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ORIGINAL PAPER

Intra-aortic balloon pump in patients with acute myocardial infarction complicated by cardiogenic shock: results of the ALKK-PCI registry

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Abstract
Aims The recommendation for the use of the intra-aortic balloon pump (IABP) as adjunct in patients with cardiogenic shock undergoing primary PCI in current guidelines is controversial. We sought to investigate the use and impact of the outcome of IABP in current practice of percutaneous coronary interventions in Germany.
Methods and results Between January 2006 and December 2011, a total of 55,008 consecutive patients with acute coronary syndromes undergoing PCI in 41 hospitals were enrolled into the prospective Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte registry. Of these, 22,039 had STEMI and 32,969 had NSTEMI, and cardiogenic shock was observed in 1,435 (6.5 %) and 478 (1.4 %), respectively. Of the total of 1,913 patients with shock, 487 (25.5 %) were treated with IABP. In-hospital mortality with and without IABP was 43.5 and 37.4 %. In the multivariate analysis, the use of IABP was associated with a strong trend for an increased mortality (odds ratio 1.45, 95 % CI 1.15–1.84).
Conclusion In the current clinical practice in Germany, IABP is used only in one quarter of patients with cardiogenic shock treated with primary PCI. We observed no benefit of IABP on outcome, which supports the findings of the randomized IABP-Shock II trial.

Keywords Percutaneous coronary intervention · Cardiogenic shock · Hospital mortality · Intra-aortic balloon pump

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Introduction

Despite the use of early revascularization therapy, cardiogenic shock is the major cause of death in patients admitted with acute myocardial infarction and associated with a mortality of around 40–50 % [1–3]. One mechanical measure to improve hemodynamics in cardiogenic shock is the intra-aortic balloon pump (IABP). IABP was introduced in 1968 and improves systemic and coronary diastolic blood pressure and reduces afterload and myocardial work [4]. These effects are believed to improve myocardial recovery during ischemia and reperfusion and, ultimately reduce mortality in patients with cardiogenic shock. Current ESC guidelines support the use of IABP (class 1c recommendation) in patients with cardiogenic shock [5]. However, a recent meta-analysis has questioned the value of IABP, especially in patients with primary PCI [6]. The recent guidelines of the German Cardiac society for cardiogenic shock are neutral regarding the recommendation for IABP in connection with primary PCI for shock [7].

Therefore, we sought to investigate the use of IABP in a large cohort of patients undergoing PCI for cardiogenic shock in Germany.

Methods

The Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte(ALKK) PCI registry

The ALKK PCI registry is a prospective registry that was initiated in 1992 to monitor quality control and contains all consecutive procedures of the participating hospitals on an intention-to-treat basis [8, 9]. Data were obtained by standardized questionnaires in the 41 participating hospitals, including the information about the medical history (prior coronary interventions, CHF, diabetes mellitus, and renal insufficiency) indication for the procedure, the adjunctive antithrombotic therapy, the procedure itself (target vessel, success rate, stent used, etc.), and the complications until hospital discharge. All data were analyzed centrally at the Karl Ludwig Neuhaus Datenzentrum, Ludwigshafen, Germany.

Patient selection

All patients receiving PCI were included on an intention-to-treat basis. We analyzed data of consecutive patients with ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI). For this analysis, we selected patients with cardiogenic shock before the start of the intervention.

Definitions

NSTEMI was diagnosed in the presence of the two following criteria: persistent angina pectoris for ≥20 min and an elevation of troponin T or I. Raised levels were considered those exceeding the upper normal level at the local laboratory at each participating site.

STEMI was diagnosed in the presence of the two following criteria: persistent angina pectoris ≥20 min and ST-segment elevation of 1 mm in ≥2 standard leads or ≥2 mm in ≥2 contiguous precordial leads or the presence of a left bundle branch block. It was later confirmed by the elevation of enzymes (creatinine kinase and its MB isoenzyme, aspartate aminotransferase, and lactic dehydrogenase) to at least twice the normal value.

Cardiogenic shock was diagnosed in patients with systolic blood pressure <90 mmHg, heart rate >100 bpm, and clinical signs of organ hypoperfusion.

Statistical methods

All analyses were performed using the SAS© statistic package, Version 9.1 (Cary, NC, USA). Data are presented as absolute numbers or percentage. Whenever possible, percentages were used to describe patient populations. The frequencies of categorical variables in four age groups were compared by Pearson–Fisher χ^2 test and by calculating odds ratios (OR) and 95 % CI. Continuous variables were compared by Mann–Whitney–Wilcoxon test. p values <0.05 were considered significant. (All p values are results of two-tailed tests).

A multivariate regression analysis for independent predictors of inhospital mortality was performed including age, gender, left main PCI, triple vessel disease, diabetes, and renal insufficiency. These values were calculated from the available cases. The computations were performed using the SAS system release 9.1 on a personal computer (SAS Institute, Inc., Cary, NC, USA).

Results

Between January 2006 and December 2011, a total of 55,008 consecutive patients with acute coronary syndromes undergoing PCI in 41 hospitals were enrolled into the registry. Of these, 22,039 had STEMI and 32,969 had NSTEMI, and cardiogenic shock was observed in 1,435 (6.5 %) and 478 (1.4 %), respectively. Of the total 1,913 patients with shock, 487 (25.5 %) were treated with IABP. The rate of shock patients treated with IABP was 26.0 % in patients with STEMI and 22.0 % in patients with NSTEMI, respectively. The rate of the use of IABP per hospital is shown in Fig. 1.

The baseline variables of patients treated with and without IABP are given in Table 1. The angiographic features and procedural details of the patients are shown in

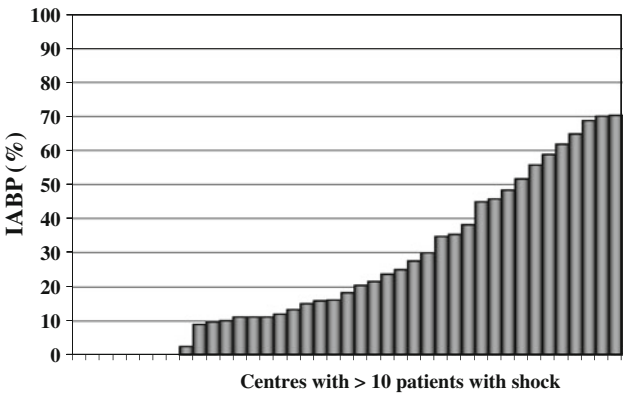

Fig. 1 Rate of use of IABP in the different hospitals with >10 patients with PCI for cardiogenic shock

Table 1 Baseline characteristics of patients with cardiogenic shock treated with primary PCI with and without IABP

	IAPB ($n = 487$)	No IAPB ($n = 1,426$)	p value
Age	67.7 years	69.9 years	<0.001
Female gender	23.6 %	32.0 %	<0.001
Prior MI	35.1 %	38.5 %	0.3
Prior PCI	18.2 %	18.1 %	0.9
Prior CABG	7.1 %	7.4 %	0.7
Prior stroke	8.9 %	8.3 %	0.9
PAD	16.2 %	19.4 %	0.2
Impaired renal function	35.5 %	37.0 %	0.5
Hypertension	73.8 %	76.0 %	0.6
Smoker	45.5 %	38.6 %	0.02
Diabetes	32.7 %	32.4 %	0.8
Hypercholesterolemia	62.5 %	62.7 %	0.7
STEMI	78.0 %	74.0 %	0.07
NSTEMI	22.0 %	26.0 %	0.07

Table 2 Angiographic findings and procedural results of patients with and without cardiogenic shock

	IAPB ($n = 487$) (%)	No IAPB ($n = 1,426$) (%)	p value
1-vessel disease	19.6	23.3	0.6
2-vessel disease	21.2	28.1	0.01
3-vessel disease	59.2	48.6	0.0003
Left main stenosis	28.9	17.8	0.004
Femoral access	94.1	95.3	0.35
Treated vessels			
RCA	30.0	35.4	0.03
Left main	15.1	10.2	0.03
LAD	56.5	48.7	0.03
CX	29.2	23.9	0.02
Bypass graft	2.9	2.9	0.6
Multi vessel PCI	27.6	18.4	<0.01
Stent implantation	87.8	83.3	0.02
Drug-eluting stent	29.1	22.7	0.01
TIMI 3 after PCI	79.1	72.8	0.01
Emergency CABG	2.4	0.6	0.01

Table 2. Thrombus aspiration was used in 30.3 versus 13.2 % of patients with and without IABP. The patients were treated with an intensive antithrombotic therapy (Table 3) with a higher use of GP IIb/IIIA inhibitors and bivalirudin in the IABP group. During PCI, inotropes were given in 81.8 % of patients with and 97.2 % of patients without IABP ($p < 0.001$), respectively. The inhospital events are shown in Fig. 2. Renal failure requiring dialysis occurred in 6.1 versus 4.7 % ($p = 0.4$) of the patients.

Table 3 Acute antithrombotic therapy in patients with and without IABP

	IABP ($n = 487$) (%)	No IABP ($n = 1,426$) (%)	p value
Aspirin	96.6	96.4	0.9
Clopidogrel	85.2	78.1	0.01
Prasugrel	7.3	5.8	0.5
Ticagrelor	1.7	3.1	0.2
GP IIb/IIIa inhibitor	64.5	54.1	0.001
Unfractionated heparin	90.7	95.3	0.001
Low molecular weight heparin	7.0	1.5	0.001
Bivalirudin	6.6	2.8	0.001

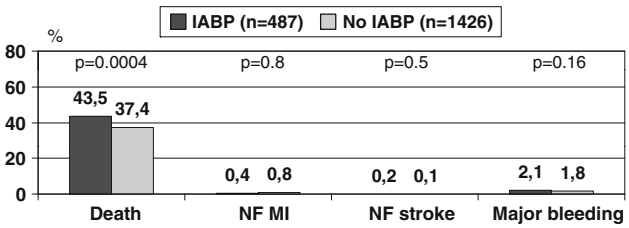

Fig. 2 In-hospital events in patients treated with or without IABP. (*NF* non-fatal, *MI* myocardial reinfarction)

Independent predictors of inhospital mortality are shown in Fig. 3. Here IABP was associated with an increased mortality (odds ratio 1.45, 95 % CI 1.15–1.84).

Discussion

Early revascularization therapy has been shown to improve the outcome of patients with acute myocardial infarction complicated by cardiogenic shock. However, mortality in these patients remains high [3, 10–15]. While current ESC-guidelines recommend the use of IABP in patients with cardiogenic shock [5], the recent shock guidelines of the German cardiac society are neutral in the recommendation [7]. In clinical practice, the utilization rate of IABP is low (15–30 %) [4, 10–14]. In our analysis with data from a large cohort of shock patients from Germany, the use of IABP was 25 % with no difference between the use in STEMI and NSTEMI. We observed large differences in the use of IABP between the hospitals ranging from 0 to 70 %. However, one reason for the overall low utilization rate of IABP in Germany might be that interventionalists are not fully convinced about the beneficial effect of IABP on top of early revascularization therapy. This skepticism is supported by a recent meta-analysis which found no mortality benefit of the IABP in patients with STEMI complicated by

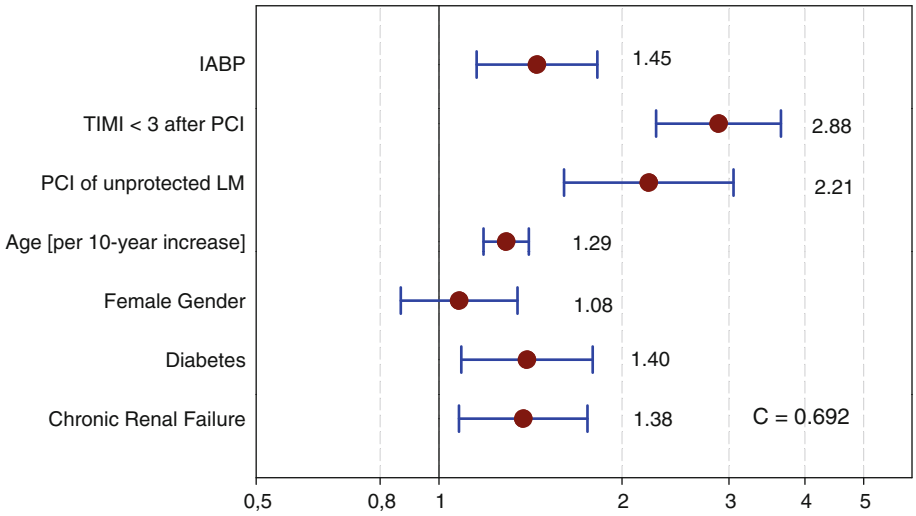

Fig. 3 Multivariate analysis with predictors of in-hospital mortality (odds ratio with 95 % confidence intervals)

cardiogenic shock treated with primary PCI [6], but an increase in major bleeding complications and stroke (Fig. 3).

Until recently, the only randomized clinical trial performed with IABP in primary PCI for shock was small and did not show any differences in the primary surrogate endpoints or any clinical endpoints [15]. Two other trials performed in high-risk patients with STEMI without cardiogenic shock did not show any beneficial effects on the routine use of IABP either [16, 17].

The results of our analysis support these findings. Anything than IABP as adjunct to primary PCI was associated with an adverse outcome. In experimental models and human experience, IABP increased the myocardial perfusion and improved hemodynamics, [18, 19]. Our findings are supported by the results of a larger cohort of patients in the NRMI registry [11]. Here, the use of IABP was associated with an increase in mortality after primary PCI in cardiogenic shock (956/2035 vs. 401/955). The mortality difference remained significant even after the adjustment for confounding factors. The same was true in an analysis of the European Heart Survey of PCI [20] and a very recent analysis of the National Cardiovascular Data Registry in the United States [21]. We can only speculate about the reasons for this increase in mortality. A possibility is that a systemic inflammation response to the device, and another explanationis that the increase in bleeding complications due to local complications at the catheterization insert site.

An interesting finding in our analysis was that patients treated with IABP were more likely to be treated with GP IIb/IIIa inhibitors, bivalirudin, thrombectomy devices, multivessel PCI, and drug-eluting stents. It seems that IABP as an adjunct to PCI is used by more "aggressive" interventionalists using more intense antithrombotic regimens and an approach of more immediate complete revascularization.

Our findings are supporting the results of the recently published IAPB-Shock II trial in which 600 patients with myocardial infarction complicated by cardiogenic shock and intended PCI were randomized to IABP or standard therapy [22]. The primary outcome of 30 day mortality did not differ between the two groups. Although IABP use was safe and not associated with an increase in complications such as sepsis, vascular complications, or bleedings, neither mortality nor any secondary endpoints were improved with IABP use. Secondary endpoints included hemodynamic parameters (blood pressure and heart rate) pre- and post revascularization, serum lactate levels measured every 8 h for 48 h, inflammatory markers, Simplified Acute Physiology Score-II (SAPS-II) measured daily during intensive care treatment, and serial creatinine-level and creatinine-clearance using the Cockcroft-Gault-formula.13 Furthermore, process of care outcomes such as time to hemodynamic stabilization, dose and duration of catecholamine therapy, requirement for renal replacement therapy, length of intensive care unit stay, requirement and length of mechanical ventilation, and requirement for active (percutaneous or surgical) left ventricular assist device implantation or heart transplantation were assessed and did not differ between the two groups.

Limitations

As always in registries a selection bias cannot fully be ruled out. Therefore, even after the adjustment for confounding for baseline variables, we cannot be sure that we were able to adjust for every factor which might have influenced the results.

Conclusions

In current clinical practice in Germany, IABP is used only in one quarter of patients with cardiogenic shock treated with primary PCI. However, we did not observe any hint for a beneficial effect of IABP on outcome, supporting the data of the recently published randomized IABP-Shock II trial. Therefore, IABP should not be considered as a routine treatment in patients with cardiogenic shock and early revascularization therapy.

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