REVIEW ARTICLE

Intraaortic balloon pump in patients with cardiogenic shock complicating myocardial infarction

A systematic review and meta-analysis of randomized trials

Sultan Altayyar[1,2], Awad Al-Omari[3,4], Abdulrahman M. Alqahtani[5], Bram Rochwerg[1], Sami Alnasser[6], Zuhoor Alqahtani[2], Alison Fox-Robichaud[1], Waleed Alhazzani[1,7]

1 Department of Medicine, Division of Critical Care, McMaster University, Hamilton, Canada
2 Department of Medicine, Prince Sultan Military Medical City, Riyadh, Saudi Arabia
3 Department of Critical Care, Security Forces Hospital, Riyadh, Saudi Arabia
4 Alfaisal University, Riyadh, Saudi Arabia
5 Department of Cardiology, University of Ottawa Heart Institute, Ottawa, Canada
6 Department of Cardiology, St Michael Hospital, University of Toronto, Toronto, Canada
7 Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Canada

KEY WORDS

cardiogenic shock, intraaortic balloon pump, meta-analysis, myocardial infarction, systematic review

ABSTRACT

INTRODUCTION Cardiogenic shock is associated with significant mortality, particularly when caused by myocardial infarction. Intraaortic balloon pump (IABP) is the primary hemodynamic adjunct in patients with cardiogenic shock; however, evidence suggests that IABP may not improve mortality in this population.

METHODS We conducted an electronic search of the Medline, EMBASE, and Cochrane trial registry databases. Two reviewers independently screened citations and identified eligible trials. The same reviewers abstracted data independently. We pooled the data using a fixed effect model and reported dichotomous outcomes as risk ratios (RRs) with 95% confidence intervals (CIs). Subsequently, we used the GRADE approach to judge the quality of evidence.

RESULTS We included 4 randomized trials with 735 patients. The use of IABP did not reduce the risk of death in patients with cardiogenic shock secondary to cardiac ischemia when compared with usual care (RR, 0.94; 95% CI, 0.79–1.13; $P = 0.52$; $I^2 = 0\%$; moderate confidence). The use of IABP was not associated with an increased risk of stroke (RR, 0.77; 95% CI 0.22–2.69; $P = 0.68$; $I^2 = 48\%$; very low confidence), limb ischemia (RR, 1.24; 95% CI, 0.59–2.59; $P = 0.58$; $I^2 = 0\%$; low confidence), or major bleeding (RR, 0.76; 95% CI, 0.34–1.72; $P = 0.52$; $I^2 = 0\%$; low confidence).

CONCLUSIONS The use of IABP in patients with cardiogenic shock complicating myocardial ischemia does not reduce mortality (moderate confidence) and is not associated with a higher risk of complications (very low to low confidence). The results should be interpreted with caution owing to limitations such as imprecision, risk of bias, and clinical heterogeneity.

Correspondence to:
Waleed Alhazzani, MD, MSc, FRCPC, McMaster University, Hamilton, Ontario, Canada, St. Joseph's Healthcare, 50 Charlton Ave., Hamilton, L8N 4A6, Ontario, Canada, phone: +1-905-522-1155, fax: +1-905-521-6068, e-mail: alhazzaw@mcmaster.ca
Received: December 24, 2014.
Revision accepted: February 18, 2015.
Published online: February 20, 2015.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2015; 125 (3): 181-190

Introduction Cardiogenic shock complicates approximately 7% to 10% of myocardial infarction (MI) events.[1] Despite the recent advances in the management of this condition, mortality remains high (40%–50%).[2,3] Intraaortic balloon pump (IABP) counterpulsation is the most common mechanical hemodynamic assist device; however, its role in cardiogenic shock has been the subject of ongoing debate.

The mechanism of action is related to the timing and frequency of balloon inflation and deflation. When the balloon inflates during diastole, blood is displaced into the proximal aorta driving blood into the coronary arteries. The effect

of IABP on coronary perfusion is variable with some studies finding little or no change in coronary blood flow,[4-6] while others reporting a significant increase.[6-8]

Subsequently, rapid balloon deflation during systole reduces aortic volume (afterload) by creating a vacuum-like effect. These effects are variable and may depend on the volume of the balloon, position in the aorta, heart rate, rhythm, and other factors.[7] The desired hemodynamic effects of IABP include a reduction in systolic blood pressure and an increase in aortic diastolic pressure, which ultimately improves coronary blood flow. The net result is lower heart rate and pulmonary capillary wedge pressure, and higher cardiac output.[7] Registry-based observational studies suggested that the use of IABP may improve hemodynamics in patients with cardiogenic shock and acute MI.[9,10]

A Cochrane review by Unverzagt et al.[11] included 3 randomized controlled trials (RCTs) comparing the use of IABP to standard of care. Given the relatively small sample size of included trials (190 patients), the results were imprecise to draw firm conclusions. Subsequently, a larger RCT (IABP SHOCK II) showed no effect on 30-day mortality when examining the effect of IABP.[3] International clinical practice guidelines recommend the use of IABP in the management of patients with cardiogenic shock caused by acute MI.[12,13] In the view of the recently published literature and the importance of this topic, a comprehensive systematic review is required to summarize and assess the quality of the existing evidence.

Methods

Study protocol We registered the study protocol in the PROSPERO international register of systematic reviews (PROSPERO 2014. CRD42014007056).[14] Subsequently, we published a study protocol that described in more detail our inclusion criteria, study methodology, quality assessment, and analysis plan.[15] We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Supplementary material online, *Table S1*).[16]

Search strategy We searched the EMBASE, MEDLINE, and CENTRAL databases from inception to November 2014. The search strategy is summarized in Supplementary material online, *Table S2*. We searched conferences and proceedings utilizing search engine provided by the McMaster University online library (PapersFirst).[17] We did not apply language or date restrictions.

Inclusion criteria Eligibility criteria included all of the following: 1) design: parallel group RCTs (crossover or pseudorandomized trials were not eligible); 2) population: adult patients with cardiogenic shock complicating acute MI; 3) intervention: IABP; studies that examined the effects of other mechanical support devices were excluded; 4) comparator: usual care including any or a combination of the following: fibrinolysis, percutaneous coronary intervention (PCI), or supportive care; 5) outcomes: all-cause mortality at hospital discharge, or if not available, the longest period at which mortality was measured is used; intensive care unit (ICU) length of stay (in days); stroke (ischemic or hemorrhagic); limb ischemia; major bleeding (any bleeding that requires transfusion of more than 2 units of blood, or that is associated with hemodynamic instability not explained by conditions other than bleeding).

In duplicate and independently, 2 of 3 reviewers selected articles by examining titles and abstracts and then full texts after identifying potentially relevant articles. We used κ statistic to measure the agreement between reviewers.[18]

Data collection and quality assessment In duplicate and independently, 2 reviewers (SA and AA) abstracted data on the design, population and demographics, intervention, comparison, and outcomes. WA and BR completed the risk of bias assessment using the Cochrane risk of bias tool. The methodology used to assess quality of evidence is described in detail in the study protocol.[15] For each of the outcomes, we independently rated the quality of evidence and confidence in effect estimates using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[19] Disagreement was resolved by discussion and consensus.

Data synthesis and analysis All statistical analyses were conducted using the RevMan 5.1 software (Review Manager [Computer program]. Version 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011). Using a fixed effect model and applying inverse variance weighting, we combined data from all trials to estimate the pooled risk ratio (RR) and associated 95% confidence intervals (CIs). The fixed effect model is probably a more conservative approach than the random effects model when a large dominating study is included in the analysis.[20] We conducted the test for subgroup interaction using a test for heterogeneity between the subgroups of interest. The I^2 statistic and P values were calculated for each subgroup interaction test.

We assessed statistical heterogeneity using the I^2 statistic[21] and interpreted substantial heterogeneity as an I^2 of more than 50%. Although we planned to conduct the Egger test and visually examine funnel plots, we could not reliably assess for publication bias owing to a small number of included trials.

Results

Trial identification Our initial search identified 244 citations, of which 10 full-text articles were assessed for eligibility, and after the application of eligibility criteria, 6 articles were excluded (FIGURE 1). Four RCTs met the eligibility criteria and were included in the quantitative and qualitative syntheses.[3,22-24] One trial was published in Spanish, and a Spanish-speaking reviewer completed data abstraction.[24] The agreement

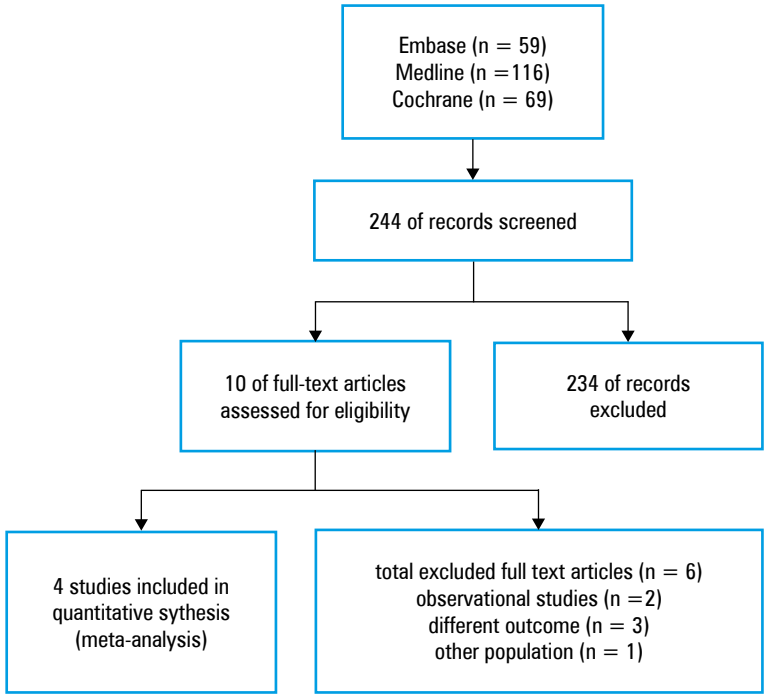


FIGURE 1 Study flow: diagram showing the process of study selection and exclusion

on eligible studies after full-text assessment was perfect (κ = 1.0).

Characteristics of studies The characteristics of the included trials are presented in TABLE 1. The trials included adult patients with cardiogenic shock secondary to acute MI. Anterior MI was the cause in 55% of all randomized patients (range, 42%–77%). The definition of cardiogenic shock was consistent across the included studies, but not identical. One trial mandated the use of pulmonary artery catheter measurements to diagnose cardiogenic shock,[24] while other trials did not require them as eligibility criteria. In the IABP-SHOCK II trial,[3] the mean age of participants was marginally higher than in the other trials (TABLE 1). One trial used fibrinolysis for all randomized patients, and only 38.6% of participants underwent PCI.[22] Although a standardized protocol for administering the drugs was provided, the choice of fibrinolytic agent was left to the discretion of the treating physician. The majority of patients (>90%) received PCI in the other 3 trials.[3,23,24] In addition, all patients received aspirin and an anticoagulation agent. In the largest trial (IABP-SHOCK II), IABP was inserted either before or immediately after PCI. One-to-one electrocardiographic triggering was used as the initial setting, and this ratio was maintained until there was sustained hemodynamic stabilization. The description of the IABP intervention in other trials is summarized separately in Supplementary material online, *Table S3*.

In all trials, crossover to IABP was allowed if patients in the control group developed mechanical complications (eg, ventricular septal defect or papillary muscle rupture).

Risk of bias Using the Cochrane risk of bias tool, 3 trials were judged to be at a high risk of bias, which is primarily due to a lack of blinding. As the adverse event outcomes were not based on clear criteria, we judged the risk of performance and ascertainment biases to be high for these outcomes. One trial was determined to be at a low risk of bias despite the lack of blinding.[3] In this trial, the outcomes of interest were rigorously defined; hence, we felt that the assessment and adjudication of the outcomes are less likely to be influenced by the lack of blinding. Upon evaluating mortality outcome, we assumed that the lack of blinding is unlikely to increase the risk of performance or ascertainment biases. Accordingly, we determined the risk of bias to be low for the mortality outcome across all trials. Finally, owing to a lack of information, we could not reliably assess the randomization method or concealment in 1 trial.[24] The details and individual components of the risk of bias are shown in Supplementary material online, *Figure S1*.

Pooled outcome A total of 4 RCTs (735 patients) reported mortality as an outcome.[3,22-24] Only 1 trial reported hospital mortality.[23] Two trials reported mortality at 30 days,[3,22] and 1 trial did not specify the time at which mortality was measured.[24] The use of IABP did not reduce the risk of death when compared with usual care (RR, 0.94; 95% CI, 0.79–1.13; P = 0.52; I^2 = 0%; moderate confidence; FIGURE 2).

Two RCTs[3,23] with a total of 638 patients reported the ICU length of stay. However, given the large unexplained statistical heterogeneity (I^2 = 71%), we did not report pooled estimates. The ICU length of stay was not significantly different in both trials (mean difference [MD], 0.00 days; 95% CI, –0.42 to 0.42; P = 1.00)[3] and (MD, –6.00 days; 95% CI, –12 to 0.02; P = 0.05).[23] Reinfarction was only reported in 1 trial; the use of IABP did not reduce the risk of reinfarction during hospital stay (RR, 2.24; 95% CI, 0.70–7.18; P = 0.16).[3]

Adverse events Three trials with 660 patients reported stroke, limb ischemia, and bleeding outcomes. Overall, the use of IABP was not associated with a statistically significant increase in the risk of stroke (RR, 0.77; 95% CI, 0.22–2.69; P = 0.68, I^2 = 48%; very low confidence), limb ischemia (RR, 1.24; 95% CI, 0.59–2.59; P = 0.58; I^2 = 0%; low confidence), or major bleeding (RR, 0.76; 95% CI, 0.34–1.72; P = 0.52; low confidence) (FIGURE 2). Of note, the event rate was low for all 3 outcomes (TABLE 1). All outcomes including confidence assessment results can be found in TABLE 2.

Subgroup analyses We defined all subgroup analyses a priori in our published protocol;[15] however, the lack of data and a small number of studies limited our ability to assess subgroup differences. The results are summarized in FIGURE 3.

TABLE 1 Characteristics of included trials

Study (No. of patients)	Population	Definition of cardiogenic shock	Intervention	Reperfusion method	Outcomes	Funding
Arias, 2005 (n = 40) Mexico	adult with STEMI age, 65.5 years male, 26 (65%)	SBP <90 mmHg for at least 1 h (refractory to administration of fluids), PCWP >18 mmHg, and a CI ≤2.2 l/min/m^2	IABP (n = 31) standard of care (n = 9)	PCI	mortality	NA
Ohman, 2005 (n = 57) USA, Australia, Europe	adults (21 to 85 years) with cardiogenic shock secondary to AMI age, 67.5 years males, 43 (75%) anterior MI, 23 (77%) in IABP group and 15 (56%) in control	anterior MI complicated by hypotension, defined as SBP ≤90 mmHg for ≥30 min or any MI complicated by hypotension (SBP ≤110 mmHg for ≥30 min, HR ≥100 bpm) or acute heart failure with SBP ≤100 mmHg for ≥30 min; unresponsive to fluid replacement and associated with signs of hypoperfusion or CI ≤2.2 l/min/m^2 (2.5 l/min/m^2 if receiving inotropic drugs)	IABP inserted within 3 h of shock onset (n = 30) standard of care (n = 27)	fibrinolysis: alteplase 15 mg bolus, then 0.75 mg/kg over 30 min, then 0.5 mg/kg over the next hour. or streprokinase 1.5 million U over 1 h or reteplase 10 units IV over 2 min (total 2 doses) angioplasty (38.6%) stent implantation (24.6%)	mortality (30 days, 6 months) stroke limb ischemia bleeding	grant from Datascope corporation
Prondzinsky, 2010 (n = 45) Germany	adults with cardiogenic shock secondary to AMI all patients underwent PCI age, 62.1 years male, 14 (74%) anterior MI, 22 (55%) APACHE II, 21.7	signs of organ hypoperfusion with one of the following: SBP ≤90 mmHg for at least 30 min or hypotension requiring inotropic/ vasopressor therapy at a HR ≥60/min or a CI ≤2.2 l/min/m^2	IABP and standard of care (n = 23) standard of care (n = 22)	PTCA (90%) stent implantation (85%)	APACHE II score hemodynamic values inflammatory markers plasma BNP level	South Cleveland Heart Fund
Thiele, 2012 (n = 600) USA	adults with cardiogenic shock secondary to AMI age, 70 years male, 202 (67.1%) anterior MI, 136 (45.1) in IABP and 116 (38.79%) in control	SBP <0 mmHg for more than 30 minutes or needed infusion of catecholamines to maintain an SBP >90 mmHg and presence of clinical signs of pulmonary congestion and evidence of impaired end-organ perfusion	IABP and standard of care (n = 301) standard of care alone (n = 299)	PCI (95.8%) fibrinolysis (8%) CABG (1%)	mortality at 30 days stroke limb ischemia bleeding reinfarction	funded by the German Research Foundation, Teleflex and Maquet Cardiopulmonary

Abbreviations: AMI, acute myocardial infarction; APACHE, acute physiology and chronic health evaluation; BNP, brain natriuretic peptide; CABG, coronary artery bypass graft; CI, cardiac index; HR, heart rate; IABP, intraaortic balloon pump; MI, myocardial infarction; NA, not available; PCI, percutaneous coronary intervention; PCWP, pulmonary capillary wedge pressure; PTCA, percutaneous transluminal coronary angioplasty; SBP, systolic blood pressure; STEMI, ST-segment-elevation myocardial infarction

Study	IABP		Control			Risk ratio	Risk ratio
	event	total	event	total	weight	M–H, fixed, 95% CI	M–H, fixed, 95% CI
mortality							
Thiele, 2012	119	300	123	298	84.5%	0.96 (0.79–1.17)	
Arias, 2005	10	31	5	9	5.3%	0.58 (0.27–1.26)	
Ohman, 2005	8	30	9	27	6.5%	0.80 (0.36–1.78)	
Prondzinsky, 2010	7	19	6	21	3.9%	1.29 (0.53–3.16)	
subtotal (95% CI)		**380**		**355**	**100%**	**0.94 (0.79–1.13)**	
total events	144		143				
heterogeneity: $\chi^2 = 2.17$, $df = 3$ ($P = 0.54$); $I^2 = 0\%$							
test for overall effect: $Z = 0.64$ ($P = 0.52$)							
stroke							
Thiele, 2012	2	300	5	298	90.3%	0.40 (0.08–2.03)	
Ohman, 2005	2	12	0	10	9.7%	4.23 (0.23–79.10)	
Prondzinsky, 2010	0	19	0	21		not estimable	
subtotal (95% CI)		**331**		**329**	**100%**		
total events	4		5				
heterogeneity: $\chi^2 = 1.93$, $df = 1$ ($P = 0.16$); $I^2 = 48\%$							
test for overall effect: $Z = 0.41$ ($P = 0.68$)							
major bleeding							
Thiele, 2012	10	300	13	298	100%	0.76 (0.34–1.27)	
Ohman, 2005	0	12	0	10		not estimable	
Prondzinsky, 2010	0	19	0	21		not estimable	
subtotal (95% CI)		**331**		**329**	**100%**		
total events	10		13				
heterogeneity: not applicable							
test for overall effect: $Z = 0.65$ ($P = 0.51$)							
limb ischemia							
Thiele, 2012	13	300	10	298	82.7%	1.29 (0.58–2.90)	
Ohman, 2005	0	12	1	10	13.4%	0.28 (0.01–6.25)	
Prondzinsky, 2010	1	19	0	21	3.9%	3.30 (0.59–2.95)	
subtotal (95% CI)		**331**		**329**	**100%**		
total events	14		11				
heterogeneity: $\chi^2 = 1.26$, $df = 2$ ($P = 0.53$); $I^2 = 0\%$							
test for overall effect: $Z = 0.56$ ($P = 0.58$)							

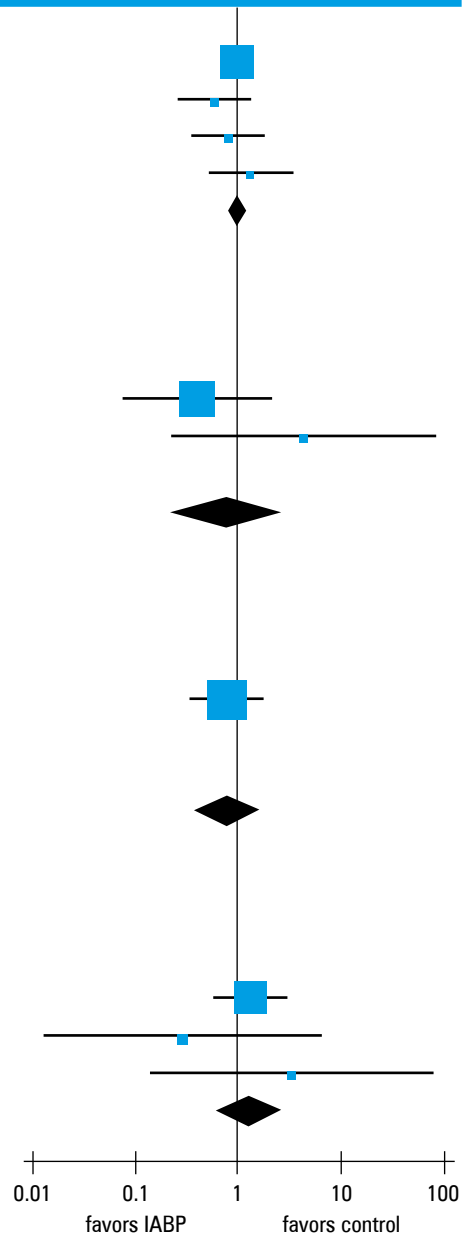


FIGURE 2 Forest plot showing the pooled effect estimates for the trials comparing the use of intraaortic balloon pump to usual care on the following outcomes: mortality, stroke, major bleeding, and limb ischemia
Abbreviations: CI, confidence interval

Sensitivity analyses All sensitivity analyses were specified a priori in the study protocol.[15] Using random-effects model did not significantly change the results for each of the outcomes. No eligible studies in an abstract form were identified; hence, we did not proceed with the second analysis. When excluding studies at a high risk of bias, only a single study was included;[3] however, the results did not change significantly. We decided to conduct a post hoc analysis excluding the study by Arias et al.[24] due to doubts about the randomization methods; however, this did not alter the results (RR, 0.96; 95% CI 0.80–1.16; $P = 0.69$; $I^2 = 0\%$).

Quality of evidence Using the GRADE approach, we judged the quality of evidence for the mortality outcome to be moderate (moderate confidence), mainly owing to concerns about imprecision. We lowered the quality of evidence for bleeding and limb ischemia outcomes (low confidence); this was primarily due to imprecision and risk of bias. Finally, we judged the quality of evidence for the stroke outcome to be very low (very low confidence). The results are presented in the form of evidence profile in TABLE 2.

Discussion The findings from this meta-analysis are consistent with the results of the most recent trial.[3] The use of IABP is not associated with a significant reduction in mortality in patients with cardiogenic shock secondary to acute MI. Furthermore, the risk of stroke, limb ischemia, and major bleeding was not significantly higher with IABP use.

These findings are based on combining the results of 4 RCTs.[3,22-24] While the previous systematic review also suggested no mortality benefit, the results were limited by imprecision and low quality of evidence. In particular, that systematic

TABLE 2 Summary of quality of evidence

Quality assessment							No. of patients (%)		Effect		Quality	Importance
No. of studies	study design	risk of bias	inconsistency	indirectness	imprecision	other considerations	IABP	no IABP	relative (95% CI)	absolute (95% CI)		
mortality												
4	randomized trials	not serious	not serious	not serious	serious[a]	none	144/380 (37.9)	143/355 (40.3)	RR, 0.94 (0.71 to 1.13)	24 fewer per 1000 (from 52 more to 117 fewer)	moderate	critical
stroke												
3	randomized trials	serious[b]	serious[c]	not serious	serious[a]	none	4/331 (1.2)	5/329 (1.5)	RR, 0.77 (0.22 to 2.69)	3 fewer per 1000 (from 12 fewer to 26 more)	very low	critical
major bleeding												
3	randomized trials	serious[b]	not serious	not serious	serious[a]	none	10/331 (3.0)	13/329 (4.0)	RR, 0.76 (0.34 to 1.72)	9 fewer per 1000 (from 26 fewer to 28 more)	low	critical
limb ischemia												
3	randomized trials	serious[b]	not serious	not serious	serious[a]	none	14/331 (4.2)	11/329 (3.3)	RR, 1.24 (0.59 to 2.59)	8 more per 1000 (from 14 fewer to 53 more)	low	critical

a confidence interval is wide and crosses the unity line; **b** we lowered the quality of evidence for risk of bias due to lack of blinding; **c** we lowered the quality of evidence due to moderate heterogeneity, $I^2 = 48\%$

Abbreviations: RR, relative risk; others, see **FIGURE 2**

review prompted the authors to subsequently conduct the largest RCT to date.[3]

IABP has been available for use for more than 4 decades. It was considered the workhorse hemodynamic tool, given the benefit shown by observational studies,[9] device availability, and operator familiarity. In a meta-analysis of RCTs by Krischan et al.,[9] which included patients with acute MI without cardiogenic shock, the use of IABP did not reduce mortality at 30 days. However, they found higher rates of bleeding and ischemic complications, which is not shown in our analysis.

In view of our results, it is important to understand whether the lack of mortality benefit is related to the intervention, population, or other factors. Shiedt et al.[6] have shown that the use of IABP decreases the mean systolic and diastolic pressure by 25% and 35%, respectively. In addition, the use of other hemodynamic support devices failed to show mortality benefit over IABP.[11] Therefore, it is plausible to assume that it is not a device performance failure that led to neutral results. Reversing hemodynamic derangements is a crucial step in managing shock; however, other factors are also of great importance. First, the timing of the intervention in relation to the onset of shock and irreversible organ damage (ischemic time). Applying reperfusion strategy with PCI (as a comparable analogy), a lowering benefit is observed with longer ischemic time; in addition, desirable effects might be lost or revered (cause harm) when performed late.[25] While in most cases the onset of myocardial ischemia is heralded by symptoms, the onset of shock is usually ambiguous and can only be retrospectively estimated. An observational study by Abdelwahhab et al.[26] demonstrated benefit with using IABP before PCI as opposed to after PCI, which could be hypothesis-generating. Unfortunately, due to the lack of data, we were not able to conduct a subgroup analysis by timing of PCI use.

Organ injury after ischemia–reperfusion is a well-established theory.[27] It is known to trigger inflammation and systemic inflammatory response syndrome that could result in organ dysfunction independent of ischemia.[27] It is not known whether this mechanism could have any influence on shock resuscitative strategy or targets.

Whether the lack of related benefit is related to the mechanistic properties of the device or to the population in which it was applied remains unclear. This certainly draws our attention to studies that investigated the efficacy of other hemodynamic support devices (eg, left ventricular assist device) and failed to show mortality benefit.[11]

Despite the popularity of using IABP in the treatment of patients with cardiogenic shock, our meta-analysis showed that it does not improve patient-important outcomes (ie, mortality). Strengths of our systematic review include adherence to a prepublished study protocol, comprehensive search strategy, inclusion of RCTs rather than observational studies, adherence to

Study	IABP		Control			Risk ratio	Risk ratio
	event	total	event	total	weight	IV, fixed, 95% CI	IV, fixed, 95% CI
A. low risk of bias							
Thiele, 2012	119	300	123	298	85.5%	0.96 (0.79–1.17)	
subtotal (95% CI)		**300**		**298**	**85.5%**	**0.96 (0.79–1.17)**	
total events	119		123				
heterogeneity: not applicable							
test for overall effect: $Z = 0.40$ ($P = 0.69$)							
A. high or unclear of bias							
Arias, 2005	10	31	5	9	5.4%	0.58 (0.27–1.26)	
Ohman, 2005	8	30	9	27	5.1%	0.80 (0.36–1.78)	
Prondzinsky, 2010	0	19	0	21	4%	1.29 (0.53–3.16)	
subtotal (95% CI)		**80**		**57**	**14.5%**	**0.81 (0.51–1.30)**	
total events	25		20				
heterogeneity: $\chi^2 = 1.74$, $df = 2$ ($P = 0.42$); $I^2 = 0\%$							
test for overall effect: $Z = 0.87$ ($P = 0.39$)							
total (95% CI)		**380**		**355**	**100%**	**0.94 (0.78–1.12)**	
total events	144		143				
heterogeneity: $\chi^2 = 2.17$, df = 3 ($P = 0.54$); $I^2 = 0\%$							
test for overall effect: $Z = 0.70$ ($P = 0.48$)							
test for subgroup differences: $\chi^2 = 0.42$, $df = 1$ ($P = 0.52$); $I^2 = 0\%$							
B. fibrinolysis							
Ohamn, 2005	8	30	9	27	6.5%	0.80 (0.36–1.78)	
subtotal (95% CI)		**30**		**27**	**6.5%**	**0.80 (0.36–1.78)**	
total events	8		9				
heterogeneity: not applicable							
test for overall effect: $Z = 0.55$ ($P = 0.58$)							
B. PCI							
Arias, 2005	10	31	5	9	5.3%	0.58 (0.27–1.26)	
Prondzinsky, 2010	7	19	6	21	3.9%	1.29 (0.53–3.16)	
Thiele, 2012	119	300	123	298	84.3%	0.96 (0.79–1.17)	
subtotal (95% CI)		**350**		**328**	**93.5 %**	**0.95 (0.79–1.15)**	
total events	136		134				
heterogeneity: $\chi^2 = 2.01$, $df = 2$ ($P = 0.37$); $I^2 = 1\%$							
test for overall effect: $Z = 0.51$ ($P = 0.61$)							
total (95% CI)		**380**		**355**	**100%**	**0.94 (0.79–1.13)**	
total events	144		143				
heterogeneity: $\chi^2 = 2.17$, $df = 3$ ($P = 0.54$); $I^2 = 0\%$							
test for overall effect: $Z = 0.64$ ($P = 0.52$)							
test for subgroup differences: $\chi^2 = 0.18$, $df = 1$ ($P = 0.68$); $I^2 = 0\%$							

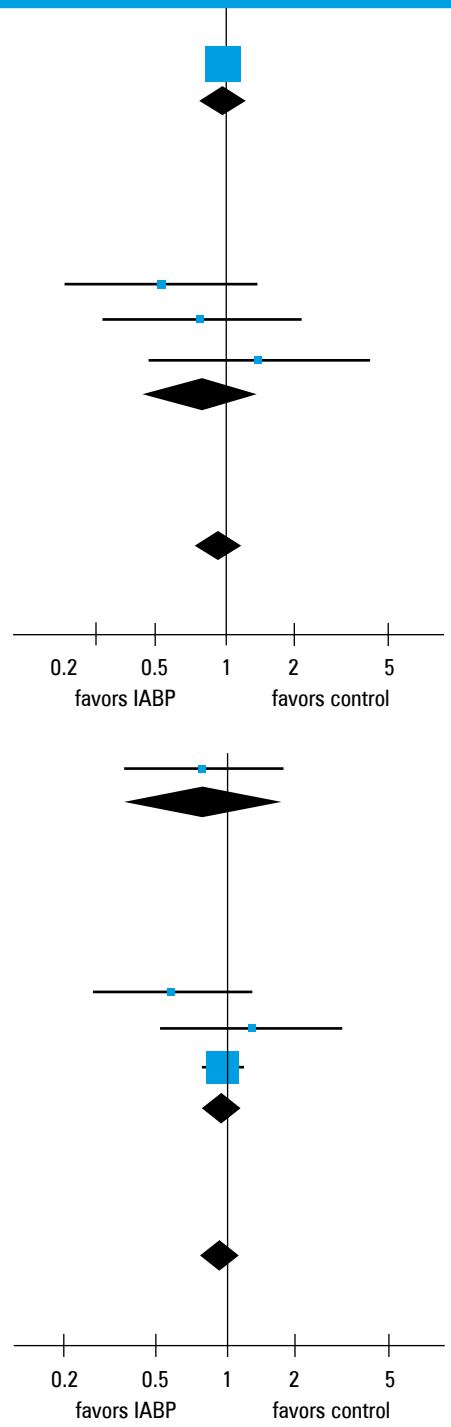


FIGURE 3 Subgroup analysis for mortality outcome; **A** – subgroup analysis by individual study risk of bias; **B** – subgroup analysis by reperfusion method (fibrinolysis vs percutaneous coronary intervention)
Abbreviations: see **FIGURE 2**

the PRISMA guidelines, and the use of GRADE methodology to assess the quality of evidence.

However, there are key limitations of the current literature that are worth discussing. First, owing to a small sample size and low event rate in the included RCTs, we were not able to reliably assess the risks of complications (harm). Hence, the quality of evidence for these outcomes was very low or low. A meta-analysis of observational studies reported a higher risk of adverse events with the use of IABP, including a higher risk of bleeding and ischemic complications.[9] We have low confidence in the estimates of adverse events provided by published RCTs. Second, the lack of some subgroup data in published trials limited our ability to conduct all subgroup analyses. Third, although we included only RCTs, 1 trial was published in Spanish and did not describe the randomization method[24]; in addition, the number of patients was not balanced in the 2 groups, which makes us question the randomization method used. For this purpose, we conducted a post hoc sensitivity analysis excluding the data of this study, but the results remained similar.

All trials included patients with evidence of acute MI and objective clinical and hemodynamic

parameters of cardiogenic shock; the generalizability of the results should be limited to this population.

While the use of IABP may be safe, there is no evidence to support its routine use in patients presenting with acute MI complicated by cardiogenic shock. Literature on high-risk patients undergoing coronary artery bypass grafting showed that the use of IABP may be of benefit in female patients with comorbidities.[28] It is unclear whether IABP has a beneficial effect in a specific subgroup, namely, in patients presenting with cardiogenic shock. Perhaps future studies should explore the potential of benefit in specific subgroups.

The results of our meta-analysis should be interpreted with caution, particularly when dealing with refractory cardiogenic shock or high-risk groups. None of the trials used IABP primarily as a rescue therapy for patients with cardiogenic shock and refractory hypotension. The generalizability of the results to this population is limited by indirectness. For instance, in our analysis, the pooled mortality rate in the control group was 40.3% (143 deaths out of 355 patients), which is lower than what is described in previous studies.[6] Furthermore, only 27% of the patients in the largest trial (IABP-SHOCK II) had a systolic blood pressure of less than 80 mmHg. On the contrary, it is challenging to conduct research (especially RCTs) when dealing with emergent and life-threatening conditions. Therefore, clinical decision making should be individualized, particularly when dealing with high-risk groups. An individual patient data meta-analysis or an RCT focusing on a high-risk population will be of great value.

Conclusions Moderate quality of evidence suggests that the use of IABP does not improve survival in patients with cardiogenic shock and acute MI. However, the results should not be used to guide clinical decision when dealing with a high-risk group or patients with refractory shock, as this population was not represented in the previously published RCTs. Low and very low quality of evidence suggests that the use of IABP is not associated with significant harm; however, these findings should be interpreted with caution as the included trials are underpowered to show any statistically significant difference. Larger trials with a homogenous population and cointerventions are required to confirm these observations.

Key messages The key messages of our paper are as follows: 1) prior systematic reviews on the use of IABP in patients with cardiogenic shock were limited by imprecision and quality of evidence; 2) a recent large RCT[3] suggested that the use of IABP in this population does not improve survival; 3) this systematic review and meta-analysis of RCTs suggests that the use of IABP in patients with cardiogenic shock complicating myocardial ischemia does not improve mortality (moderate quality of evidence); and 4) low and very low quality of evidence suggests that the use of IABP is not associated with a higher risk of complications.

Acknowledgments We would like to acknowledge the help of Dr. Itziar Etxeandia in data abstraction from a non-English study.

REFERENCES

1 Khalid L, Dhakam SH. A review of cardiogenic shock in acute myocardial infarction. Curr Cardiol Rev. 2008; 4: 34-40.

2 Fox KA, Steg PG, Eagle KA, et al. Decline in rates of death and heart failure in acute coronary syndromes, 1999-2006. JAMA. 2007; 297: 1892-1900.

3 Thiele H, Zeymer U, Neumann FJ, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med. 2012; 367: 1287-1296.

4 Port SC, Patel S, Schmidt DH. Effects of intraaortic balloon counterpulsation on myocardial blood flow in patients with severe coronary artery disease. J Am Coll Cardiol. 1984; 3: 1367-1374.

5 Williams DO, Korr KS, Gewirtz H, et al. The effect of intraaortic balloon counterpulsation on regional myocardial blood flow and oxygen consumption in the presence of coronary artery stenosis in patients with unstable angina. Circulation. 1982; 66: 593-597.

6 Scheidt S, Wilner G, Mueller H, et al. Intra-aortic balloon counterpulsation in cardiogenic shock. Report of a co-operative clinical trial. N Engl J Med. 1973; 288: 979-984.

7 Mueller H, Ayres SM, Conklin EF, et al. The effects of intra-aortic counterpulsation on cardiac performance and metabolism in shock associated with acute myocardial infarction. J Clin Invest. 1971; 50: 1885-1900.

8 Kern MJ, Aguirre FV, Tatineni S, et al. Enhanced coronary blood flow velocity during intraaortic balloon counterpulsation in critically ill patients. J Am Coll Cardiol. 1993; 21: 359-368.

9 Sjauw KD, Engstrom AE, Vis MM, et al. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? Eur Heart J. 2009; 30: 459-468.

10 Barron HV, Every NR, Parsons LS, et al. The use of intra-aortic balloon counterpulsation in patients with cardiogenic shock complicating acute myocardial infarction: data from the National Registry of Myocardial Infarction 2. Am Heart J. 2001; 141: 933-939.

11 Unverzagt S, Machemer MT, Solms A, et al. Intra-aortic balloon pump counterpulsation (IABP) for myocardial infarction complicated by cardiogenic shock. Cochrane Database Syst Rev. 2011: CD007398.

12 Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). Circulation. 2004; 110: e82-292.

13 Van de Werf F, Bax J, Betriu A, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J. 2008; 29: 2909-2945.

14 Waleed Alhazzani, Sultan Altayyar, Bram Ruchworg, et al. Intra-aortic balloon pump in patients with cardiogenic shock complicating myocardial infarction: a systematic review and meta-analysis of randomized trials. PROSPERO 2014:CRD42014007056 Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014007056. Accessed February 10, 2015.

15 Altayyar S, Rochwerg B, Alnasser S, et al. Intra-aortic balloon pump in patients with cardiogenic shock complicating myocardial infarction: a systematic review and meta-analysis of randomized trials (protocol). Syst Rev. 2014; 3: 24.

16 Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009; 339: b2535.

17 PapersFirst. http://library.mcmaster.ca/articles/papersfirst. Accessed November 12, 2014.

18 Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. Fam Med. 2005; 37: 360-363.

19 Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008; 336: 924-926.

20 Guyatt GH, Norris SL, Schulman S, et al. Methodology for the development of antithrombotic therapy and prevention of thrombosis guidelines: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012; 141: 53S-70S.

21 Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ. 2003; 327: 557-560.

22 Ohman EM, Nanas J, Stomel RJ, et al. Thrombolysis and counterpulsation to improve survival in myocardial infarction complicated by hypotension and suspected cardiogenic shock or heart failure: results of the TACTICS Trial. J Thromb Thrombolysis. 2005; 19: 33-39.

23 Prondzinsky R, Lemm H, Swyter M, et al. Intra-aortic balloon counterpulsation in patients with acute myocardial infarction complicated by cardiogenic shock: the prospective, randomized IABP SHOCK Trial for attenuation of multiorgan dysfunction syndrome. Crit Care Med. 2010; 38: 152-160.

24 Arias EA, Gonzalez-Chon O, Garcia-Lopez SM, et al. [Impact of the intra-aortic balloon pump in the mortality due to cardiogenic shock secondary to acute myocardial infarction]. Arch Cardiol Mex. 2005; 75: 260-266. Spanish.

25 Hochman JS, Lamas GA, Buller CE, et al. Coronary intervention for persistent occlusion after myocardial infarction. N Engl J Med. 2006; 355: 2395-2407.

26 Abdel-Wahab M, Saad M, Kynast J, et al. Comparison of hospital mortality with intra-aortic balloon counterpulsation insertion before versus after primary percutaneous coronary intervention for cardiogenic shock complicating acute myocardial infarction. Am J Cardiol. 2010; 105: 967-971.

27 Carden DL, Granger DN. Pathophysiology of ischaemia-reperfusion injury. J Pathol. 2000; 190: 255-266.

28 Wilczynski M, Krzych LJ, Bis J, et al. Effect of gender on efficacy of preoperative intra-aortic balloon pump in high risk patients undergoing surgical coronary revascularisation. Kardiol Pol. 2010; 68: 1361-1368.

ARTYKUŁ POGLĄDOWY

Kontrapulsacja wewnątrzaortalna u chorych we wstrząsie kardiogennym wikłającym zawał serca

Przegląd systematyczny i metaanaliza badań z randomizacją

Sultan Altayyar[1,2], Awad Al-Omari[3,4], Abdulrahman M. Alqahtani[5], Bram Rochwerg[1], Sami Alnasser[6], Zuhoor Alqahtani[2], Alison Fox-Robichaud[1], Waleed Alhazzani[1,7]

1 Department of Medicine, Division of Critical Care, McMaster University, Hamilton, Kanada
2 Department of Medicine, Prince Sultan Military Medical City, Riyadh, Arabia Saudyjska
3 Department of Critical Care, Security Forces Hospital, Riyadh, Arabia Saudyjska
4 Alfaisal University, Riyadh, Arabia Saudyjska
5 Department of Cardiology, University of Ottawa Heart Institute, Ottawa, Kanada
6 Department of Cardiology, St Michael Hospital, University of Toronto, Toronto, Kanada
7 Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Kanada

SŁOWA KLUCZOWE

kontrapulsacja wewnątrzaortalna, metaanaliza, przegląd systematyczny, wstrząs kardiogenny, zawał serca

STRESZCZENIE

WPROWADZENIE Wstrząs kardiogenny, zwłaszcza spowodowany zawałem serca, wiąże się z dużą śmiertelnością. Kontrapulsacja wewnątrzaortalna (*intraaortic balloon pump* – IABP) jest główną metodą wspomagania hemodynamicznego u pacjentów we wstrząsie kardiogennym; dane sugerują jednak, że IABP może nie zmniejszać śmiertelności u tych chorych.

METODY Przeprowadzono elektroniczną kwerendę w bazach danych Medline, EMBASE i Cochrane. Dwóch autorów niezależnie przejrzało opisy bibliograficzne i zidentyfikowało odpowiednie badania. Ci sami autorzy niezależnie ekstrahowali dane. Dane połączono stosując model z efektami stałymi, a wyniki dychotomiczne przedstawiono w postaci współczynników ryzyka (*risk ratio* – RR) z 95% przedziałami ufności (*confidence interval* – CI). Następnie zastosowano system GRADE do oceny jakości danych.

WYNIKI Uwzględniono 4 badania z randomizacją obejmujące 735 chorych. Stosowanie IABP, w porównaniu ze zwykłą opieką, nie zmniejszyło ryzyka zgonu chorych we wstrząsie kardiogennym wtórnym do niedokrwienia mięśnia sercowego (RR: 0,94; 95% CI: 0,79–1,13; p = 0,52; I^2 = 0%, ufność umiarkowana). Stosowanie IABP nie wiązało się ze zwiększonym ryzykiem udaru (RR: 0,77; 95% CI: 0,22–2,69; p = 0,68; I^2 = 48%; ufność bardzo mała), niedokrwienia kończyn (RR: 1,24; 95% CI: 0,59–2.59; p = 0,58; I^2 = 0%; ufność mała) ani poważnego krwawienia (RR: 0,76; 95% CI: 0,34–1,72; p = 0,52; I^2 = 0%; ufność mała).

WNIOSKI Stosowanie IABP u chorych we wstrząsie kardiogennym wikłającym niedokrwienie mięśnia sercowego nie zmniejsza śmiertelności (ufność umiarkowana) i nie wiąże się z większym ryzykiem powikłań (ufność bardzo mała lub mała). Wyniki należy interpretować ostrożnie ze względu na ograniczenia związane z małą precyzją ich oszacowania, ryzykiem błędu systematycznego i niejednorodnością kliniczną.

Adres do korespondencji:
Waleed Alhazzani, MD, MSc, FRCPC, McMaster University, Hamilton, Ontario, Kanada, St. Joseph's Healthcare, 50 Charlton Ave., Hamilton, L8N 4A6, Ontario, Kanada, tel.: +1-905-522-1155, fax: +1-905-521-6068, e-mail: alhazzaw@mcmaster.ca

Praca wpłynęła: 24.12.2014.
Przyjęta do druku: 18.02.2015.
Publikacja *online*: 20.02.2015.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2015; 125 (3): 181-190

Supplementary material online

Table S1. PRISMA Check List

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2,3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5

Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9,10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective	8

		reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9,10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7,8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10,11,12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of	3

		identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Table S2. Search Strategy

1. exp cardiogenic shock/
2. exp shock/
3. exp heart left ventricle failure/
4. 2 and 3
5. 1 or 4
6. exp intraaortic balloon pump/
7. 5 and 6
8. exp clinical trial/ or clin$ trial$.mp.
9. exp Randomized controlled trial/
10. exp Randomization/
11. Single-Blind Method/
12. Double-Blind Method/
13. exp Random Allocation/
14. RCT.tw.

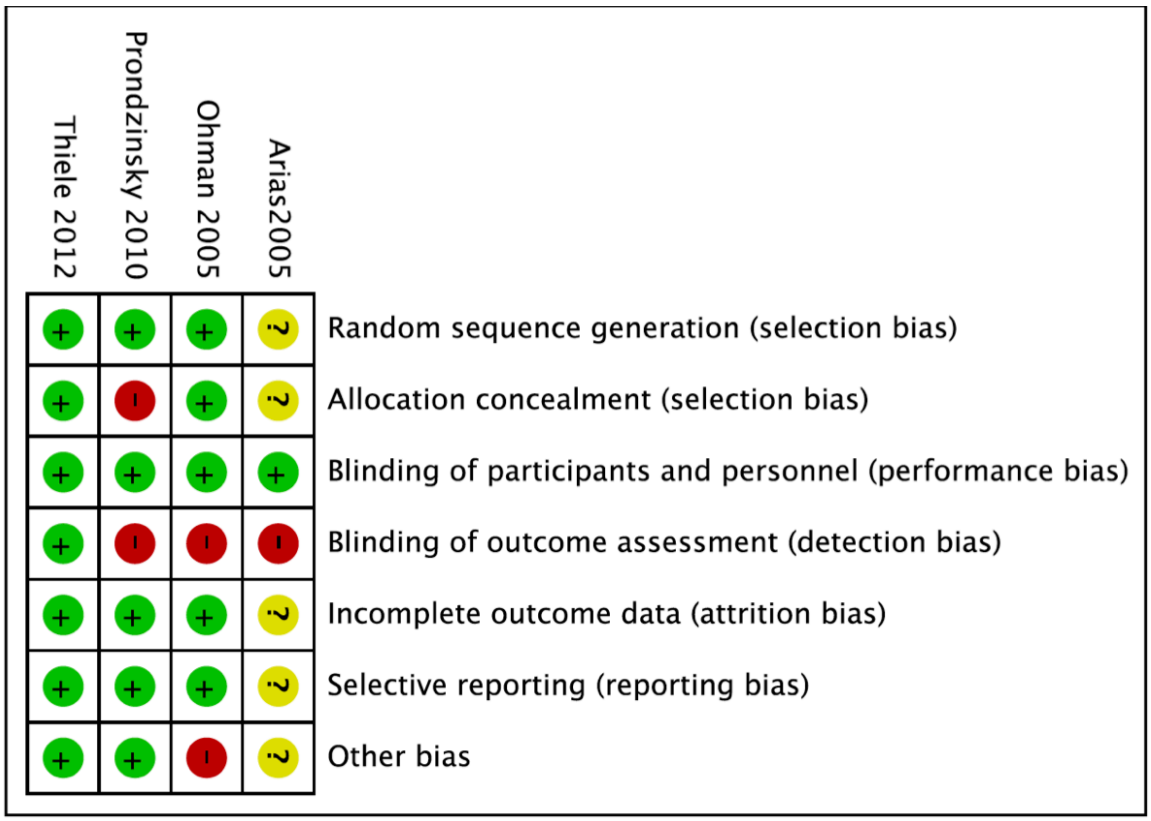
15. random$.mp.
16. (Single blind$ or Double blind$ or ((treble or triple) adj2 blind$)).tw.
17. comparative study/
18. controlled study/
19. Prospective study/
20. placebo:.mp.
21. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. 7 and 21

Table S3. Description of IABP use in included trials

Studies	Description of IABP use
Arias 2005	No description provided
Ohman 2005	The IABP catheter (Datascope, Inc., Montvale, New Jersey) was inserted with in 3 hours of receiving fibrinolytic therapy. Initial rate at 1:1 for 48 hours, weaning was done gradually over 12 hours. In patients who remained hypotensive (SBP<90mmHg) or developed ischemia the IABP was continued.
Prondzinsky 2010	A 40 mL balloon IABP (IABP System 97, Datacope; Fairfield, NJ) was inserted immediately after PCI. IABP device was continued for a minimum of 48 hrs. Rate and weaning strategy was not described.
Thiele 2012	IABP was inserted either before or immediately after PCI, 1:1 electrocardiographic triggering was used as initial the setting, this ratio was maintained until there was sustained hemodynamic stabilization.

IABP: intra-aortic balloon pump; PCI: primary percutaneous intervention; SBP: systolic blood pressure.

Figure S1. Summary of Risk of Bias


Thiele 2012
Prondzinsky 2010
Ohman 2005
Arias2005
Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias

Supplementary material online

Table S1. PRISMA Check List

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2,3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language,	5

		publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9,10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8

Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9,10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7,8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10,11,12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	3

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Table S2. Search Strategy

1. exp cardiogenic shock/
2. exp shock/
3. exp heart left ventricle failure/
4. 2 and 3
5. 1 or 4
6. exp intraaortic balloon pump/
7. 5 and 6
8. exp clinical trial/ or clin$ trial$.mp.
9. exp Randomized controlled trial/
10. exp Randomization/
11. Single-Blind Method/
12. Double-Blind Method/
13. exp Random Allocation/
14. RCT.tw.
15. random$.mp.
16. (Single blind$ or Double blind$ or ((treble or triple) adj2 blind$)).tw.
17. comparative study/

18. controlled study/
19. Prospective study/
20. placebo:.mp.
21. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. 7 and 21

Table S3. Description of IABP use in included trials

Studies	Description of IABP use
Arias 2005	No description provided
Ohman 2005	The IABP catheter (Datascope, Inc., Montvale, New Jersey) was inserted with in 3 hours of receiving fibrinolytic therapy. Initial rate at 1:1 for 48 hours, weaning was done gradually over 12 hours. In patients who remained hypotensive (SBP<90mmHg) or developed ischemia the IABP was continued.
Prondzinsky 2010	A 40 mL balloon IABP (IABP System 97, Datacope; Fairfield, NJ) was inserted immediately after PCI. IABP device was continued for a minimum of 48 hrs. Rate and weaning strategy was not described.
Thiele 2012	IABP was inserted either before or immediately after PCI, 1:1 electrocardiographic triggering was used as initial the setting, this ratio was maintained until there was sustained hemodynamic stabilization.

IABP: intra-aortic balloon pump; PCI: primary percutaneous intervention; SBP: systolic blood pressure.

Figure S1. Summary of Risk of Bias