



# Effectiveness of pulmonary artery catheter monitoring for patients with cardiogenic shock of various causes: a systematic review and meta-analysis

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**Background:** Cardiogenic shock is associated with significant morbidity and mortality. Invasive hemodynamic monitoring with pulmonary artery catheterization (PAC) can be useful in the assessment of changes in cardiac function and hemodynamic status; however, the benefits of PAC in the management of cardiogenic shock are not known well.

**Methods:** We performed a systematic review and meta-analysis of observational studies and randomized controlled trials, comparing in-hospital mortality between PAC and non-PAC groups of cardiogenic shock patients with various underlying causes. Articles were obtained from MEDLINE, Embase, and Cochrane CENTRAL. We reviewed titles, abstracts, and full articles and evaluated the quality of evidence using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) framework. We used a random-effects model to compare studies in terms of in-hospital mortality findings.

**Results:** We included twelve articles in our meta-analysis. Mortality among patients with cardiogenic shock was not significantly different between the PAC and the non-PAC groups [risk ratio (RR) 0.86, 95% confidence interval (CI): 0.73–1.02,  $I^2=100%$ ,  $P<0.01$ ]. Two studies investigating cardiogenic shock caused by acute decompensated heart failure determined lower in-hospital mortality in the PAC group than in the non-PAC group (RR 0.49, 95% CI: 0.28–0.87,  $I^2=45%$ ,  $P=0.18$ ). Six studies investigating cardiogenic shock of any cause determined lower in-hospital mortality in the PAC group than in the non-PAC group (RR 0.84, 95% CI: 0.72–0.97,  $I^2=99%$ ,  $P<0.01$ ). There was no significant difference in in-hospital mortality between the PAC and non-PAC groups of patients with cardiogenic shock secondary to acute coronary syndrome (RR 1.01, 95% CI: 0.81–1.25,  $I^2=99%$ ,  $P<0.01$ ).

**Conclusions:** Overall, our meta-analysis demonstrated no significant association between PAC monitoring and in-hospital mortality among patients managed for cardiogenic shock. The use of PAC in the management of cardiogenic shock caused by acute decompensated heart failure was associated with lower in-hospital mortality, but there was no association between PAC monitoring and in-hospital mortality among patients with cardiogenic shock caused by acute coronary syndrome.

**Keywords:** Pulmonary artery catheterization (PAC); pulmonary artery catheter monitoring; cardiogenic shock (CS); acute decompensated heart failure (ADHF)

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## Introduction

Cardiogenic shock (CS) is characterized by sustained hypotension and systemic hypoperfusion caused by a primary cardiac pump failure in one or both ventricles (1,2). The morbidity and mortality associated with CS remain significant, necessitating sophisticated management even from the time of diagnosis (3). CS is most often caused by acute myocardial infarction; however, there are several causes of shock, and the rates of CS from non-ischemic cardiomyopathy or cardiac causes other than primary myocardial dysfunction have been increasing (4). Therefore, the management of these types of shock is complicated.

During critical care of patients with circulatory failure, it is important to evaluate cardiac function—either directly or indirectly, respectively, through the monitoring of cardiac output or intracardiac pressure—to understand the underlying pathophysiological mechanisms, make a differential diagnosis, and establish appropriate therapeutic goals (5,6). Invasive hemodynamic monitoring with pulmonary artery catheterization (PAC) can be useful for assessing cardiac function (7). Moreover, PAC can provide continuous measurements of several hemodynamic variables, which can facilitate an accurate diagnosis and guide appropriate interventions. Nevertheless, according to the negative results of previous studies, including the ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial, the routine use of PAC in the management of acute decompensated

heart failure (ADHF) is not recommended (8). However, most such previous studies excluded patients with CS. A recent large cohort study demonstrated a decline in PAC use for CS despite improved outcomes (7). Recent studies have shown that PAC guidance is useful in the management of CS, especially in the contexts of specific subtypes, such as postcardiotomy shock or CS from ADHF (9,10). Meanwhile, other studies have yielded controversial findings associated with CS complicating acute myocardial infarction (11). These conflicting data regarding the role of PAC in the management of CS have warranted an organized synthesis of the existing research findings to identify the CS patient most suitable for PAC monitoring. We performed a systematic review and meta-analysis of PAC studies and compared in-hospital mortality among patients with CS of various causes. We present the following article in accordance with the PRISMA reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-22-1139/rc>).

## Methods

### Article selection

Eligible articles included patient groups diagnosed with ADHF or CS. The shock criteria were those used in the SHOCK (Should We Emergently Revascularized Occluded Coronaries for Cardiogenic Shock) and IABP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock II) trials. Patients were categorized dichotomously according to whether or not they underwent hemodynamic monitoring with PAC. The eligible study designs were observational studies or randomized controlled trials. Study outcomes must have included in-hospital mortality. We excluded nonhuman studies and articles using datasets with patients already included in our systematic review and meta-analysis.

### Search strategy

We searched for related articles published from 2008 through January 2022 using keywords, such as “pulmonary artery catheterization” and “cardiogenic shock,” in the MEDLINE, Cochrane CENTRAL, and Embase databases. We screened the articles according to our inclusion criteria. Two reviewers analyzed each article separately and reviewed the full text. Disagreements among reviewers were settled by discussions until consensus was reached, with the assistance of a third-party adjudicator if necessary. Data from meta-analyses were extracted by reviewers using prepiloted data collection forms ([Appendix 1](#)).

### Highlight box

#### Key findings

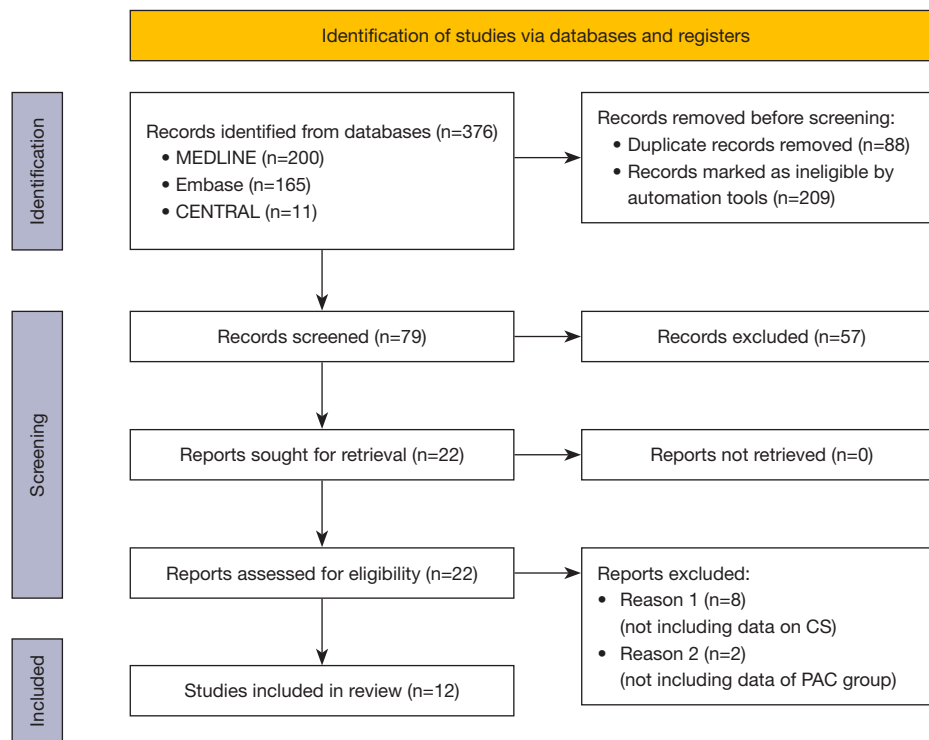
- There was no significant association between PAC monitoring and in-hospital mortality among patients managed for cardiogenic shock.

#### What is known and what is new?

- Invasive hemodynamic monitoring with PAC can be useful in the assessment of changes in cardiac function and hemodynamic status.
- We found that the use of PAC in the management of cardiogenic shock was not associated with lower in-hospital mortality, even though it might be beneficial among patients with cardiogenic shock caused by acute decompensated heart failure but not among patients with cardiogenic shock caused by acute coronary syndrome.

#### What is the implication, and what should change now?

- It is important to select patients with cardiogenic shock who may benefit from PAC.



**Figure 1** PRISMA flow diagram. CS, cardiogenic shock; PAC, pulmonary artery catheterization.

### Risk-of-bias assessment

Using the Office of Health Assessment and Translation (OHAT) risk-of-bias method, two reviewers assessed the risk of bias for each article and rated it as either low risk, high risk, or unclear risk of bias according to the following categories: selection bias, confounding bias, assessment of cointervention (performance bias), exclusion bias, detection bias, and selective reporting bias.

### Statistical analysis

A random-effects model with an inverse variance method was applied to the analysis to evaluate the effectiveness of PAC for each CS category (according to underlying cause), and Hartung–Knapp adjustment was conducted in the confidence-interval (CI) estimation of treatment effect (12). Chi-square and  $I^2$  analyses were conducted to determine statistical heterogeneity assessment, and the Paule-Mandel estimator and Q-profile methods were used for the point and interval estimations of  $\tau^2$  (13). Publication bias was evaluated using funnel plot. The R package ‘meta’ was used for data analysis in R (R Foundation for Statistical Computing, Vienna, Austria).

### Results

The search strategy flow diagram is shown in *Figure 1*. Seventy-nine articles were excluded according to the predetermined criteria. Twelve articles were included in the analysis, and approximately 1,854,569 patients met the eligibility criteria. Nine articles reported on retrospective cohort studies, and three reported on prospective cohort studies. No articles reporting on randomized controlled trials met the inclusion criteria. Entire articles were divided according to the cause of CS. Four articles included patients who were close to CS due to acute coronary syndrome (ACS) (14-17), two articles included patients with ADHF without ACS (18,19), and the causes of CS were not accurately described in the other six articles (20-25). The overall baseline characteristics are summarized in *Table 1* and *Table S1*. The mean age of the PAC group was 65.6 years, and there was a male preponderance (66.7%). The inclusion criteria of each study are also summarized in *Table 1*. In the studies that the cause of CS was not accurately described, the proportions of patients with ACS in the overall cardiogenic shock groups ranged from approximately 40% to 75%. These data were summarized in *Table 2*.

**Table 1** Summary and characteristics of included studies

Study ID	N (%)	Design	Population	Inclusion and exclusion criteria	Definition of CS	Mortality (PAC vs. no PAC)
Ashraf 2020 (14)	20,758: PAC 1,892 (9.1%), no PAC 18,866 (90.9)	Retrospective cohort, adjusted	National Inpatient Sample (2005–2014)	Inclusion: all patients with AMI-CS who underwent revascularization (PCI or tPA) with MCS	Not provided	31.18% vs. 28.62%
Ha 2018 (15)	89,718: PAC 5,503 (6.1%), no PAC 84,215 (93.9%)	Retrospective cohort, adjusted	National Inpatient Sample	Inclusion: patients who underwent coronary angiography for the management of AMI complicated by CS Exclusion: other forms of shock or underwent cardiac surgery, mission information	Not provided	34.9% vs. 29.4%
Vallabhajosyula 2020 (16)	364,001: PAC 29,609 (8.1%), no PAC 334,392 (91.9%)	Retrospective cohort, adjusted	National inpatient Sample (2000–2014)	Inclusion: patient admitted due to AMI-CS Exclusion: concomitant cardiac surgery or non-AMI etiology for CS	Not provided	46.3% vs. 42.0%
Oneill 2018 (17)	13,984: PAC 5,217 (37.3%), no PAC 8,767 (62.7)	Retrospective cohort	Registry that the patient in the US treated with an Impella device (2009–2016)	Inclusion: patient with AMI-CS who were implanted Impella device Exclusion: not provided	Systolic blood pressure <90 mmHg, or need for vasopressor to maintain a systolic blood pressure >90 mmHg	37% vs. 51%
Sotomi 2014 (18)	1,004: PAC 502 (50%), no PAC 502 (50%)	Prospective cohort, propensity score matched	ATTEND Registry enrolled patients (2007–2011)	Inclusion: acute heart failure syndrome patients who met the modified Framingham criteria Exclusion: patients aged <20 years, acute coronary syndrome, defined unsuitable by attending physicians	Not provided	1.4% vs. 4.4%
Rossello 2017 (19)	65: PAC 43 (66.1%), no PAC 22 (33.9%)	Prospective cohort, adjusted	Single-center registry (2005–2009)	Inclusion: first admission for CS Exclusion: acute coronary syndrome	Not provided	49% vs. 82%
Doshi 2018 (20)	842,369: PAC 71,452 (8.5%), no PAC 770,917 (91.5%)	Retrospective cohort, adjusted	National Inpatients sample (2005–2014)	Inclusion: hospitalization with CS Exclusion: younger than 18 years of age	Not provided	33.9% vs. 38.8%
Hernandez 2019 (21)	22,278: PAC 11,139 (50%), no PAC 11,139 (50%)	Retrospective cohort, (propensity score matched)	National Inpatient sample (2004–2014)	Inclusion: diagnosis of CS Exclusion: <18 years of age, missing mortality data	Not provided	34.9% vs. 37%
Ranka 2020 (22)	269,475: PAC 25,840 (9.6%), no PAC 243,635 (90.4%)	Retrospective cohort, adjusted	Nationwide readmissions Database (2016–2017)	Inclusion: hospitalizations with CS Exclusion: not provided	Not provided	25.8% vs. 39.5%
Sionis 2020 (23)	219: PAC 82 (37.4%), no PAC 137 (62.6%)	Prospective cohort	Nine hospitals in 8 European countries (Czech Republic, Denmark, Finland, Greece, Italy, Poland, Portugal, and Spain) (2010–2012)	Inclusion: patients aged >18 years within 6 hours from the identification of CS, with hypotension or severe low output syndrome Exclusion: shock after cardiac or noncardiac surgery, ongoing hemodynamically significant arrhythmia as the cause of hypotension	Systolic blood pressure <90 mmHg for 30 minutes; need for vasopressor therapy to maintain systolic blood pressure >90 mmHg; symptom and/or signs of systemic and/or pulmonary congestion; symptoms and/or signs of hypoperfusion (altered mental status/confusion, cold periphery, oliguria <0.5 mL/kg/h for the previous 6 hours, blood lactate >2 mmol/L)	42% vs. 34%
Osman 2021 (24)	124,440: PAC 62,220 (50%), no PAC 62,220 (50%)	Retrospective cohort, adjusted (propensity score matching)	National Inpatient Sample (2015–2018)	Inclusion: patient with CS Exclusion: patients who underwent only left heart catheterization, missing mortality, age, or sex data, younger than 18 years of age, patients who received concomitant cardiac surgery, transcatheter aortic valve replacement, mitral clipping, or catheter ablation during the same hospitalization; patients who died on the day of admission; patients with the diagnosis of primary pulmonary hypertension; patients who were admitted electively to the hospital; patients who received the IHM after or on the same day of receiving durable LVADs or HT	Not provided	24.1% vs. 30.6%
Sidhu 2017 (25)	106,258: PAC 7,440 (7%), no PAC 98,818 (93%)	Retrospective cohort, propensity score matching	National Inpatient sample (2010–2014)	Inclusion: diagnosis of CS Exclusion: not provided	Not provided	30.3% vs. 37.4%

CS, cardiogenic shock; PAC, pulmonary artery catheterization; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; tPA, tissue plasminogen activator; HT, heart transplantation; LVAD, left ventricular assist devices; MCS, mechanical circulatory support; IHM, invasive hemodynamic monitoring.

**Risk of bias**

Twelve articles were compared and analyzed according to the OHAT risk-of-bias assessment method; they were classified as either low risk, high risk, or unclear according to each category of bias, as shown in *Figure 2*. Publication bias assessment was performed by funnel plot analysis, which did not reveal significant asymmetries (*Figure S1*).

**Mortality**

Based on findings from the twelve articles in our meta-analysis, PAC application did not significantly impact in-

hospital mortality in the overall CS patient sample [risk ratio (RR) 0.86, 95% CI: 0.73–1.02,  $I^2=100\%$ ,  $P<0.01$ ] (*Figure 3*). However, two studies investigating CS due to ADHF determined a lower in-hospital mortality in the PAC groups than in the non-PAC groups (RR 0.49, 95% CI: 0.28–0.87,  $I^2=45\%$ ,  $P=0.18$ ). Additionally, six studies investigating CS of unspecified cause observed lower in-hospital mortality in the PAC groups than in the non-PAC groups (RR 0.84, 95% CI: 0.72–0.97,  $I^2=99\%$ ,  $P<0.01$ ). However, there was no significant difference in in-hospital mortality between the PAC and non-PAC groups among patients with CS caused by ACS (RR 1.01, 95% CI: 0.81–1.25,  $I^2=99\%$ ,  $P<0.01$ ).

**Quality of evidence**

The overall quality of the evidence was deemed to be low because of the high amount of observational data used.

**Discussion**

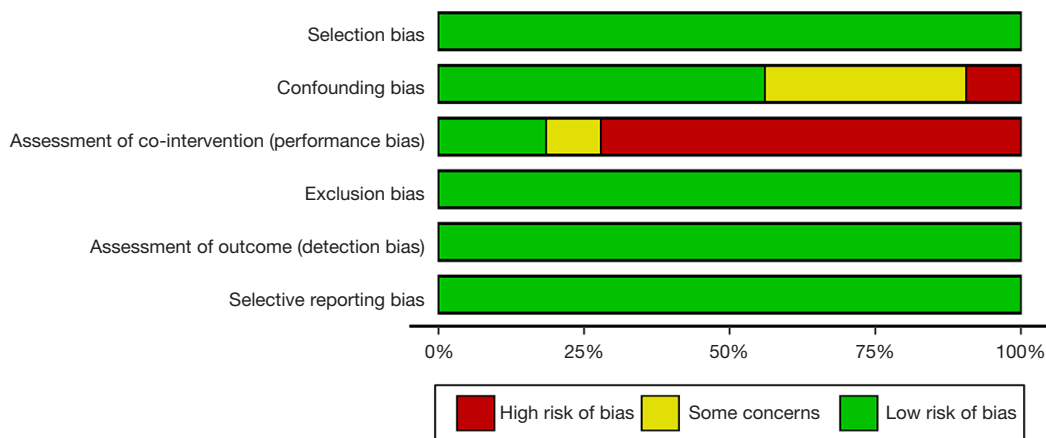
In this systematic review and meta-analysis comprising twelve observational studies, the use of PAC did not significantly impact in-hospital mortality among CS patients overall; however, a nonsignificant trend favoring PAC use was found. The results of this review were inconsistent with the results of earlier studies that found PAC to be useful in the management of CS. However, the results of this analysis highlight the need for more evidence based on prospective, randomized clinical trials investigating PAC use in the management of CS.

Since the publication of the ESCAPE trial data in

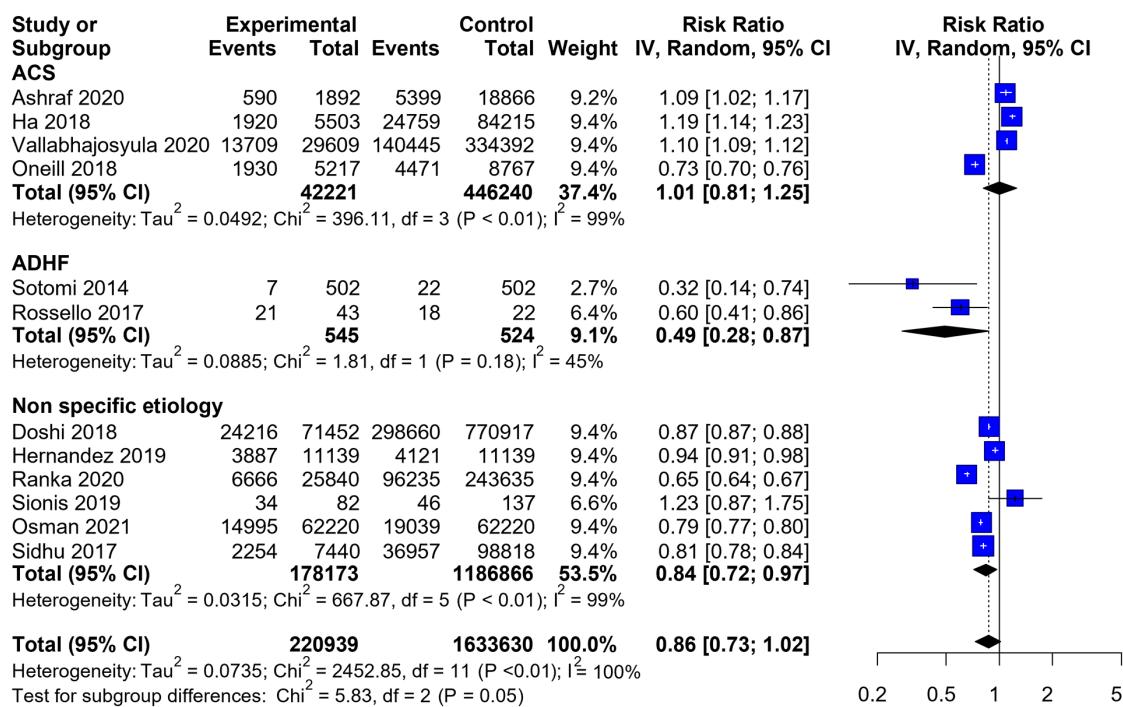
**Table 2** Summary of proportions of patients with ACS among those with cardiogenic shock in the studies of non-specific causes

Study ID	PAC	No PAC
Doshi 2018 (20)	ACS: 45.5%	ACS: 53.2%
Hernandez 2019 (21)	STEMI 24.3%	
	Non-STEMI 12.9%	
	Acute HF 11.4%	
Ranka 2020 (22)	Unknown	Unknown
Sionis 2020 (23)	ACS 74%	ACS 85%
Osman 2021 (24)	STEMI 19.9%	STEMI 20.3%
	Non-STEMI 21.9%	Non-STEMI 22.2%
Sidhu 2017 (25)	Unknown	Unknown

ACS, acute coronary syndrome; PAC, pulmonary artery catheterization; STEMI, ST-segment elevation myocardial infarction; HF, heart failure.



**Figure 2** Bar chart of risk of bias.



**Figure 3** In-hospital mortality patients who underwent pulmonary artery catheterization *vs.* those who did not undergo pulmonary artery catheterization. Each study's risk ratio point estimate is displayed by a square marker, with the size of the square being proportional to the weight of the study in the meta-analysis. The solid diamond represents the estimated 95% CI for the effect size of all the meta-analyzed data, and the horizontal lines represent the 95% CIs. ACS, acute coronary syndrome; ADHF, acute decompensated heart failure; CI, confidence interval.

2005, the use of PAC has decreased in the management of heart failure (7). Interestingly, the use of PAC has also decreased in CS management, even though data regarding its role are insufficient. Most studies investigating PAC monitoring of patients with CS have been retrospective, observational studies with small sample sizes. Several studies have even demonstrated that invasive hemodynamic monitoring with PAC reduces mortality and reduces the need for mechanical circulatory support in a multiplicity of shock contexts (10,18,20). We, therefore, gathered all of the relevant data that we could find and analyzed the role of PAC in CS management. Recently, several meta-analyses have investigated CS-related topics. Chow *et al.* found that the use of PAC was associated with superior in-hospital mortality outcomes compared with the non-use of PAC (26). In our analysis, the use of PAC did not yield statistically significant results in terms of an association with in-hospital mortality among patients with CS overall. In the meta-analysis conducted by Chow *et al.*, one article reporting on postcardiotomy shock was highly weighted

despite its small sample size, and this may have contributed disproportionately to the overall findings and conclusions, pushing the trend toward a more positive effect. Bertaina *et al.* also conducted a meta-analysis demonstrating the positive role of PAC in the management of CS (27). However, they analyzed only six articles, and there was a possibility of selection bias. To date, the benefit of PAC in CS management remains controversial.

The use of PAC monitoring for patients with CS has decreased even though its use has shown clinical benefits (21). One reason has been the difficulty in interpreting data obtained from PAC studies and the consequent difficulty with clinical decision-making. Another reason has been the poor quality of evidence regarding the use of PAC. Many CS studies have been retrospective, observational studies. Moreover, many of the relevant randomized controlled studies have not proven improvements in outcomes associated with PAC monitoring in the management of various conditions (28,29). It could be argued that sicker patients may receive PAC and have a high a risk of mortality

that is not specifically related to the PAC use itself. However, PAC has been reported to cause complications, such as bleeding or infection (8). In this review and meta-analysis, PAC use was not significantly associated with in-hospital mortality among CS patients, even though a nonsignificant trend favoring PAC use was found. This result does not imply that PAC should not be used in the management of CS; rather, the findings may point to an emphasis on better selection of patients who may benefit from PAC.

In the present study, we hypothesized that outcomes associated with invasive hemodynamic monitoring would vary depending on the cause of CS. We found that a specific subgroup of patients with CS caused by ADHF potentially derived a survival benefit from PAC use, while patients with CS caused by ACS did not. Also, the use of PAC did not have a significant benefit in the subgroup of patients with CS cause by non-specific etiology, but the proportion of ACS in these studies was about 40% to 70%. These factors would affect entire analysis. This analysis provides the first evidence of varying PAC-related outcomes according to the underlying cause of shock. Additionally, this is the first meta-analysis to reveal a beneficial effect of PAC for CS caused by ADHF, a result that conflicts with the conventional belief that PAC is not useful in the management of ADHF.

There are several possible explanations for why PAC monitoring was associated with lower in-hospital mortality among patients with CS caused by ADHF but not among patients with CS caused by ACS. In some studies, the hemodynamic profiles of patients with CS caused by ADHF differed from those of patients with CS caused by ACS (10,30). One study found cardiac power output and cardiac index, which are not easily changed, to be key predictors of mortality among patients with CS caused by myocardial infarction, although venous congestion and right-sided heart failure were significant predictors of death in ADHF-CS patients (31,32). Another study demonstrated that right atrial pressure or pulmonary capillary wedge pressure discriminated mortality better in association with CS secondary to heart failure than in association with CS secondary to myocardial infarction (10). These results indicate that invasive hemodynamic monitoring can be more beneficial for patients with CS caused by heart failure because it can be used to monitor hemodynamic profiles in real time and guide decision-making for optimal treatment to improve prognosis. Additionally, the prognosis of CS caused by ACS may be affected by revascularization

procedures and interventional outcomes (33). Moreover, the study designs in the included articles may have partly explained the finding of an insignificant benefit of PAC in the management of CS caused by ACS. Most studies used retrospective data, and the proportions of patients using PAC were small overall. This analysis included two articles reporting on CS caused by ADHF without ACS. Although the studies reported in these two articles had relatively small sample sizes, they provided more powerful evidence because they were prospective studies. Additionally, among patients who had CS secondary to ACS, PAC would have been administered to patients with disease of greater severity requiring mechanical circulatory support; this may have contributed to the lack of a significant difference found in the in-hospital mortality between the two groups (16).

There were several limitations to our analysis. First, the quality of evidence was quite low, given that most of the findings were based on observational studies. Second, much of the data were from the National Inpatient Sample. Although this is a large database of patients managed in the United States, even though the studies varied in terms of sampling periods and the presence or absence of adjustments for confounding variables, many studies have overlapping time frames, and there is potential for unmeasured confounding. Caution should, therefore, be taken when interpreting the results. Third, there were only two articles reporting on CS caused by ADHF without ACS, and recent advances in treatment options were not sufficiently reflected in the included studies. Currently, the use of PAC for patients with CS is generally not recommended; however, many studies and meta-analyses have shown that PAC can be useful in specific contexts (according to patient characteristics or the cause of CS, for example). Moreover, because most of the included articles reported on observational studies and lacked high-quality evidence, further prospective studies or randomized controlled trials are warranted to provide strong evidence for these findings.

## Conclusions

In this meta-analysis and systematic review of PAC use for patients with CS of various causes, the PAC in monitoring had no significant association with in-hospital mortality. However, in the subgroup of patients with CS without ACS, especially those with CS secondary to ADHF, PAC monitoring may be associated with lower in-hospital mortality. Further research is needed to firmly identify the

specific CS patients who may benefit from PAC monitoring.

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## Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## Appendix 1 Search strategy

(pulmonary artery catheterization[MeSH Terms]) AND (pulmonary artery catheter [MeSH Terms]) OR (invasive hemodynamic monitoring[MeSH Terms]) OR (hemodynamic [MeSH Terms]) OR (hemodynamic monitoring[MeSH Terms]) AND (catheterization, swan ganz[MeSH Terms]) AND (shock, cardiogenic[MeSH Terms]) OR (heart failure[MeSH Terms]) OR (Acute decompensated heart failure) AND (cardiogenic shock[MeSH Terms])

Table S1 Baseline characteristics of included studies

Study ID	Age	Sex	MCS rate	Vasopressors and/or inotropes	Mechanical ventilator support	Renal replacement therapy
Ashraf 2020 (14)	Mean age 66 years (overall)	Male 70% (overall)	-	-	-	5.18(PAC) 3.66(No PAC)
Ha 2018 (15)	-	-	-	-	-	-
Vallabhajosyula 2020 (16)	68.3(12.5) (PAC) 70.1 (13.4)(No PAC)	62.3(PAC) 59 (No PAC)	55.8 (PAC) 39.2(No PAC)		61.4 (PAC) 42.1(No PAC)	5.8 (PAC) 2.9 (No PAC)
Oneill 2018 (17)	-	-	-	-	-	-
Sotomi 2014 (18)	66.7 (13.9) (PAC), 68.0 (14.9) (No PAC)	63.3 (PAC), 62.7 (No PAC)	-	21.5 (PAC), 22.3 (No PAC)	7.8(PAC), 8.4 (No PAC)	1.2 (PAC), 1.0 (No PAC)
Rossello 2017 (19)	66 (15.5) (PAC), 71 (12.5) (No PAC)	65 (PAC), 65 (No PAC)	37 (PAC), 22 (No PAC)	98 (PAC), 85 (No PAC)	71 (PAC), 54 (No PAC)	25 (PAC), 13 (No PAC)
Doshi 2018 (20)	65 (PAC), 69 (No PAC)	64.3 (PAC), 59.5 (No PAC)	-	-	-	-
Hernandez 2019 (21)	64 (14.7) (PAC), 68.1 (14.4) (No PAC)	63.8 (PAC), 59.3 (No PAC)	39 (PAC), 25.8 (No PAC)	-	56.9 (PAC), 50.8 (No PAC)	9.8 (PAC), 6.1 (No PAC)
Ranka 2020 (22)	-	-	-	-	-	-
Sionis 2020 (23)	65(12) PAC, 68(11) No PAC	78 (PAC), 72 (No PAC)	68 (PAC), 44 (No PAC)	93 (PAC), 77 (No PAC)	89 (PAC), 47(No PAC)	22 (PAC), 9 (No PAC)
Osman 2021 (24)	64 (55-72) (PAC), 68 (58-78) (No PAC)	66.9 (PAC), 61.4 (No PAC)	44.7 (PAC), 28.8 (No PAC)	-	39.7 (PAC), 49.1 (No PAC)	9.4 (PAC), 9 (No PAC)
Sidhu 2017 (25)	-	-	-	-	-	-

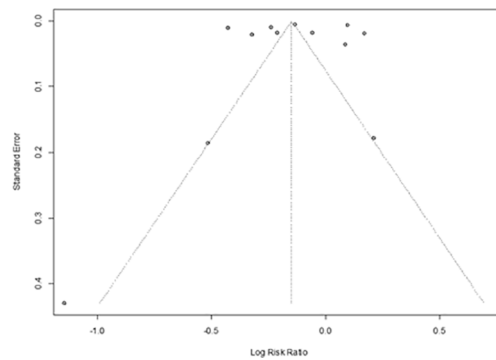


Figure S1 Funnel plot of studies used in meta-analysis.