JAMA®

Impact of the Pulmonary Artery Catheter in Critically Ill Patients: Meta-analysis of Randomized Clinical Trials

Monica R. Shah; Vic Hasselblad; Lynne W. Stevenson; et al.

Correction	Contact me if this article is corrected.
Citations	This article has been cited 91 times. Contact me when this article is cited.
Topic collections	Revascularization; Cardiovascular System; Quality of Care; Evidence-Based Medicine; Surgery; Surgical Interventions; Cardiovascular/ Cardiothoracic Surgery; Review; Cardiovascular Intervention Contact me when new articles are published in these topic areas.
Related Articles published in the same issue	Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness: The ESCAPE Trial The ESCAPE Investigators and ESCAPE Study Coordinators*. *JAMA*. 2005;294(13):1625. Searching for Evidence to Support Pulmonary Artery Catheter Use in Critically Ill Patients Jesse B. Hall. *JAMA*. 2005;294(13):1693.

Impact of the Pulmonary Artery Catheter in Critically Ill Patients
Meta-analysis of Randomized Clinical Trials

Monica R. Shah, MD, MHS, MSJ

Vic Hasselblad, PhD

Lynne W. Stevenson, MD

Cynthia Binanay, RN, BSN

Christopher M. O'Connor, MD

George Sopko, MD, MPH

Robert M. Califf, MD

T HE PULMONARY ARTERY CATH-
eter (PAC) is used to diag-
nose various diseases and
physiological states, monitor
the progress of critically ill patients, and
guide the selection and adjustment of
medical therapy.[1] The PAC is often con-
sidered a cornerstone of critical care and
a hallmark of the intensive care unit
(ICU).[2] Approximately 1 million PACs
are used annually in the United States.[3]
However, despite widespread use of
these devices, there are conflicting data
about their utility. The majority of non-
randomized studies in critically ill pa-
tients have suggested that the PAC is
associated with increased morbidity and
mortality.[4] Conversely, some nonran-
domized studies have shown im-
proved quality of life when the PAC was
used to direct a specific therapeutic ap-
proach.[5-7]

Since the mid-1980s, randomized
clinical trials (RCTs) have been con-
ducted to evaluate the efficacy of the
PAC. However, none of these trials have
been persuasive individually, because

See also pp 1625 and 1693.

Context Randomized clinical trials (RCTs) evaluating the pulmonary artery catheter (PAC) have been limited by small sample size. Some nonrandomized studies suggest that PAC use is associated with increased morbidity and mortality.

Objective To estimate the impact of the PAC device in critically ill patients.

Data Sources MEDLINE (1985-2005), the Cochrane Controlled Trials Registry (1988-2005), the National Institutes of Health ClinicalTrials.gov database, and the US Food and Drug Administration Web site for RCTs in which patients were randomly assigned to PAC or no PAC were searched. Results from the ESCAPE trial of patients with severe heart failure were also included. Search terms included *pulmonary artery catheter*, *right heart catheter*, *catheter*, and *Swan-Ganz*.

Study Selection Eligible studies included patients who were undergoing surgery, in the intensive care unit (ICU), admitted with advanced heart failure, or diagnosed with acute respiratory distress syndrome and/or sepsis; and studies that reported death and the number of days hospitalized or the number of days in the ICU as outcome measures.

Data Extraction Information on eligibility criteria, baseline characteristics, interventions, outcomes, and methodological quality was extracted by 2 reviewers. Disagreements were resolved by consensus.

Data Synthesis In 13 RCTs, 5051 patients were randomized. Hemodynamic goals and treatment strategies varied among trials. A random-effects model was used to estimate the odds ratios (ORs) for death, number of days hospitalized, and use of inotropes and intravenous vasodilators. The combined OR for mortality was 1.04 (95% confidence interval [CI], 0.90-1.20; $P=.59$). The difference in the mean number of days hospitalized for PAC minus the mean for no PAC was 0.11 (95% CI, −0.51 to 0.74; $P=.73$). Use of the PAC was associated with a higher use of inotropes (OR, 1.58; 95% CI, 1.19-2.12; $P=.002$) and intravenous vasodilators (OR, 2.35; 95% CI, 1.75-3.15; $P<.001$).

Conclusions In critically ill patients, use of the PAC neither increased overall mortality or days in hospital nor conferred benefit. Despite almost 20 years of RCTs, a clear strategy leading to improved survival with the PAC has not been devised. The neutrality of the PAC for clinical outcomes may result from the absence of effective evidence-based treatments to use in combination with PAC information across the spectrum of critically ill patients.

JAMA. 2005;294:1664-1670   www.jama.com

Author Affiliations: Department of Cardiology, Columbia University Medical Center, New York, NY (Dr Shah); Biostatistics and Bioinformatics, Duke Clinical Research Institute, Durham, NC (Dr Hasselblad); Cardiovascular Division, Brigham and Women's Hospital, Boston, Mass (Dr Stevenson); Project Leadership, Duke Clinical Research Institute, Durham, NC (Ms Binanay); Division of Cardiology, Duke University Medical Center, and Duke Clinical Research Institute, Durham, NC (Drs O'Connor and Califf); and Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md (Dr Sopko).
Corresponding Author: Vic Hasselblad, PhD, Duke Clinical Research Institute, Biostatistics and Bioinformatics, PO Box 17969, Durham, NC 27705 (victor.hasselblad@duke.edu).

they are limited by small sample sizes in heterogeneous populations. Ivanov et al performed 2 meta-analyses on PAC use through 1996.[8,9] One study focused on mortality from 16 RCTs of the PAC[8] and the other focused on major morbidity from 12 RCTs[9]; however, neither study restricted the randomization specifically to catheter vs no catheter use. There was no difference found in mortality, but there was a statistically significant difference in major morbidity, which was defined separately for each organ system.[8,9]

Despite the overwhelmingly negative tenor of the literature, clinicians continue to use the PAC in ICUs based on personal experience and the belief that careful monitoring will improve decision making and clinical outcomes. To provide a broad perspective for the recently completed ESCAPE trial,[10] in which patients with advanced heart failure were randomized to the PAC or clinical assessment alone, we performed a meta-analysis of 13 recently published clinical trials testing the safety and efficacy of the PAC.

METHODS
Study Search
We searched MEDLINE (1985-2005), the Cochrane Controlled Trials Registry (1988-2005), the National Institutes of Health ClinicalTrials.gov database, and the US Food and Drug Administration Web site (http://www.fda.gov) for reports of articles pertaining to the PAC. The MEDLINE search results included all articles yielded by other search methods. The search terms used were *pulmonary artery catheter*, *right heart catheter*, *catheter*, and *Swan-Ganz*.

For the MEDLINE search, we used the term *pulmonary artery catheter* as a keyword. We then searched the subject headings *catheterization*, *Swan-Ganz*, and *pulmonary artery catheter*. The search was limited to articles that were written in English, included only human beings, and published between 1985 and 2005. These citations were then manually searched to identify articles that were RCTs, system-atic reviews, prospective cohort studies, or editorial letters and comments. The references from the citations were also searched to identify additional RCTs.

Eligibility and Data Abstraction
We reviewed references identified by the search method specified above. Additional references were identified by manually searching the bibliographies of these articles. These citations were included in our meta-analysis. We included trials if the randomization scheme included groups that assigned patients to treatment guided by the PAC or treatment without the PAC. We only included trials if they reported death and number of days hospitalized or the number of days in the ICU as outcome measures. Studies were excluded if the randomization scheme did not specify groups as PAC or no PAC, if patients were not randomized to a conventional PAC, if investigators combined randomized and nonrandomized groups when reporting outcomes, or if there were no outcome data on death or hospitalizations.

Eligibility assessment and data abstraction were performed independently in an unblinded standardized manner by 2 reviewers (M.R.S. and V.H.). Abstracted data included eligibility criteria, baseline characteristics, interventions, outcomes, and methodological quality. The outcome of interest was the number of deaths from any cause and the number of days hospitalized. Trial methodological quality was assessed by abstracting reported use of intention-to-treat analysis and reported allocation generation and allocation concealment. Disagreements between reviewers were resolved by consensus.

Data Analysis
Random-effects models were used for the meta-analysis of both mortality and days hospitalized. Mortality was summarized by odds ratio (OR) with 95% confidence intervals (CIs). Days hospitalized were summarized as the difference in mean number of days. The measures were combined using an empirical Bayes random-effects estimator,[11] which also provides an estimate of heterogeneity. The calculations were performed by using FAST*PRO software version 1.80.[12] $P<.05$ was considered statistically significant.

Some of the studies had zero deaths in a particular group, which is problematic for conventional meta-analysis methods. Meta-regression analysis is an alternative method of estimating the pooled OR. Based on the assumption used in standard meta-analysis, we assumed that the OR for mortality remained constant across studies, except for some additional random variation. The model was fitted using a logistic-normal model as implemented in EGRET for Windows.[13] These results were used as a check on the empirical Bayes estimator.
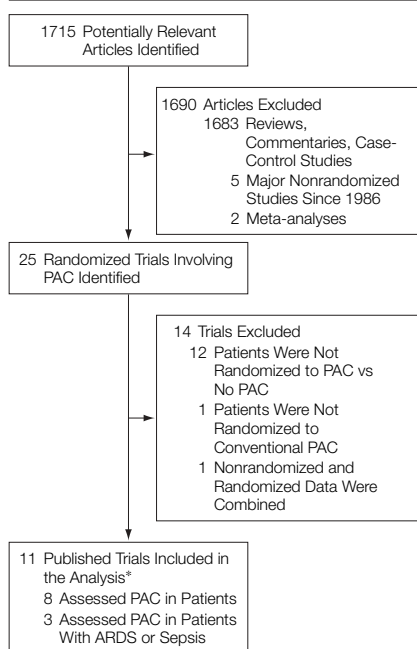
RESULTS
Search Results
We identified 2305 articles with the subject headings *catheterization*, *Swan-Ganz*, or *pulmonary artery catheter* (**FIGURE 1**). We limited our analysis to articles that were written in English, included only human beings, and were published between 1985 and 2005, which yielded 1715 articles. We manually searched these citations and identified 11 RCTs evaluating the PAC that met the prespecified criteria. In addition, we included 2 recently published trials. The first trial, Evaluation of the Clinical Care and Cost Effectiveness of Pulmonary Artery Flotation Catheters in Intensive Care (PAC-Man), was conducted in England and completed in March 2004.[14] The second trial, the ESCAPE trial,[10] was presented at the American Heart Association meeting on November 9, 2004.

Qualitative Findings
In total, 5051 patients were randomized into the 13 trials included in our meta-analysis.[10,14-25] Eight studies focused on patients undergoing major general, abdominal, vascular, or orthopedic surgery.[15-18,20-22,24] These trials included 2667 (52.8%) of 5051 patients

PAC indicates pulmonary artery catheter; ARDS, acute respiratory distress syndrome.
*Results from the ESCAPE trial[10] and the recently published PAC-Man trial[14] were also included.

in the meta-analysis. Three studies evaluated patients admitted to the ICU who were diagnosed with sepsis or acute respiratory distress syndrome.[19,23,25] These trials included 910 patients (18.0%) of the meta-analysis study population. Only 1 study, ESCAPE,[10] focused primarily on patients with advanced heart failure.

Baseline Characteristics

Treatment Protocols. Specific hemodynamic targets were outlined in 7 studies[10,16,18,20-22,24] (**TABLE 1**). Six studies[10,18,20-22,24] targeted a specific pulmonary capillary wedge pressure as 1 of the therapeutic goals, 6 studies[16,18,20-22,24] used the cardiac index, 3 studies[16,22,24] aimed at oxygen delivery, and 4 studies[18,20-22] focused on systemic vascular resistance.

Five studies[15,17,19,23,25] did not require investigators to achieve specific hemodynamic targets. The protocols of these studies called for clinicians to use their own judgment in assessing thera-

peutic goals and designing treatment strategies.

In contrast, 2 studies[10,16] clearly outlined hemodynamic targets but did not specify which therapies should be selected to achieve these goals. The protocol of the ESCAPE trial[10] encouraged the use of vasodilators and diuretics and discouraged inotropes but did not mandate use of these drugs.

The 5 most specific protocols focused on the surgical population.[18,20-22,24] These trials outlined treatment strategies to achieve specific hemodynamic goals. A summary of fluids and therapies used in the 13 trials is shown in **TABLE 2**.

Quantitative Findings. Overall, there was a significantly higher rate of use of vasodilator agents in patients randomly assigned to PAC (OR, 2.35; 95% CI, 1.75-3.15; $P<.001$). In addition, use of inotropes was also significantly higher in patients randomly assigned to PAC (OR, 1.58; 95% CI, 1.19-2.12; $P=.002$).

The meta-analysis of death in the 13 RCTs demonstrated that the PAC did not significantly increase mortality. More importantly, the use of the PAC also did not improve survival (OR, 1.04; 95% CI, 0.90-1.20; $P=.59$) (**FIGURE 2**).

In addition, the meta-analysis of the number of days hospitalized showed that the PAC did not have a significant impact on this end point (mean for PAC – mean for no PAC, 0.11 days; 95% CI, –0.51 to 0.74; $P=.73$) (**FIGURE 3**).

COMMENT

Our meta-analysis of 13 RCTs evaluating the safety and efficacy of the PAC demonstrates that use of the catheter neither improves outcomes in critically ill patients nor increases mortality or days in hospital. This provides a broader confirmation of the recent results of the ESCAPE trial,[10] which showed that the routine use of the PAC in patients with advanced heart failure did not reduce or increase death or days in hospital.

PAC: A Diagnostic Tool

Previous clinical trials have evaluated the PAC as an intervention, although

it is only a diagnostic tool, similar to a chest radiograph or an echocardiogram. To expect a diagnostic device to increase survival may be unrealistic unless there is a therapeutic intervention associated with it that improves outcomes. Our meta-analysis emphasizes the lack of consensus about the goals of therapy in critically ill populations, the paucity of standard guidelines on how to use the PAC, and the dearth of therapies that have met modern criteria for evidence, which provide clinical benefit in acutely ill populations.

Use of the PAC in Different Populations

The PAC may be used differently in the spectrum of critical illnesses. Because the role of the PAC in different disease states varies, the catheter may benefit some patients and harm others. The specific role the device plays in treating patients may be a factor in determining its ultimate impact on clinical outcomes. For example, in the ICU and surgical populations, the focus of the PAC is on diagnosis of volume and perfusion status and the selection and titration of drugs. In contrast, in the heart failure population, the PAC is used not only to diagnose volume and perfusion status and titrate therapy, but also to refine drug combinations and select equivalent oral doses of intravenous medications. Because the use of the PAC may vary by disease state, combining the results of different trials may not give an accurate estimate of the impact of the device in specific patient populations. However, none of the individual trials included in our meta-analysis showed a significantly positive effect of the PAC on outcomes, so heterogeneity of response as an explanation for the neutral results would have to be within each trial. We are unable to address this issue because we do not have the individual patient data.

Therapies Associated With the PAC

Another potential reason that the results of our meta-analysis were neutral may be that use of the PAC increased the accuracy of diagnosis, potentially leading to increased survival, but that

Table 1. Overview of Major Randomized Clinical Trials Evaluating the Safety and Efficacy of the PAC

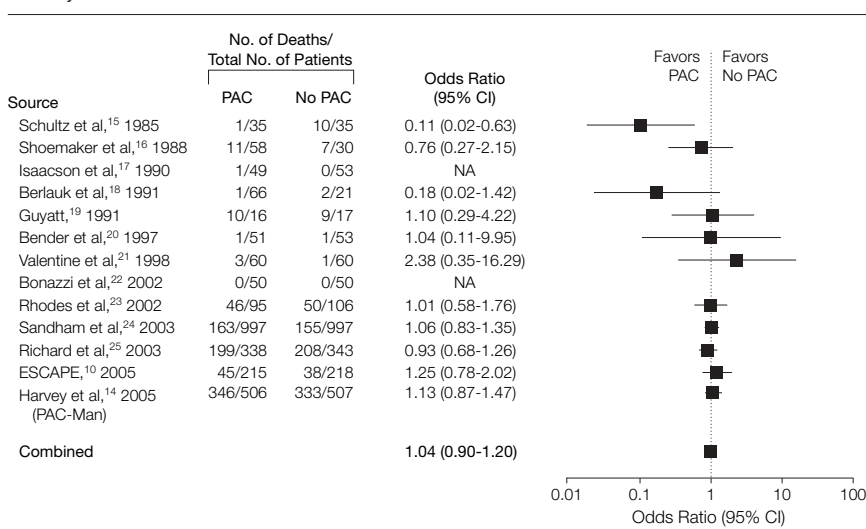| Source, y	No. of Patients	PAC vs No PAC	Population	Design	Hemodynamic Targets	Treatment Strategy	End Points	Results PAC vs No PAC
Harvey et al,[14] 2005	1041	519/522	Adult ICU patients	Group 1: PAC Group 2: no PAC	No	No	Days in ICU Death	Death: PAC: 346 of 506 (68%) No PAC: 33 of 507 (66%)
Schultz et al,[15] 1985	70	35/35	Hip fracture; orthopedic surgery	PAC vs no PAC	No	No	Death	1 vs 10
Shoemaker et al,[16] 1988	88	30/30/28	High-risk general surgery patients	Group 1: no PAC Group 2: PAC with normal goals Group 3: PAC with supranormal goals	Yes Group 2: cardiac index 2.8-3.5, O_2 delivery 400-550, VO_2 120-140 Group 3: cardiac index >4.5, O_2 delivery >600, VO_2 >170	No	Death Days hospitalized	Death: group 1: 7; group 2: 10; group 3:1; group 3 vs group 1 (P<.01) Days hospitalized: group 1: mean (SD), 22.2 (2.8); group 2: mean (SD), 25.2 (3.4); group 3: mean (SD), 19.3 (2.4)
Isaacson et al,[17] 1990	102	49/53	Abdominal aortic reconstructive surgery	PAC vs no PAC	No	No	Complications Days in ICU Days hospitalized Death	17 vs 16 2.7 vs 2.1; P = .13 10.2 vs 9.4; P = .60 1 vs 0
Berlauk et al,[18] 1991	89	45/23/21	Limb salvage arterial surgery	Group 1: PAC 12 h pre-operation vs Group 2: PAC 3 h pre-operation vs Group 3: no PAC	Yes PCWP ≤15 Cardiac index ≥2.8 SVR ≤1100	Yes SVR >1100 Systolic BP >110 (vasodilator) SVR ≤1100 (inotrope) PCWP <15 (fluids) Cardiac index <2.8 (inotrope)	Days hospitalized Death	Days hospitalized: group 1: mean (SD), 19.4 (11.6); group 2: mean (SD), 18.0 (12.0); group 3: mean (SD), 15.4 (7.5) Death: group 1: 1; group 2: 0; group 3: 1
Guyatt,[19] 1991	33	16/17	ICU patients	PAC vs usual care	No	No	Days hospitalized APACHE score Death	10.3 vs 8.1 14.4 vs 11.1 10 vs 9
Bender et al,[20] 1997	104	51/53	Elective vascular surgery	PAC vs no PAC	Yes PCWP ≤14 Cardiac index ≥2.8 SVR ≤1100	Yes PCWP (crystalloid) Cardiac index (dopamine) SVR (nitroprusside)	Days in ICU Days hospitalized Death	2.7 vs 2.6 12.5 vs 12 1 vs 1
Valentine et al,[21] 1998	120	60/60	Aortic surgery	PAC vs no PAC	Yes PCWP <15 Cardiac index ≥2.8 SVR ≤1000	Yes PCWP (Ringer's lactate) Cardiac index (dopamine) SVR (nitroprusside, nitroglycerin)	Days in ICU Days hospitalized Death	8 vs 7 13 vs 13 3 vs 1
Bonazzi et al,[22] 2002	100	50/50	Aortic reconstructive surgery	PAC vs no PAC	Yes PCWP ≤18 Cardiac index ≥3.0 SVR <1450 O_2 delivery >600	Yes PCWP (Ringer's lactate, normal saline) Cardiac index (dobutamine) SVR (nitroglycerin)	Acute coronary syndrome, heart failure, arrhythmias Days hospitalized Renal failure Death	2 vs 4 12 vs 11 0 vs 0 0 vs 0
Rhodes et al,[23] 2002	201	96/105	ICU patients	PAC vs no PAC	No	No	Renal failure Days hospitalized Death	22 vs 12 13 vs 14; P = .81 46 vs 50; P>.99
Sandham et al,[24] 2003	1994	997/997	High-risk major surgery patients	PAC vs no PAC	Yes O_2 delivery >600 Cardiac index ≥3.5 Mean arterial pressure, 70 PCWP ≤18 Heart rate <120/min Hematocrit, 27%	Yes To achieve hemodynamic goals, the following were tried in order: Fluid loading Inotropes Vasodilators Vasopressors Blood transfusion	Days hospitalized In-hospital death Death at 360 d In-hospital morbidity Pulmonary embolism	10 vs 10; P = .41 78 vs 77; P = .93 163 vs 155 504 vs 523 8 vs 0; P = .004
Richard et al,[25] 2003	676	335/341	ICU patients with ARDS, sepsis, or both	PAC vs no PAC	No	No	28-d death Days hospitalized	199 vs 208; RR, 0.97; 95% CI, 0.86-1.1; P = .67 14 vs 14; P = .67
ESCAPE,[10] 2005	433	215/218	NYHA class IV heart failure patients	PAC vs no PAC	Yes PCWP ≤15 Right arterial pressure ≤8	No	Days dead or hospitalized over 180 d	HR, 1.00; 95% CI, 0.83-1.21

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; ARDS, acute respiratory distress syndrome; BP, blood pressure; CI, confidence interval; HR, hazard ratio; ICU, intensive care unit; NYHA, New York Heart Association; PAC, pulmonary artery catheter; PCWP, pulmonary capillary wedge pressure; RR, relative risk; SVR, systemic vascular resistance.

Table 2. Therapies in PAC vs No PAC Groups

	No. of Patients		Hemodynamic Targets	Treatment Strategy	Crystalloid, mL*		Colloid, mL*		Packed Red Blood Cells, Units*		No. of Inotropes (%)		No. of Vasodilators (%)	
	PAC	No PAC			PAC	No PAC	PAC	No PAC	PAC	No PAC	PAC	No PAC	PAC	No PAC
Harvey et al,[14] 2005	519	522	No	No	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Schultz et al,[15] 1985	35	35	No	No	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Shoemaker et al,[16] 1988	30; 30	28	Yes	No	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Isaacson et al,[17] 1990	49	53	No	No	3308 (1547)	2979 (1044)	93 (189)	115 (261)	0.2 (0.7)	0.2 (0.5)	NA	NA	NA	NA
Berlauk et al,[18] 1991	43; 23	21	Yes	Yes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Guyatt,[19] 1991	16	17	No	No	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bender et al,[20] 1997	51	53	Yes	Yes	5137 (315)	3789 (306)	NA	NA	1.3 (0.1)	1.8 (1.5)	NA	NA	NA	NA
Valentine et al,[21] 1998	60	60	No	Yes	5100 (270)†	4060 (190)	NA	NA	NA	NA	NA	NA	NA	NA
Bonazzi et al,[22] 2002	50	50	Yes	Yes	4500 (3250-6500)†	3250 (2500-4750)	NA	NA	825 (500-1500)	975 (500-2000)	NA	NA	NA	NA
Rhodes et al,[23] 2002	96	105	No	No	4953 (3140-7000)†	4295 (2535-6049)	NA	NA	NA	NA	24 (28.2)	21 (23.6)	NA	NA
Sandham et al,[24] 2003	997	997	Yes	Yes	NA	NA	546 (54.8)†	446 (47.7)	564 (56.6)	469 (47.0)	488 (48.9)	327 (32.8)	847.5 (8.5)	39 (3.9)
Richard et al,[25] 2003	338	343	No	No	NA	NA	NA	NA	NA	NA	296 (88.6)	307 (90.3)	NA	NA
ESCAPE,[10] 2005	215	218	Yes	No	NA	NA	NA	NA	NA	NA	94 (43.7)	86 (39.4)	78 (36.3)	41 (18.8)

Abbreviations: NA, not available; PAC, pulmonary artery catheter.
*Data are presented as mean (SD) or mean (range).
†$P<.05$.

Figure 2. Odds Ratio (PAC vs No PAC) for Mortality of RCTs Evaluating the Safety and Efficacy of the PAC

Source	No. of Deaths/ Total No. of Patients		Odds Ratio (95% CI)
	PAC	No PAC	
Schultz et al,[15] 1985	1/35	10/35	0.11 (0.02-0.63)
Shoemaker et al,[16] 1988	11/58	7/30	0.76 (0.27-2.15)
Isaacson et al,[17] 1990	1/49	0/53	NA
Berlauk et al,[18] 1991	1/66	2/21	0.18 (0.02-1.42)
Guyatt,[19] 1991	10/16	9/17	1.10 (0.29-4.22)
Bender et al,[20] 1997	1/51	1/53	1.04 (0.11-9.95)
Valentine et al,[21] 1998	3/60	1/60	2.38 (0.35-16.29)
Bonazzi et al,[22] 2002	0/50	0/50	NA
Rhodes et al,[23] 2002	46/95	50/106	1.01 (0.58-1.76)
Sandham et al,[24] 2003	163/997	155/997	1.06 (0.83-1.35)
Richard et al,[25] 2003	199/338	208/343	0.93 (0.68-1.26)
ESCAPE,[10] 2005	45/215	38/218	1.25 (0.78-2.02)
Harvey et al,[14] 2005 (PAC-Man)	346/506	333/507	1.13 (0.87-1.47)
Combined			1.04 (0.90-1.20)

CI indicates confidence interval; NA, not available; PAC, pulmonary artery catheter; RCT, randomized clinical trial. *P* for heterogeneity=.36.

hemodynamic data also triggered use of therapies that worsened outcomes. Four studies included in our analysis presented information on how frequently intravenous inotropes and vasodilators were used.[10,23-25]

It may be that inotropes and vasodilators were used more frequently in patients who received the PAC because objective hemodynamic goals were present. There are few data, and no RCT data, that show either class of drugs improves outcomes in acutely ill patients. In fact, the use of inotropic agents and some vasodilators have been associated with increased morbidity and mortality in the advanced heart failure population.[26,27] In addition, there is little evidence from RCTs to support the use of fluid loading, blood transfusions, or intravenous vasodilators to achieve hemodynamic goals.[28] Although use of the PAC may have allowed physicians to diagnose clinical and hemodynamic status more accurately, it may have also triggered the use of drugs that ultimately worsened outcomes.

Quality of Hemodynamic Data

Quality of hemodynamic data is also a critical factor in determining the impact of the device on clinical outcomes. Eleven studies in our analysis did not include a protocol for interpretation of hemodynamic wave-

forms. Thus, there may have been inaccuracies in the hemodynamic data, which had an impact on morbidity and mortality. In addition, only the ESCAPE trial required study nurses to undergo formal training in hemodynamic waveform interpretation. Without standard protocols for the PAC, there may have been errors in gathering hemodynamic data, which may have ultimately affected clinical outcomes.
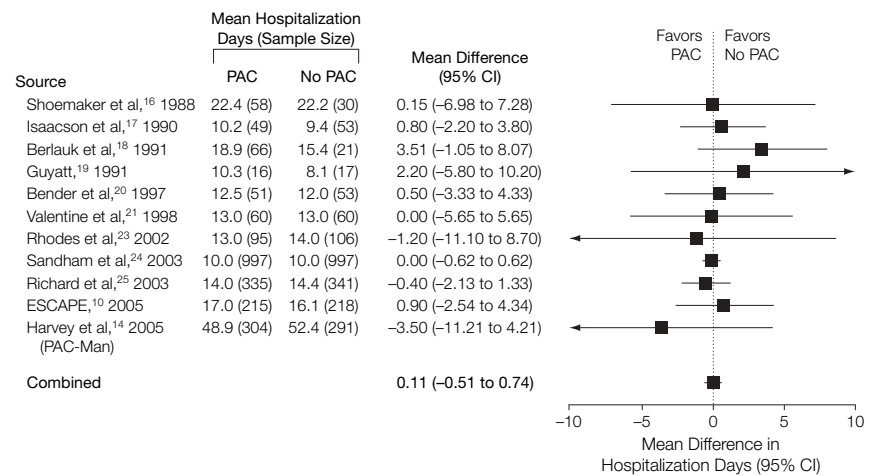
Hemodynamic Targets: The Wrong Surrogates?

Although many of the studies included in our meta-analysis outlined specific hemodynamic goals, there are few definitive data to support the use of any hemodynamic target. The decision to optimize filling pressures in the ESCAPE trial was based mostly on the positive results of single-center, nonrandomized studies using these targets.[29,30] In contrast, there are few data, even from nonrandomized studies, to support maximizing cardiac index and oxygen delivery.[31] It may be that the observed neutral effect of the PAC was because investigators were targeting drugs, fluid, and blood replacement to the wrong end points.

Ongoing Randomized Studies

We identified 1 additional unpublished trial evaluating the safety and efficacy of the PAC. The Fluids and Catheter Treatment Trial focused on 1000 patients with acute respiratory distress syndrome.[32,33] Patients were randomized in a 2×2 factorial design to a liberal vs conservative fluid treatment strategy and to therapy guided by a PAC or central venous catheter. The primary end point was death at 60 days. The investigators outlined specific hemodynamic goals and treatment strategies for the use of inotropes, vasopressors, fluids, and diuretics. The trial was started in 2001 but was suspended by the Office for Human Protections From Research[32] for questions about the ethics of the protocol. After extended review by external consultants, the trial was restarted in 2002 with no major revisions to the protocol.

Figure 3. Mean Difference in the Average Number of Days Hospitalized in PAC Randomized Controlled Trials (Mean for PAC − Mean for No PAC)

Source	Mean Hospitalization Days (Sample Size)		Mean Difference (95% CI)
	PAC	No PAC	
Shoemaker et al,[16] 1988	22.4 (58)	22.2 (30)	0.15 (−6.98 to 7.28)
Isaacson et al,[17] 1990	10.2 (49)	9.4 (53)	0.80 (−2.20 to 3.80)
Berlauk et al,[18] 1991	18.9 (66)	15.4 (21)	3.51 (−1.05 to 8.07)
Guyatt,[19] 1991	10.3 (16)	8.1 (17)	2.20 (−5.80 to 10.20)
Bender et al,[20] 1997	12.5 (51)	12.0 (53)	0.50 (−3.33 to 4.33)
Valentine et al,[21] 1998	13.0 (60)	13.0 (60)	0.00 (−5.65 to 5.65)
Rhodes et al,[23] 2002	13.0 (95)	14.0 (106)	−1.20 (−11.10 to 8.70)
Sandham et al,[24] 2003	10.0 (997)	10.0 (997)	0.00 (−0.62 to 0.62)
Richard et al,[25] 2003	14.0 (335)	14.4 (341)	−0.40 (−2.13 to 1.33)
ESCAPE,[10] 2005	17.0 (215)	16.1 (218)	0.90 (−2.54 to 4.34)
Harvey et al,[14] 2005 (PAC-Man)	48.9 (304)	52.4 (291)	−3.50 (−11.21 to 4.21)
Combined			0.11 (−0.51 to 0.74)

CI indicates confidence interval; PAC, pulmonary artery catheter. *P* for heterogeneity = .91.

Future Studies

The overview by Ivanov et al[9] suggests that nonfatal end points may be improved by disease-specific targeting of therapy and the ESCAPE trial[10] suggested the possibility of quality of life improvement. Future trials should look at alternate clinical end points, particularly symptom status. Furthermore, given the absence of harm for major clinical end points, renewed emphasis should be placed on the development of novel therapies that might be effective when coupled with the diagnostic information obtained from the PAC.

Conclusions

During the past 60 years, the PAC has evolved from a simple diagnostic tool to a device that is used for monitoring and determining goal-directed therapy. Our meta-analysis shows that despite the widespread acceptance of the PAC, use of this device across a variety of clinical circumstances in critically ill patients does not improve survival or decrease the number of days hospitalized. The patients included were those in whom physicians had clinical equipoise about the use of the PAC. That is, clinicians were uncertain about the use of the PAC before they randomized patients.

Although our results suggest that the PAC should not be a standard of care,

all of the trials excluded patients in whom clinicians thought a PAC was required for treatment. Thus, it is possible that patients who are outside the boundaries of these trials, such as those who are evaluated for heart and lung transplantation, derive benefit from the PAC. However, these results suggest that the PAC should not be used for the routine treatment of patients in the ICU, patients with decompensated heart failure, or patients undergoing surgery until or unless effective therapies can be found that improve outcomes when coupled with this diagnostic tool.

collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

REFERENCES

1. Trottier SJ, Taylor RW. Physicians' attitudes toward and knowledge of the pulmonary artery catheter: Society of Critical Care Medicine membership survey. *New Horiz*. 1997;5:201-206.
2. Dalen JE. The pulmonary artery catheter—friend, foe, or accomplice? *JAMA*. 2001;286:348-350.
3. Chalfin DB. The pulmonary artery catheter: economic aspects. *New Horiz*. 1997;5:292-296.
4. Connors AF Jr, Speroff T, Dawson NV, et al; SUPPORT Investigators. The effectiveness of right heart catheterization in the initial care of critically ill patients. *JAMA*. 1996;276:889-897.
5. Johnson W, Omland T, Hall C, et al. Neurohormonal activation rapidly decreases after intravenous therapy with diuretics and vasodilators for class IV heart failure. *J Am Coll Cardiol*. 2002;39:1623-1629.
6. Fonarow GC, Stevenson LW, Walden JA, et al. Impact of a comprehensive heart failure management program on hospital readmission and functional status of patients with advanced heart failure. *J Am Coll Cardiol*. 1997;30:725-732.
7. Chomsky DB, Lang CC, Rayos G, Wilson JR. Treatment of subclinical fluid retention in patients with symptomatic heart failure: effect on exercise performance. *J Heart Lung Transplant*. 1997;16:846-853.
8. Ivanov RI, Allen J, Sandham JD, Calvin JE. Pulmonary artery catheterization: a narrative and systematic critique of randomized controlled trials and recommendations for the future. *New Horiz*. 1997;5:268-276.
9. Ivanov R, Allen J, Calvin JE. The incidence of major morbidity in critically ill patients managed with pulmonary artery catheters: a meta-analysis. *Crit Care Med*. 2000;28:615-619.
10. The ESCAPE Investigators and ESCAPE Study Coordinators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA*. 2005;294:1625-1633.
11. Hedges LV, Olkin I. *Statistical Methods for Meta-Analysis*. Orlando, Fla: Academic Press; 1985.

12. Eddy DM, Hasselblad V. *FAST*PRO: Software for Meta-analysis by the Confidence Profile Method*. Orlando, Fla: Academic Press; 1992.
13. *EGRET for Windows*. Cambridge, Mass: Cytel Software Corp; 1999.
14. Harvey S, Harrison DA, Singer M, et al; PAC-Man Study Collaboration. Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. *Lancet*. 2005;366:472-477.
15. Schultz RJ, Whitfield GF, LaMura JJ, Raciti A, Krishnamurthy S. The role of physiologic monitoring in patients with fractures of the hip. *J Trauma*. 1985; 25:309-316.
16. Shoemaker WC, Appel PL, Kram HB, Waxman K, Lee TS. Prospective trial of supranormal values of survivors as therapeutic goals in high-risk surgical patients. *Chest*. 1988;94:1176-1186.
17. Isaacson IJ, Lowdon JD, Berry AJ, et al. The value of pulmonary artery and central venous monitoring in patients undergoing abdominal aortic reconstructive surgery: a comparative study of two selected, randomized groups. *J Vasc Surg*. 1990;12:754-760.
18. Berlauk JF, Abrams JH, Gilmour IJ, O'Connor SR, Knighton DR, Cerra FB. Preoperative optimization of cardiovascular hemodynamics improves outcome in peripheral vascular surgery: a prospective, randomized clinical trial. *Ann Surg*. 1991;214:289-297.
19. Guyatt G. A randomized control trial of right-heart catheterization in critically ill patients: Ontario Intensive Care Study Group. *J Intensive Care Med*. 1991;6:91-95.
20. Bender JS, Smith-Meek MA, Jones CE. Routine pulmonary artery catheterization does not reduce morbidity and mortality of elective vascular surgery: results of a prospective, randomized trial. *Ann Surg*. 1997; 226:229-237.
21. Valentine RJ, Duke ML, Inman MH, et al. Effectiveness of pulmonary artery catheters in aortic surgery: a randomized trial. *J Vasc Surg*. 1998;27:203-211.
22. Bonazzi M, Gentile F, Biasi GM, et al. Impact of perioperative haemodynamic monitoring on cardiac morbidity after major vascular surgery in low risk patients: a randomised pilot trial. *Eur J Vasc Endovasc Surg*. 2002;23:445-451.

23. Rhodes A, Cusack R, Newman PJ, Grounds RM, Bennett ED. A randomised, controlled trial of the pulmonary artery catheter in critically ill patients. *Intensive Care Med*. 2002;28:256-264.
24. Sandham JD, Hull RD, Brant RF, et al; Canadian Critical Care Clinical Trials Group. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med*. 2003;348: 5-14.
25. Richard C, Warszawski J, Anguel N, et al; French Pulmonary Artery Catheter Study Group. Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2003;290: 2713-2720.
26. Stevenson LW. Clinical use of inotropic therapy for heart failure: looking backward or forward? part I: inotropic infusions during hospitalization. *Circulation*. 2003;108:367-372.
27. Sackner-Bernstein JD, Kowalski M, Fox M, Aaronson K. Short-term risk of death after treatment with nesiritide for decompensated heart failure: a pooled analysis of randomized controlled trials. *JAMA*. 2005; 293:1900-1905.
28. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care: Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med*. 1999;340:409-417.
29. Steimle AE, Stevenson LW, Chelimsky-Fallick GC, et al. Sustained hemodynamic efficacy of therapy tailored to reduce filling pressures in survivors with advanced heart failure. *Circulation*. 1997;96:1165-1172.
30. Stevenson LW, Steimle AE, Fonarow G, et al. Improvement in exercise capacity of candidates awaiting heart transplantation. *J Am Coll Cardiol*. 1995;25: 163-170.
31. Matuschak GM. Supranormal oxygen delivery in critical illness. *New Horiz*. 1997;5:233-238.
32. Drazen JM. Controlling research trials. *N Engl J Med*. 2003;348:1377-1380.
33. Steinbrook R. How best to ventilate? trial design and patient safety in studies of the acute respiratory distress syndrome. *N Engl J Med*. 2003;348: 1393-1401.