patients treated with primary percutaneous coronary intervention (PCI) in our hospital were entered into a dedicated database ($n=3038$). The primary PCI was performed with standard techniques and prior to the procedure patients were treated with heparin and aspirin. For the present study all patients prospectively registered as being in CS by the attending cardiologist ($n=292$) were selected. We have previously published about this CS cohort [11–13]. From the selected cohort of 292, a total of 199 patients received IABP therapy ('IABP group') and 93 patients received no additional support ('no IABP group').

For analyses on timing of initiation of IABP therapy, the IABP group was divided in two subgroups: a group of patients with IABP therapy initiated prior to PCI ('IABP pre-PCI'; $n=59$) and a group with IABP therapy initiated after PCI ('IABP post-PCI'; $n=140$).

Data collection

Baseline characteristics including demographics, clinical presentation, angiographic characteristics and hospital procedural data were obtained from a prospectively built dedicated database of all PCI procedures performed in our hospital. All data were checked for completeness and inconsistencies. In addition, haemodynamic data and specific IABP therapy-related data were collected retrospectively by review of the electronic medical records and hospital case records. Characteristics that were not described were considered absent. Finally, information on vital status was obtained from the Dutch national population registry (Statistics Netherlands, Voorburg, the Netherlands) per January 2007.

Definitions

The state of cardiogenic shock was determined by the attending operator guided by a definition similar to the SHOCK trial, i.e. a systolic blood pressure (BP) persistently ≤ 90 mmHg or vasopressors required to maintain BP > 90 mmHg, evidence of end-organ hypoperfusion (e.g. urine output < 30 ml or cold/diaphoretic extremities or altered mental status), and evidence of elevated filling pressures [14]. The ischaemic time was defined as the interval between onset of symptoms and first balloon dilatation of the culprit artery. The number and dose of inotropic agents/vasopressors refers to inotropics given from admission to the catheterisation laboratory, coronary care unit (CCU) or intensive care unit (ICU).

Endpoints

The primary endpoint of the study was all-cause mortality at 30 days. For multivariate analyses odds ratios for 30-day mortality were determined. Finally, rates of bleeding requiring transfusion and stroke were assessed.

Statistical analysis

Data are presented as mean $\pm$ SD for continuous variables and as frequencies for categorical variables. Normal distribution of variables was assessed visually. Differences between the IABP group versus the no IABP group, and the IABP pre-PCI versus the IABP post-PCI group in continuous variables were tested with the Student's *t* test or with the Mann–Whitney *U* test as appropriate. Differences in categorical variables were tested by the chi-square test.

Odds ratios of 30-day mortality for the IABP versus the no-IABP group, and the IABP pre-PCI versus the IABP post-PCI group were derived from univariate analyses and, in an attempt to minimise the influence of bias and confounding, from both propensity stratification analyses and multivariate logistic regression analyses.

To generate the propensity score for each patient, logistic regression modelling was used to first model the likelihood that patients were to receive IABP therapy and subsequently the likelihood that patients received IABP therapy prior to PCI versus after PCI, based on covariates independently associated with treatment assignment. Discriminative ability of the derived propensity scores was assessed by the c-statistic (> 0.8 good discriminative ability). For the propensity score stratification analyses, strata were created based on quintiles of the score. Creation of 5 strata based on the propensity score has shown to remove > 90 % of the bias in each of the included covariates in the propensity model [15].

Multivariate stepwise logistic regression analyses were performed including all covariates that were associated with outcome in univariate analyses.

All tests were two-tailed and a p -value of <0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS inc., Chicago, IL, USA; version 14.0.) for Windows.

Results

IABP versus no IABP

The study cohort of 292 CS patients on admission treated with primary PCI either or not in combination with intra-aortic balloon counterpulsation consisted of 67 % males with a mean age of 64 ± 13 years. Baseline characteristics for the study cohort divided by no IABP ($n=93$) versus IABP ($n=199$) are detailed in Table 1. Patients in the IABP group were older and more often had prior CABG. They were more likely to have multivessel disease and the LAD as the infarct-related artery. Ischaemic time between the two groups was equal, although there was a trend towards shorter ischaemic times in the IABP group. Finally, patients who received IABP were given more inotropic agents and abciximab compared with those who did not receive IABP therapy.

All-cause 30-day mortality for the total cohort of 292 CS patients was 41 %. All-cause 30-day mortality for the IABP versus the no IABP group was 47 % vs. 28 %, respectively. The rate of bleeding requiring transfusion and stroke rate in the IABP versus the no IABP group was 25 % vs. 19 % (NS) and 1.5 % vs. 1.1 % (NS), respectively.

Univariate analysis of mortality showed a significantly greater odds for mortality in the IABP group compared with the no IABP group (OR 1.7; 95 % CI 1.2–2.4).

The final propensity score model to predict the likelihood of the use of IABP therapy included seven independent predictor variables (age, admission creatinine, admission glucose, mean blood pressure, heart rate, LAD-related infarction, and multivessel disease). The c-statistic for the propensity score model was 0.85, indicating adequate discrimination. The odds for mortality after stratification by quintiles of the propensity score are detailed in Table 2. The negative odds ratio of mortality for IABP therapy versus no IABP therapy was neutralised with adjustment by the propensity stratification model (OR 1.09; 95 % CI 0.64 to 1.89). Adjustment by the propensity stratification model resulted in an odds for mortality of 1.10 (95 % CI 0.64 to 1.89). However, also by logistic regression there was no longer a significant difference in odds for mortality (OR 1.40; 95 % CI 0.68 to 2.61). Table 3 summarises both univariate and multivariate analyses.

Initiation of IABP therapy pre-PCI versus post-PCI

As detailed, the IABP group was divided into two subgroups based on the timing of initiation of support, i.e. the

‘IABP-pre PCI’ group ($n=59$) and the ‘IABP post PCI’ group ($n=140$). Differences were smaller between these last two groups than between the no IABP and the IABP groups. The baseline characteristics according to timing of initiation of IABP therapy are detailed in Table 4.

Patients in the IABP pre-PCI group were more likely to be male and were less likely to have diabetes mellitus. Finally, they had higher lactate levels on admission and received more inotropic agents/vasopressors as opposed to patients from the IABP post-PCI group.

All-cause 30-day mortality for the IABP pre-PCI versus the IABP post-PCI group was 62 % vs. 40 %, respectively. Univariate analysis, consequently, showed a significantly greater odds for mortality in the IABP pre-PCI group compared with the IABP post-PCI group (OR 1.56; 95 % CI 1.18–2.08).

The final propensity score model to predict the likelihood of the use of IABP therapy pre-PCI included eight independent predictor variables (age, male gender, admission glucose, LAD-related infarction, admission lactate, previous myocardial infarction, previous CABG, and TIMI flow 0 before PCI). The c-statistic was 0.94. The odds for mortality after stratification by quintiles of the propensity score are detailed in Table 5. The negative odds ratio of mortality for IABP pre-PCI versus post-PCI was diminished to a non-significant difference in mortality estimates with adjustment by the propensity stratification model (OR 1.42; 95 % CI 0.81 to 3.25). Adjustment by logistic regression also neutralised the negative odds ratio for mortality in univariate analysis (OR 1.13; 95 % CI 0.51 to 2.54). Table 6 summarises both univariate and multivariate analyses.

Discussion

This study reflects a representative single-centre population of STEMI patients with CS on admission over a long range of years (1997–2005). The overall 30-day mortality rate of 41 % was comparable with rates observed in other cohort studies [1, 2]. We conducted a retrospective analysis to compare outcomes of concomitant IABP therapy versus no IABP in patients with STEMI complicated by CS undergoing primary PCI. In addition we investigated whether timing of initiation of IABP therapy is of influence on outcome.

The principal finding of this study is that IABP therapy in addition to primary PCI showed neither a significant positive nor a negative odds ratio with regard to 30-day mortality after multivariate adjustment.

Univariate analysis showed a negative 30-day mortality odds ratio of IABP therapy in addition to primary PCI (OR 1.67; 95 % CI 1.16 to 2.39). However, analyses adjusting outcomes by a propensity stratification model (OR 1.09; 95 % CI 0.64 to 1.89) and logistic regression model (OR

Table 1 Characteristics of cardiogenic shock patients divided by no IABP vs. IABP

Variable	No IABP (n=92)	IABP (n=199)	p-value
Clinical characteristics and risk factors			
Age (year)	61.5±13.8	64.7±12.7	0.058
Male (%)	61 (65.6)	136 (68.3)	0.640
BMI (kg/m ²)	26.6±3.7	26.7±3.3	0.813
Hypertension (%)	29 (31.2)	69 (34.7)	0.556
Diabetes mellitus (%)	16 (17.2)	36 (18.1)	0.854
Hypercholesterolaemia (%)	32 (34.4)	42 (21.1)	0.015
Current smoker (%)	49 (52.7)	72 (36.2)	0.008
Family history of CVD (%)	33 (35.5)	64 (32.2)	0.200
Prior stroke (%)	5 (5.4)	8 (4.0)	0.483
Previous myocardial infarction (%)	22 (23.7)	60 (30.2)	0.250
Previous coronary angioplasty (%)	6 (6.5)	18 (9.0)	0.452
Previous CABG (%)	1 (1.1)	15 (7.5)	0.008
Peripheral artery disease (%)	2 (2.2)	14 (7.0)	0.087
Haemodynamics pre-PCI			
Heart rate (bpm)	87.3±25.3	85.3±24.2	0.509
Systolic BP (mmHg)	104.7±30.3	103.3±28.9	0.710
Diastolic BP (mmHg)	63.5±18.2	62.0±17.0	0.487
Mean BP (mmHg)	77.2±21.4	75.7±19.4	0.564
Laboratory			
Haemoglobin (mmol/l)	8.0±1.2	8.0±1.4	0.833
Lactate (mmol/l)	4.9±2.8	6.0±4.3	0.190
Serum creatinine (μmol/l)	91.7±34.7	106.2±60.2	0.010
Plasma glucose (mmol/l)	10.3±4.4	13.2±5.8	<0.001
Angiographic characteristics			
LAD-related infarction (%)	26 (28.0)	119 (59.8)	<0.001
Multi-vessel disease (%)	37 (39.8)	125 (62.8)	<0.001
TIMI0-pre (%)	65 (69.9)	146 (73.4)	0.537
TIMI3-post (%)	69 (74.2)	135 (67.8)	0.270
Ischaemic time	4h03m±2h34m	3 h34 m±2 h08 m	0.112
Treatment-related characteristics			
Inotropics (%)	35 (37.6)	146 (73.4)	<0.001
Number of inotropics	0.6±1.0	1.6±1.4	<0.001
Abciximab (%)	15 (16.1)	90 (45.2)	<0.001

BMI body mass index; BP blood pressure; CABG coronary artery bypass grafting; CVD cardiovascular disease; IABP intra-aortic balloon pump; PCI: percutaneous coronary intervention; TIMI thrombolysis in myocardial infarction

Table 2 Propensity score stratification analysis IABP vs. no IABP in cardiogenic shock

Strata	Propensity Score	No IABP n/N	IABP n/N	OR	95 % CI
1	0–0.46	2/40	3/18	3.800	0.627–23.040
2	0.46–0.66	10/25	14/34	1.050	0.363–3.034
3	0.66–0.78	6/17	21/41	1.925	0.597–6.202
4	0.78–0.89	6/8	21/51	0.233	1.169–0.047
5	0.89–1	2/3	34/55	0.810	9.656–0.068
Overall ^a		26/93	93/199	1.097	0.637–1.890

Comparison of effect of IABP therapy in CS on 30-day mortality across strata (quintiles) of propensity score

IABP intra-aortic balloon pump; OR odds ratio, CI confidence interval; n number of patients who died; N total number of patients in group

^a Mantel-Haenszel pooled estimate (p=0.739)

Table 3 Unadjusted and adjusted OR (IABP vs. no IABP) of 1-month mortality

Analysis	OR	95 % CI
Unadjusted	1.672	1.168–2.392
Adjusted by propensity stratification	1.097	0.637–1.890
Adjusted by logistic regression ^a	1.402	0.688–2.613

IABP intra-aortic balloon pump; *OR* odds ratio; *CI* confidence interval; *IRA* infarct-related artery; *LM* left main coronary artery; *CTO* chronic total occlusion; *LAD* left descending artery; *RCA* right coronary artery

^a Included covariates: ischaemic time, glucose, TIMI 3 flow post PCI, IRA LM, admission lactate, abciximab administration, CTO LAD and RCA

1.40; 95 % CI 0.68 to 2.61), respectively, neutralised this negative odds ratio.

In respect to the timing of initiation of IABP therapy, our study did not show any significant difference in odds of mortality. Univariate analysis resulted in an odds ratio in favour of initiation of IABP therapy after PCI (OR 1.56; 95 % CI 1.18 to 2.08). However, adjustment by propensity analysis (OR 1.42; 95 % CI 0.81 to 3.3) and multivariate logistic regression analysis (OR 1.13; 95 % CI 0.51 to 2.54), respectively, showed no significant difference in odds of 30-day mortality.

Concomitant acute circulatory support and left ventricular unloading has been suggested to provide superior infarct salvage and therefore improved long-term outcome

Table 4 Characteristics of cardiogenic shock patients divided by IABP pre PCI vs. IABP post PCI

Variable	IABP pre PCI (n=59)	IABP post PCI (n=140)	p-value
Clinical characteristics and risk factors			
Age (year)	65.1±12.7	64.6±12.7	0.806
Male (%)	47 (79.7)	89 (63.6)	0.026
BMI (kg/m ²)	27.4±3.3	26.4±3.3	0.059
Hypertension (%)	22 (37.3)	47 (33.6)	0.615
Diabetes mellitus (%)	9 (15.3)	27 (19.3)	0.000
Hypercholesterolaemia (%)	15 (25.4)	27 (19.3)	0.332
Current smoker (%)	18 (30.5)	54 (38.6)	0.280
Family history of CVD (%)	17 (28.8)	47 (33.6)	0.512
Prior stroke (%)	3 (5.1)	5 (3.6)	0.620
Previous MI (%)	17 (28.8)	43 (30.7)	0.790
Previous coronary angioplasty (%)	6 (10.2)	12 (8.6)	0.720
Previous CABG (%)	7 (11.9)	8 (5.7)	0.133
Peripheral artery disease (%)	5 (8.5)	9 (6.4)	0.606
Haemodynamics pre-PCI			
Heart rate (bpm)	84.2±24.5	85.7±24.1	0.683
Systolic BP (mmHg)	109.7±50.0	104.8±29.9	0.228
Diastolic BP (mmHg)	60.4±16.5	62.2±17.2	0.389
Mean BP (mmHg)	73.5±18.4	76.7±19.8	0.273
Laboratory			
Haemoglobin (mmol/l)	7.9±1.3	8.0±1.4	0.723
Lactate (mmol/l)	7.5±5.5	5.4±3.6	0.002
Serum creatinine (μmol/l)	109.7±49.9	104.8±64.0	0.562
Plasma glucose (mmol/l)	14.0±5.7	12.8±5.8	0.184
Angiographic characteristics			
LAD-related infarction (%)	33 (55.9)	86 (61.4)	0.470
Multivessel disease (%)	38 (64.4)	87 (62.1)	0.763
TIMI0-pre (%)	39 (66.1)	107 (76.4)	0.132
TIMI3-post (%)	38 (64.4)	97 (69.3)	0.501
Ischaemic time	3h50m±2h26m	3h27m±1h59m	0.300
Treatment-related characteristics			
Inotropics (%)	48 (81.4)	98 (70.0)	0.098
Number of inotropics	1.7±1.4	1.6±1.4	0.499
Abciximab (%)	25 (52.4)	65 (46.4)	0.600

BMI body mass index; *BP* blood pressure; *CABG* coronary artery bypass grafting; *CVD* cardiovascular disease; *IABP* intra-aortic balloon pump; *MI* myocardial infarction; *PCI* percutaneous coronary intervention; *BMI* body mass index; *TIMI* thrombolysis in myocardial infarction

Table 5 Propensity score stratification analysis IABP pre PCI vs. IABP post PCI in CS

Strata	Propensity score	Post PCI n/N	Pre PCI n/N	OR	95 % CI
1	0–0.06	10/38	0/1	2.800	0.058–135.437
2	0.06–0.19	9/33	3/7	2.000	0.371–10.769
3	0.19–0.31	15/30	7/10	2.333	0.506–10.750
4	0.31–0.51	15/28	8/13	1.387	0.357–5.382
5	0.89–1	7/11	19/28	1.206	0.274–5.302
Overall ^a		56/140	37/59	1.418	0.805–3.254

Comparison of effect of IABP therapy pre-PCI vs. post-PCI in CS on 30-day mortality across strata (quintiles) of propensity score

IABP intra-aortic balloon pump; OR odds ratio; CI confidence interval; *n* number of patients who died; *N* total number of patients in group

^a Mantel-Haenzel pooled estimate ($p=0.176$)

over reperfusion alone. Intra-aortic balloon counterpulsation is still the most used method of LV unloading and haemodynamic support in the catheterisation laboratory [5]. However, the use of IABP therapy concomitant to primary PCI remains controversial, due to lack of sufficient (randomised) scientific support, as evidenced recently by a meta-analysis from our group [10]. Nonetheless, the ACC-AHA 2011 guidelines still list the use of IABP therapy (or another haemodynamic support device) in the setting of CS as a class IB recommendation [16], albeit, in contrast to the former 2008 version of the guidelines, with the statement that there are no data to support a reduction in mortality rates [17]. The European Society of Cardiology guidelines report an IC recommendation for IABP therapy in the setting of cardiogenic shock (i.e. expert opinion) [18].

The results of our study concerning the use of IABP therapy per se are in concordance with a recent study from Prondzinsky et al., which reported on the first randomised controlled trial investigating concomitant IABP ($n=23$) versus no IABP ($n=22$) therapy immediately post-PCI in the setting of CS [9]. The study showed neither a significant difference in APACHE II scores (primary endpoint) nor in mortality between both groups. In contrast, in the large NRM Registry mortality was significantly higher, even

after multivariate analysis, for patients receiving IABP therapy in addition to primary PCI in the setting of CS [19]. Another important consideration is that complications of IABP therapy (i.e. bleeding, stroke) may outweigh any putative benefits [10]. Overall, the currently available data do not seem to be conclusive with regard to the role of IABP therapy in the setting of primary PCI for STEMI complicated by CS [9, 19].

Finally due to a paucity of data an ongoing debate remains as to whether IABP therapy should be initiated before or after PCI in order to be able to beneficially affect outcome. Experimental research suggests that unloading prior to revascularisation might result in an additional reduction in infarct size [20, 21]. In line with this hypothesis a small retrospective study ($n=48$) recently showed an improved outcome when IABP was used before as opposed to after PCI [7]. However there were significant differences in mean values of cardiac enzymes between the two groups in favour of the IABP-assisted PCI group, i.e. both presentation and peak levels were lower, suggesting earlier presentation and less extensive infarction. Although multivariate analysis was attempted to correct for this difference, patients from the IABP post-PCI group due to the delayed presentation may have been a priori in a more progressed state of cardiogenic shock and multiple organ failure, as also evidenced by the higher trends in need for vasopressors, mechanical ventilation and renal replacement therapy.

To our knowledge the present study represents the largest cohort used to investigate the issue of timing of initiation of IABP therapy in the setting of STEMI complicated by CS. Our data suggest no difference in effect on outcome between initiation of IABP therapy either before or after primary PCI, which is in accordance to a subgroup analysis of a prior randomised trial by Thiele et al. investigating concomitant left ventricular assist device support versus IABP therapy in the setting of CS [22].

Of note, a recent large randomised trial (BCIS-1) of IABP-assisted PCI versus no IABP in the setting of elective PCI did

Table 6 Unadjusted and adjusted OR (IABP pre PCI vs. post PCI in CS) of 1-month mortality

Analysis	OR	95 % CI
Unadjusted	1.568	1.182–2.080
Adjusted by propensity stratification	1.418	0.805–3.254
Adjusted by logistic regression ^a	1.133	0.506–2.536

^a Included covariates: age, admission creatinine, glucose, MBP, HR, inotropic use, IRA LAD

ABP intra-aortic balloon pump; OR odds ratio; CI: confidence interval; IRA infarct-related artery; LAD left descending artery MBP mean blood pressure; HR heart rate

not prove to reduce major adverse cardiac and cerebral events [23]. In addition in the setting of STEMI without haemodynamic derangement, the CRISP-AMI (Counterpulsation to Reduce Infarct Size Pre-PCI-Acute Myocardial Infarction) trial [24], again randomising between IABP-assisted PCI vs. PCI without IABP support, also did not show improved outcomes, i.e. MRI-determined infarct size at 4 days, death or reinfarction at 30 days and six months.

In summary, to date there does not seem to be strong support for IABP-assisted primary PCI in the setting of STEMI complicated by CS. Recent trials even show IABP therapy to be discouraged in the setting of elective PCI and stable STEMI patients. However, mechanical cardiac assist in general, due to its intuitive and experimentally supported rationale, remains an appealing treatment strategy. Perhaps use of the more potent percutaneous left ventricular assist devices, which are increasingly being used, will show a benefit for initiation of LV support either before, during or after PCI. However, currently there is no evidence supporting the routine use of percutaneous LVAD, as shown in a recent meta-analysis by Cheng et al. [8]. Moreover, with the strong scientific evidence for primary PCI as the cornerstone of treatment and time being muscle for STEMI patients, including those with CS, one should consider whether the benefits of LV support, when initiated prior to PCI, will outweigh a delay in reperfusion. Perhaps answers will follow from the running IABP-SHOCK II trial (NCT00491036) investigating IABP versus no IABP in addition to primary PCI in the setting of cardiogenic shock.

Limitations

Despite the concordant results of the propensity stratification and logistic regression analyses, it remains important to note that in the present study, there still might be residual confounding and bias. With both methods, hidden bias may remain due to the presence of (dormant) unobserved confounders. Furthermore in propensity analysis the decision for the investigated treatment is assumed to be at one point in time.

In normal practice it is obvious that the decision whether or not to insert an IABP is not taken at a single point in time. First, in some cases the operators may insert the IABP before primary PCI as a stabilising measure in the presence of an unstable haemodynamic condition of the patient or in patients in whom further deterioration is foreseen due to reperfusion injury, a large myocardial area at risk or other causes. Second, indications may also arise after primary PCI for the operators to decide upon initiation of IABP therapy, i.e. in case of unanticipated haemodynamic deterioration after PCI, in case of persistent instability, or as a last resort. As our database only provided haemodynamic and laboratory data recorded at admission, we could not correct for

factors influencing late decisions to start IABP treatment. Therefore, without formalised criteria for the indication of IABP therapy, indication bias seems inevitable. Possibly, operators may have intuitively selected patients expected to respond well to IABP treatment. On the other hand, operators may have preferentially given IABP treatment to patients in a poorer condition. It is difficult to withhold patients from active treatment with IABP, even if their prognosis is extremely bleak. Therefore, the results of this analysis must be interpreted cautiously. The indication bias detailed above can only be prevented by proper randomisation. Of note, the point in time chosen for randomisation will be a matter of debate, and it is not certain whether it will be possible to address the different indications for IABP therapy in the setting of STEMI complicated by CS in one single trial.

Conclusion

In our cohort of patients with STEMI complicated by CS treated with primary PCI we observed a difference in mortality between those treated with IABP and those treated without IABP in favour of the ‘no IABP’ group. The mortality difference was eliminated after adjustment for differences in case mix by propensity stratification or by logistic regression analysis. Neither did we observe any difference in mortality between patients whose IABP treatment was initiated before or immediately after PCI. However, limitations of the propensity stratification and logistic regression analyses in eliminating bias and confounding must be recognised. Therefore the results of this study need to be interpreted cautiously.

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