European Heart Journal (2009) **30**, 459–468
doi:10.1093/eurheartj/ehn602

CLINICAL RESEARCH
Coronary heart disease

A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines?

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Received 9 June 2008; revised 18 November 2008; accepted 17 December 2008; online publish-ahead-of-print 23 January 2009

See page 389 for the editorial comment on this article (doi:10.1093/eurheartj/ehp030)

Aims Intra-aortic balloon counterpulsation (IABP) in ST-segment elevation myocardial infarction (STEMI) with cardiogenic shock is strongly recommended (class IB) in the current guidelines. We performed meta-analyses to evaluate the evidence for IABP in STEMI with and without cardiogenic shock.

Methods and results Medical literature databases were scrutinized to identify randomized trials comparing IABP with no IABP in STEMI. In absence of randomized trials, cohort studies of IABP in STEMI with cardiogenic shock were identified. Two separate meta-analyses were performed respectively. The first meta-analysis included seven randomized trials ($n = 1009$) of STEMI. IABP showed neither a 30-day survival benefit nor improved left ventricular ejection fraction, while being associated with significantly higher stroke and bleeding rates. The second meta-analysis included nine cohorts of STEMI patients with cardiogenic shock ($n = 10529$). In patients treated with thrombolysis, IABP was associated with an 18% [95% confidence interval (CI), 16–20%; $P < 0.0001$] decrease in 30 day mortality, albeit with significantly higher revascularization rates compared to patients without support. Contrariwise, in patients treated with primary percutaneous coronary intervention, IABP was associated with a 6% (95% CI, 3–10%; $P < 0.0008$) increase in 30 day mortality.

Conclusion The pooled randomized data do not support IABP in patients with high-risk STEMI. The meta-analysis of cohort studies in the setting of STEMI complicated by cardiogenic shock supported IABP therapy adjunctive to thrombolysis. In contrast, the observational data did not support IABP therapy adjunctive to primary PCI. All available observational data concerning IABP therapy in the setting of cardiogenic shock is importantly hampered by bias and confounding. There is insufficient evidence endorsing the current guideline recommendation for the use of IABP therapy in the setting of STEMI complicated by cardiogenic shock. Our meta-analyses challenge the current guideline recommendations.

Keywords Myocardial infarction • Intra-aortic balloon pump • Angioplasty • Cardiogenic shock • Meta-analysis

Introduction

The intra-aortic balloon pump (IABP) was introduced in 1968.[1] It improves diastolic coronary and systemic blood flow, and reduces afterload and myocardial work.[2] These physiologic effects are believed to lead to improved myocardial and organ recovery after ST-segment elevation myocardial infarction (STEMI).[3,4] Animal studies suggest improved myocardial salvage

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by IABP therapy.[5] Alternatively, IABP is suggested to act as a stabilizing measure or to prevent catheterization laboratory events.[6] After almost four decades of use, IABP has become a mature technology. It is the most common method of mechanical cardiac assistance in acute cardiology today.

The American College of Cardiology and American Heart Association (ACC/AHA) STEMI guidelines list IABP therapy in cardiogenic shock as a class IB recommendation.[7] The European Society of Cardiology (ESC) STEMI guidelines also strongly recommend supportive treatment with an IABP in cardiogenic shock patients.[8] Despite the strong recommendations, the utilization rate of adjunctive IABP in STEMI complicated by cardiogenic shock is low (20–39%).[9,10]

The body of evidence supporting IABP therapy in STEMI and in STEMI with cardiogenic shock remains limited. Only a few relatively small randomized clinical trials have studied IABP therapy in STEMI. Moreover, no randomized clinical trials of IABP support have been performed specifically for STEMI complicated by cardiogenic shock. The current recommendations for the usage of IABP in STEMI complicated by cardiogenic shock are based on non-randomized studies only. Meta-analyses may thoroughly assess available sources of clinical evidence, achieving more precise effect estimates. Therefore, we sought to perform a meta-analysis of all randomized clinical trials comparing adjunctive IABP support with no IABP support in the setting of STEMI. Because no randomized trials of IABP therapy have been specifically performed in STEMI with cardiogenic shock, we also performed a meta-analysis of all cohort studies that evaluated IABP therapy in this setting.

Methods

Inclusion criteria

In our first meta-analysis, we included the results of randomized clinical trials comparing additional IABP therapy with no IABP therapy in STEMI patients. In our second meta-analysis, we included the results of cohort studies comparing concurrent groups of STEMI patients with cardiogenic shock that were treated either with additional IABP therapy or no IABP therapy. All studies required that either in-hospital or 30 day mortality was available for at least 90% of the patients. In-hospital or 30 day mortality hereinafter is referred to as 30 day mortality.

Data sources

We performed a search of MEDLINE (source PubMed, 1966 through December 2007), the Cochrane Controlled Clinical Trials Register Database (through December 2007) and the ClinicalTrials.gov website for randomized controlled trials comparing additional IABP therapy vs. no IABP therapy in the setting of STEMI and cohort studies comparing concurrent groups of patients with STEMI complicated by cardiogenic shock receiving either IABP therapy or no IABP therapy. Searches included the keywords and corresponding Medical Subject Headings (MeSH) for counterpulsation, IABP, myocardial infarction (subheading therapy), and cardiogenic shock. Non-English and non-human studies, case reports, and reviews were excluded from the initial search. All potentially relevant articles were independently reviewed by two investigators (K.D.S. and A.E.E.) to establish eligibility for either of the two meta-analyses. Disagreements were resolved by discussion. Review of the reference lists of the eligible studies and previous reviews of IABP therapy in STEMI did not identify additional potentially eligible articles.

The flow chart of the search strategy and selection of studies is depicted in *Figure 1*. We identified and included seven randomized clinical trials for our first meta-analysis of IABP therapy in the setting of STEMI.[11–17] Ten cohort studies were identified for inclusion in our meta-analysis of IABP therapy in the setting of STEMI complicated by cardiogenic shock. One study only published as abstract was excluded because there was an overlap of patients with another identified study and the reported data were insufficient for correct analysis.[18] Furthermore, one study was excluded as it did only report 1 year mortality instead of the primary endpoint of 30 day mortality.[19] Finally, we included the results of a comparative cohort study of IABP in the setting of STEMI complicated by cardiogenic shock from our own research group (AMC CS cohort). We have previously published about this cardiogenic shock cohort.[20,21] Therefore, a total of

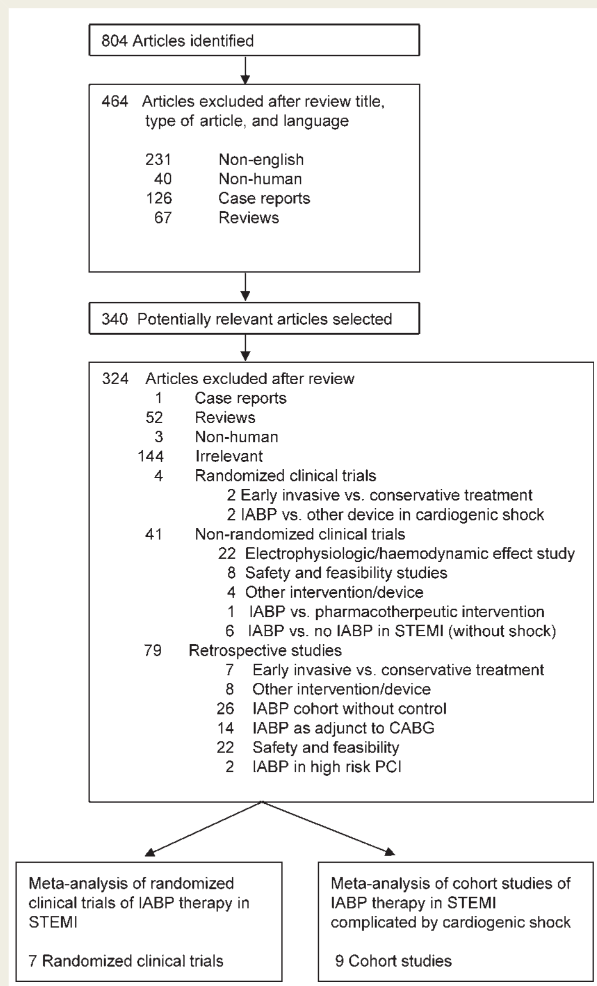

Figure 1 Flow chart of the search strategy and selection of studies for the two meta-analyses. A total of seven randomized controlled trials were identified for the meta-analysis of IABP therapy in STEMI and a total of nine cohort studies were identified for the meta-analysis of IABP therapy in STEMI complicated by cardiogenic shock. IABP, intra-aortic balloon counterpulsation; STEMI, ST-segment elevation myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

nine cohort studies were included in our meta-analysis in the setting of STEMI with cardiogenic shock.[20–29]

Data extraction and quality assessment

Pre-specified patient and outcome data were independently extracted by two investigators (K.D.S. and A.E.E.). The same investigators also evaluated all randomized trials for the adequacy of allocation concealment, analysis by intention to treat, completeness of study and follow-up, adjudication of adverse events, funding source, and database controller. The quality of the cohort studies was assessed with standard criteria: control for confounders, measurement of exposure, and completeness of follow-up and blinding. The findings of the quality assessment for the randomized trials and the cohort studies are, respectively, summarized in *Tables 1* and *2*.

Data synthesis and analysis

The primary efficacy endpoint for both meta-analyses was all cause-mortality at 30 days. The secondary efficacy endpoint, left ventricular ejection fraction (LVEF), and the safety endpoints, stroke and bleeding, were only evaluated in the first meta-analysis of randomized trials, as the cohort studies did not uniformly report on these endpoints.

Studies in both meta-analyses are grouped and presented by type of reperfusion therapy: no reperfusion, thrombolysis, or primary percutaneous coronary intervention (PCI). Subgroups of patients with different reperfusion therapy within individual studies are presented as separate studies.

Results are presented as absolute risk differences for binary outcome measures and absolute mean differences for continuous outcome measures together with 95% confidence intervals (CI). Binary and continuous outcomes from individual studies were combined, respectively, with the Mantel–Haenzel or inverse variance fixed-effect models. We examined heterogeneity across studies by the Cochran's Q statistic and the I^2 statistic. Potential publication bias was assessed by visual assessment of constructed funnel plots. Tests were two-tailed and a *P*-value of $<$0.05 was considered statistically significant. The study was performed in compliance with the Quality of Reporting of Meta-analysis (QUOROM) guidelines.[30] Review Manager (version 4.2.10) was used for statistical analysis.

Results

Meta-analysis of randomized trials of intra-aortic balloon pump therapy in high-risk STEMI patients

Seven randomized trials of IABP therapy in STEMI included 1009 patients.[11–17] *Table 3* shows the study characteristics of the trials. All trials focussed on high-risk STEMI patients, albeit with varying inclusion criteria, such as STEMI with suboptimal PCI result, STEMI with poor ST-elevation resolution, failed thrombolysis, Killip class $>$1, or a large ischaemic area at risk. The trials included a typical STEMI population in terms of age and gender. Generally, treatment groups were well-matched.

Figure 2A shows the absolute numbers of deaths in each treatment group, with the absolute risk difference for each trial. In total, there were 45 deaths in patients who received IABP support and 43 deaths in patients without IABP support. Overall, IABP support in the setting of STEMI was not associated with a change in 30 day mortality (risk difference 1%; 95% CI, -3 to 4%; $P = 0.75$). *Figure 2B* shows the LVEF $\pm$ SD at follow up in

Table 1 Design of the randomized clinical trials of intra-aortic balloon pump in STEMI

Study	Method of allocation	Power calculation	Outcome assessors masked?	Adjudication of adverse events	ITT analysis	Number of patients lost to FUP	Early termination	Study design	Control of database
O'Rourke *et al.*[11]	Predetermined randomization list/ sealed envelopes	No	NR	NR	NR	0	No	Investigator	NR
Flaherty *et al.*[12]	Zelen randomization technique	No	Yes	NR	NR	0	No	Investigator	NR
Kono *et al.*[13]	Predetermined randomization list/ sealed envelopes	No	Yes	NR	Yes	0	No	Investigator	NR
Ohman *et al.*[14] (TACTICS)	Central telephone in USA/sealed envelopes in non-USA	Yes	NR	DSMB	Yes	0	Yes	Investigator	Independent TCC
Ohman *et al.*[15]	Stratified by site and permuted block design	Yes	Yes	NR	NR	Angiographic FUP: 9 IABP group, 11 controls	No	Investigator	Independent TCC
Stone *et al.*[16] (PAMI-2)	NR	Yes	Yes	DSMB	Yes	0	No	Investigator	Independent TCC
van 't Hof *et al.*[17]	NR	Yes	Yes	NR	Yes	0	Yes	Investigator	Investigator

IABP, intra-aortic balloon pump; STEMI, ST-elevation myocardial infarction; ITT, intention to treat; FUP, follow up; NR, not reported; DSMB, data safety monitoring.

Table 2 Design of cohort studies of intra-aortic balloon pump in STEMI complicated by cardiogenic shock

Study	Control for confounders	*A priori* addressed confounders	Measurement of exposure to IABP therapy	Number of patients lost to FUP	Inclusion in cohort without knowledge of outcome
Moulopoulos *et al.*[22]	–	None	+	0	– (group allocation biased by knowledge of contra-indication for IABP in control group)
Stomel *et al.*[23]	–	CS definition, STEMI definition	+	0	+
Kovack *et al.*[24]	–	CS definition, STEMI definition	+	0	+
Bengtson *et al.*[25]	–	CS definition	+	0	+
Waksman *et al.*[26]	–	CS definition, STEMI definition	+	0	+
GUSTO-I[27]	– (subgroup analysis from randomized trial)	CS definition	+	5	± (IABP after day 1 considered as no IABP)
NRMI-2[28]	±	CS definition, STEMI definition, demographics, hospital presentation factors, hospital course parameters	+	0	+
SHOCK registry[29]	±	CS definition, only CS due to LV failure, timing of IABP therapy	+	0	+
AMC CS cohort[20,21]	±	CS definition, STEMI definition, demographics, hospital presentation factors, hospital course parameters	+	0	+

+ denotes that the issue is properly addressed; ± denotes that the issue could be a cause of bias; – denotes that bias due to the issue is likely.

Table 3 Characteristics of randomized controlled trials of intra-aortic balloon pump in STEMI

Study	No. of patients	Type of reperfusion	Setting	Period	Inclusion criteria	CS excluded	Primary outcome	Mean age (years)		Male sex (%)	
								IABP	Control	IABP	Control
O'Rourke et al.[11]	30	No	Multicentre	1976–1979	<12 h, Q's/STT↑ ≥2 mm 2 leads, Killip II–IV	No	Hospital/long-term mortality/infarct size	60	54	86	75
Flaherty et al.[12]	20	No	Single centre	NR	<12 h, STT↑/↓ ≥2 mm, thallium defect score ≥7, Killip I–II (III)	Yes	14 day mortality/infarct size	52	53	90	90
Kono et al.[13]	45	Thrombolysis	Single centre	1992–1995	<12 h, STT↑ ≥1 mm 2 leads, failed TT on CAG	Yes	Patency of IRA at 3 week FUP	54	60	87	73
Ohman et al.[14] (TACTICS)	57	Thrombolysis	Multicentre	1996–1999	<12 h, STT↑ ≥1 mm 2 leads or LBBB, STT↓ ≥2 mm AND anterior AMI with sysRR ≤90 mmHg OR any MI with sysRR ≤110 mmHg, HR ≥100 b.p.m. OR Killip III–IV	No	All cause mortality at 6 m	68	67	77	74
Ohman et al.[15]	182	Primary PCI	Multicentre	1989–1992	Chest pain or persistent STT↑ ≥2 mm, emergency CAG <24 h, TIMI flow 2 or 3 by rescue PCI or intracoronary TT	Yes	Re-occlusion of IRA during hospitalization	56	55	74	76
Stone et al.[16] (PAMI-2)	437	Primary PCI	Multicentre	1993–1995	<12 h, STT↑ ≥1 mm 2 leads, LBBB with IRA and LVEF↓ AND high risk: age>70, 3VD, LVEF ≤45%, SVG occlusion, suboptimal PCI result, malignant VT	Yes	Composite of death, re-MI, stroke, hypotension/CHF	65	64	75	75
van 't Hof et al.[17]	238	Primary PCI	Single centre	1993–1996	<3 h, cumulative ΔSTT >20 mm	No	Composite of death, re-MI, stroke, LVEF <30% at 6 m FUP	59	56	84	85

IABP, intra-aortic balloon pump; STEMI, ST-elevation myocardial infarction; CS, cardiogenic shock; <12 h less, than 12 h from symptom onset; STT↑ or ↓, ST-segment elevation or depression; ΔSTT, ST-segment deviation; TT, thrombolytic therapy; sysRR, systolic blood pressure (mmHg); NR, not reported; CI, cardiac index; PCI, percutaneous coronary intervention; CAG, coronary angiography; TIMI, thrombolysis in myocardial infarction; LVEF, left ventricular ejection fraction; IRA, infarct related artery; SVG, saphenous vein graft; VT, ventricular tachycardia; CHF, chronic heart failure, FUP, follow up.

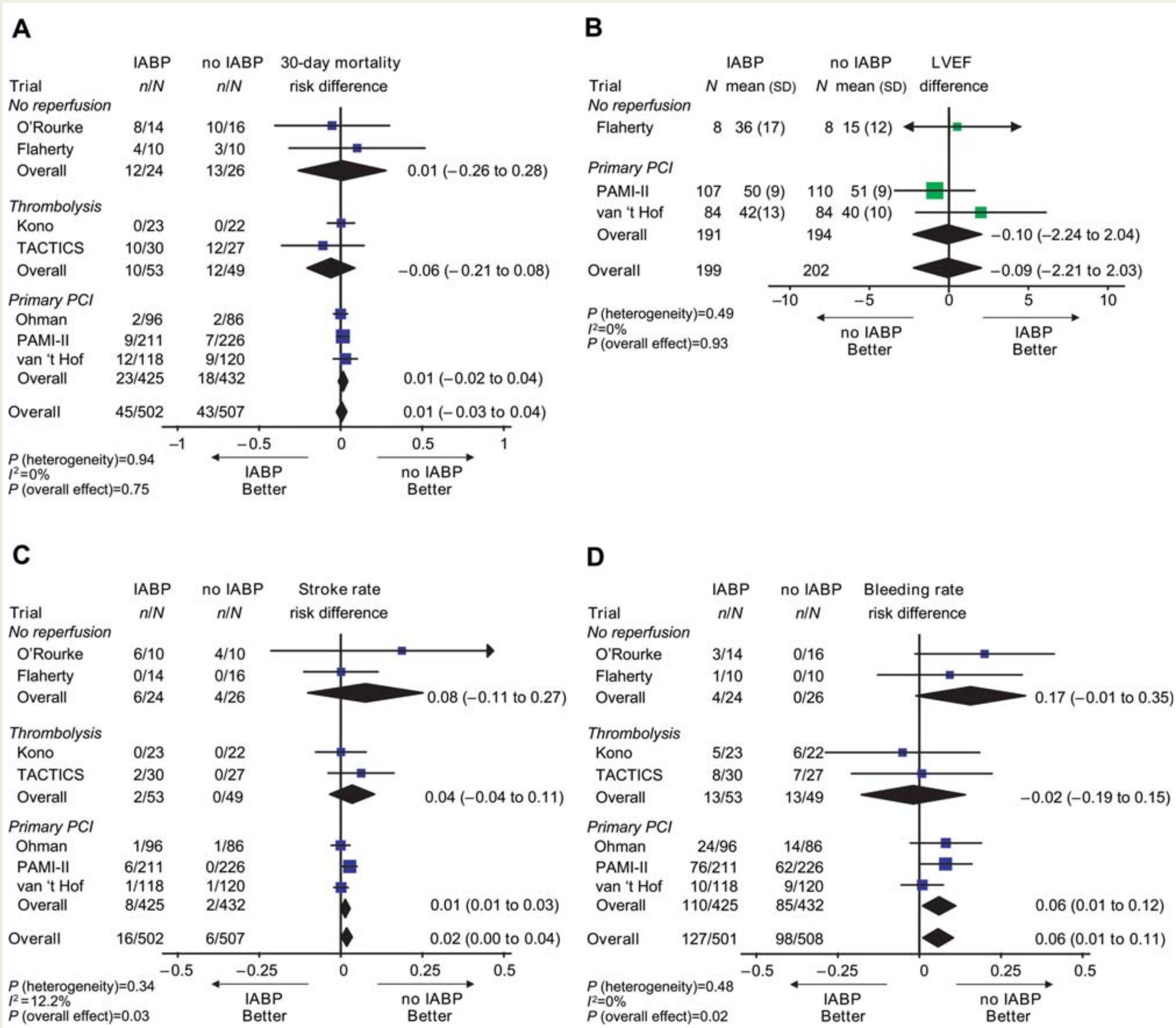

Figure 2 Meta-analysis of randomized clinical trials of IABP therapy in STEMI. All meta-analyses show effect estimates for the individual trials, for each type of reperfusion therapy and for the overall analysis. The size of each square is proportional to the weight of the individual trial. (*A*) The risk differences in 30 day mortality. (*B*) The mean differences in left ventricular ejection fraction (LVEF). (*C* and *D*) The risk differences in stroke and major bleeding rate. IABP, intra-aortic balloon counterpulsation; PCI, percutaneous coronary intervention.

each treatment group, with the mean difference for three trials that reported on left ventricular function. Overall, IABP support in the setting of STEMI was not associated with a change in LVEF at follow up (mean difference −0.1%; 95% CI, −2.2 to 2.0%; $P = 0.93$). *Figure 2C* and *D* shows the absolute numbers of stroke and bleeding in each treatment group, together with the respective absolute risk differences for each trial. Overall, the use of IABP was associated with an increased stroke rate of 2% (95% CI, 0–4%; $P = 0.03$) and an increased bleeding rate of 6% (95% CI, 1–11%; $P = 0.02$). Analyses by type of reperfusion therapy yielded similar results to those of the comprehensive analyses. There was no evidence of heterogeneity across the seven trials. None of the funnel plots showed skewed distributions, suggesting that no publication bias was involved.

Meta-analysis of cohort studies of intra-aortic balloon pump therapy in STEMI patients with cardiogenic shock

Nine cohort studies of IABP therapy in STEMI patients with cardiogenic shock included a total of 10 529 patients.[20–29] *Table 4* shows the study characteristics. Patients in the IABP group were younger (66 vs. 73 years) and more often male (63 vs. 53%). *Figure 3A* shows the absolute numbers of deaths in each treatment group, with the absolute risk difference for each cohort study. The thrombolysis studies showed adjunctive IABP therapy to be associated with an absolute decrease in 30 day mortality of 18% (95% CI, 16–20%; $P < 0.0001$). Contrariwise, the primary PCI studies showed IABP therapy to be associated with an absolute increase

Table 4 Characteristics of cohort studies of intra-aortic balloon pump therapy in STEMI complicated by cardiogenic shock

Study	No. of Patients	Type of reperfusion	Setting	Period	Cardiogenic shock definition	Mean age (years)		Male sex (%)	
						IABP	Control	IABP	Control
Moulopoulos et al.[22]	49	No reperfusion	Single centre	<1985	SysRR ≤80, urine output <20 mL/h, clinical signs of hypoperfusion	60	61	85	87
Stomel et al.[23]	64	Thrombolysis/rescue PCI	Single centre	1985–1991	SysRR ≤80 unresponsive to fluids CI ≤2.0 L/min/m^2, PCWP ≥18 mmHg, clinical signs of hypoperfusion	66§	66§	45*	62*
Kovack et al.[24]	46	Thrombolysis/rescue PCI	Multicentre	1985–1995	SysRR ≤90 unresponsive to fluids, CI ≤2.2 L/min/m^2, clinical signs of hypoperfusion	62	64	59	63
Bengtson et al.[25]	200	Thrombolysis/rescue PCI	Single centre	1987–1988	≥30 min sysRR <90 unless IABP/ pressors, CI ≤2.2 L/min/m^2 and PCWP ≥18, clinical signs of hypoperfusion	64	67	–	–
Waksman et al.[26]	41	Thrombolysis/rescue PCI	Single centre	1989	SysRR ≤90 unresponsive to fluids, clinical signs of hypoperfusion	66	68	70	71
GUSTO-I[27]	310	Thrombolysis/rescue PCI	Multicentre	1990–1993	SysRR ≤90 unresponsive to fluids, CI ≤2.2 L/min/m^2, clinical signs of hypoperfusion	64	68	68	62
NRMI-2[28†]	8671	Thrombolysis/rescue PCI or primary PCI	Multicentre	1994–1998	SysRR ≤90 unresponsive to fluids, clinical signs of hypoperfusion	67*	74*	61*	51*
SHOCK registry[29]	856	Thrombolysis/rescue PCI	Multicentre	1995–2000	SysRR ≤90 unresponsive to fluids, CI ≤2.2 L/min/m^2, clinical signs of hypoperfusion	65§*	72§*	67§*	60§*
AMC CS cohort[20,21]	292	Primary PCI	Single centre	1997–2005	SysRR ≤90 unresponsive to fluids, CI ≤2.2 L/min/m^2, clinical signs of hypoperfusion	65	62	68	66

IABP, intra-aortic balloon pump; STEMI, ST-elevation myocardial infarction; sysRR, systolic blood pressure (mmHg); NR, not reported; CI, cardiac index; PCI, percutaneous coronary intervention, LV left ventricle.
*$P < 0.05$.
†The NRM1-2 study reported about a thrombolysis and a primary PCI cohort.
§Calculated from the extracted data.

in 30 day mortality of 6% (95% CI, 3–10%; $P = 0.0008$). There was statistically significant heterogeneity across the trials ($I^2 = 94\%$). The funnel plot did not show a skewed distribution.

Figure 3B shows the revascularization rates [rescue PCI and coronary artery bypass grafting (CABG)] for the seven cohorts of STEMI patients with cardiogenic shock treated with thrombolysis. The revascularization rate in IABP-treated patients (39%) exceeded that in control patients (9%), with a relative risk of 4.0 (95% CI, 3.6–4.5; $P < 0.001$).

Discussion

We conducted two meta-analyses comparing IABP therapy with no IABP therapy for the treatment of STEMI and the treatment of STEMI complicated by cardiogenic shock. The principal findings of the meta-analysis of randomized clinical trials of IABP therapy in STEMI showed no efficacy benefit of adjunctive IABP therapy. We neither observed a 30 day survival benefit nor improved LVEF. Instead, IABP therapy was associated with a significant absolute increase in the rates of stroke and bleeding of, respectively, 2 and 6%. These clinically relevant higher complication rates are not outweighed by any clinical benefit.

In the absence of randomized studies, we performed a separate meta-analysis of all available observational studies comparing IABP therapy vs. no IABP therapy in STEMI complicated by cardiogenic shock. The most striking observation in this meta-analysis was the heterogeneity in the effect estimates of IABP therapy between the thrombolysis and the primary PCI studies. The overall effect estimate in the thrombolysis cohorts favoured IABP therapy, whereas the overall effect estimate in the primary PCI cohorts disfavoured IABP therapy. This observation does not render support to the concept that potential beneficial effects of IABP on outcome in STEMI complicated by cardiogenic shock would be independent of the type of reperfusion therapy.

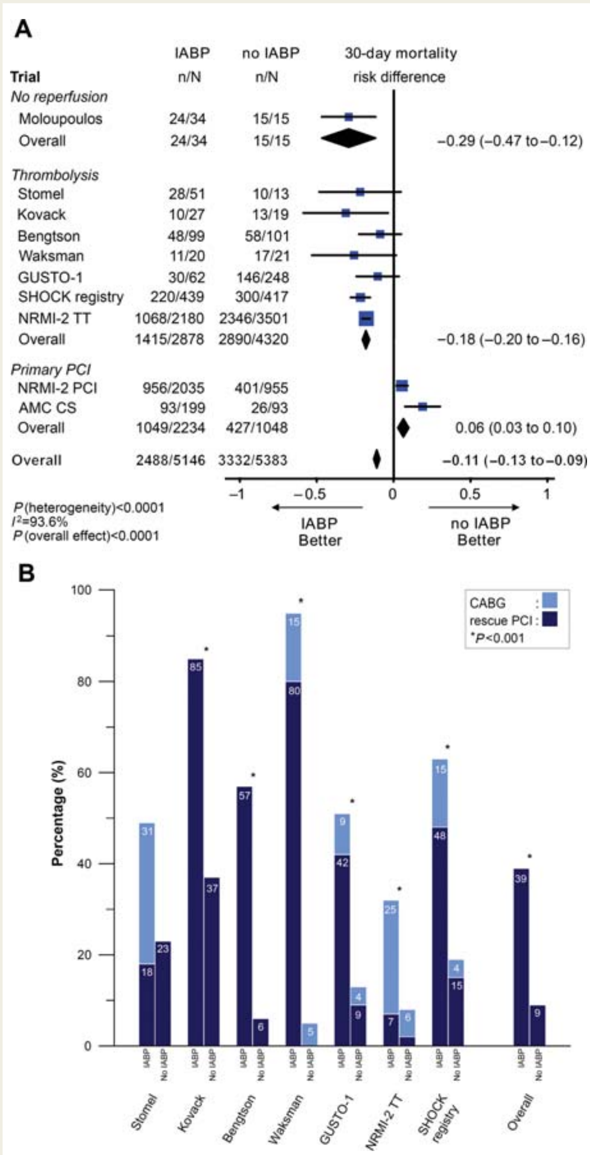

Figure 3 Meta-analysis of cohort studies of IABP therapy in STEMI complicated by cardiogenic shock. (*A*) The risk differences in 30 day mortality for the individual studies, for each type of reperfusion therapy and for the overall analysis. The size of each square is proportional to the weight of the individual study. (*B*) The revascularization procedures, i.e. rescue percutaneous coronary intervention (dark blue) and coronary artery bypass grafting (light blue) in the thrombolysis studies by IABP group and no IABP group, as well as the weighted overall revascularization rate. Single-coloured bars are used if separate figures for percutaneous coronary intervention and coronary artery bypass grafting could not be given. IABP denotes intra-aortic balloon counterpulsation, NRMI-2 TT denotes cohort from NRMI-2 study of patients treated with thrombolysis, and NRMI-2 PCI denotes cohort from NRMI-2 study of patients treated with primary percutaneous coronary intervention.

The observed beneficial effect of IABP therapy as an adjunct to thrombolysis would support the rationale for IABP therapy of myocardial and organ recovery.[31] Furthermore, it would support the hypothesis that IABP increases the efficacy of thrombolytic therapy in STEMI patients with cardiogenic shock by increasing coronary perfusion.[32] However, there are at least three other explanations for the observed lower mortality in the IABP group in this setting. First, the IABP-treated patients were on average 7 years younger and the frequency of men was 10% higher. As known from the current literature, the odds for mortality increase by 49–60% for every 10 years increase in age.[33,34] Also, men have a lower clinical risk profile than women, particularly in the setting of cardiogenic shock.[35] Second, in the thrombolysis studies, co-treatment with coronary revascularization was substantially more frequent in patients who received IABP therapy than in patients who did not receive IABP therapy. The SHOCK trial clearly showed that revascularization effectively reduced mortality in cardiogenic shock patients.[36] The revascularization rates in the SHOCK trial in the emergent revascularization arm and the conservative medical treatment arm, respectively, were 87 and 25% (relative risk 3.4), whereas the rate of IABP therapy was 86% in both groups. In comparison, the overall revascularization rates in the thrombolysis studies from the meta-analysis in the IABP and no IABP group were 39 and 9% (relative risk 4.0), respectively. Third, in the thrombolysis studies, the sicker patients may have been considered too ill to benefit from IABP therapy and others may have died before they could receive IABP therapy. This phenomenon may have induced a severe bias towards poor outcomes in the 'no IABP' group. Selection bias tends to make treatment effects appear larger than they are and the size of these distortions can be as large or larger than the size of the effects that are being measured.[37] In summary, the lower mortality of the patients who received IABP adjunctive to thrombolysis can be explained by confounding and bias, rather than by a beneficial effect of IABP therapy *per se*.

The observed detrimental effect of IABP therapy as an adjunct to primary PCI in STEMI with cardiogenic shock is contrary to the expectation that IABP might improve survival in these patients. It would oppose the suggestion that the underutilization of IABP therapy is one of the causes of the remainingly high mortality in this setting.[9,10] However, there are two important issues that need to be addressed concerning the outcome of IABP therapy in the primary PCI cohorts. First, we cannot rule out the influence of confounders in non-randomized studies. Nevertheless, in the NRMI-2 cardiogenic shock cohort, IABP therapy was independently associated with a higher 30 day mortality after multivariate adjustment for age, several clinical risk factors, PCI, and CABG. Second, IABP therapy may have been preferentially given to patients in worse condition. In a catheterization setting, it is difficult to withhold patients from active treatment with IABP, even if their prognosis is extremely grim. Alternatively, the negative treatment effect of IABP therapy could also reflect a longer ischaemic time, as IABP support may have been used for transfer to a primary PCI facility. Either way, these phenomena may have induced a severe bias towards poor outcomes in the IABP group, which is in contrast to the bias noted in the thrombolysis studies. In summary, one cannot reliably distinguish between an unexpected, truly detrimental effect of IABP therapy as an adjunct to primary PCI in STEMI complicated by cardiogenic shock and the influence of bias and confounding inherent to cohort studies. Therefore, the results of this analysis must be interpreted cautiously.

Our findings may have several implications for the clinical practice guidelines and ongoing research. Currently, the ACC/AHA and ESC guidelines do not explicitly address the use of IABP therapy in high-risk STEMI. The pooled randomized data do not support IABP therapy in this setting. As many practitioners still use IABP therapy in high-risk STEMI patients, a guideline statement about IABP therapy according to the appropriate classification of recommendation and level of evidence should be considered for this indication.

Cardiogenic shock, when not quickly reversed by pharmacologic therapy, is listed in the ACC/AHA guidelines as a class IB recommendation.[7] The ESC guidelines also strongly recommend IABP therapy in STEMI with cardiogenic shock.[8] Our study challenges these recommendations. Combining both meta-analyses, one may conclude that there is insufficient evidence endorsing the current recommendation for IABP therapy in STEMI with cardiogenic shock. Hence, any recommendation for adjunctive IABP therapy at this time can be based on expert opinion only. Concomitant IABP therapy along with other various available pharmacologic and mechanical therapeutic means may have some specific indications in cardiogenic shock patients. However, this study implies that greater nuances with regard to IABP therapy in this setting are needed than given in the current guidelines.

Ultimately, to clarify its role in contemporary treatment of STEMI with cardiogenic shock, including stenting and the use of glycoprotein IIb/IIIa inhibitors,[38] a randomized controlled trial of IABP therapy vs. no support adjunctive to primary PCI should be undertaken. After all, mechanical cardiac assist, due to its intuitive and experimentally supported rationale, remains an appealing treatment strategy, especially, since mortality in cardiogenic shock is still unacceptably high. The recent introduction of percutaneous left ventricular assist devices is very promising.[39–41] They may be a superior alternative to IABP therapy. However, as we can learn from the TRIUMPH trial and two recent trials on mechanical cardiac assist, we should realize that improved haemodynamic status, either pharmacologically or mechanically induced, is not a surrogate marker for survival.[39,42,43] Therefore, also for these new devices, we need evidence from properly powered randomized controlled trials with regard to their effect on outcome, before we herald these devices as a new therapeutic option. Although virtually all trials in STEMI with cardiogenic shock were prematurely halted, the SHOCK trial and the recent TRIUMPH trial prove that randomized controlled trials can be executed in this important setting.[36,42]

Limitations

The meta-analysis of randomized trials in STEMI may have been hampered by the sample size. Nevertheless, the total sample size was sufficient to detect moderate reductions in 30 day mortality (i.e. from 10 to 5%). Moreover, the sample size for LVEF was relatively large for a study with a quantitative outcome parameter and sufficient to detect a difference of 2.5 absolute ejection fraction points. The limitations of the meta-analysis of cohort studies of IABP in STEMI complicated by cardiogenic shock are thoroughly detailed above.

Conclusions

The meta-analysis of randomized studies did not support the use of routine IABP in high-risk STEMI. The meta-analysis of cohort studies in the setting of STEMI complicated by cardiogenic shock supported IABP therapy adjunctive to thrombolysis. In contrast, the observational data did not support IABP therapy adjunctive to primary PCI. All available observational data concerning IABP therapy in the setting of cardiogenic shock is importantly hampered by bias and confounding. There is insufficient evidence endorsing the current guideline recommendation for the use of IABP therapy in the setting of STEMI complicated by cardiogenic shock. Our meta-analyses challenge the current guideline recommendations.

Conflict of interest: none declared.

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