Review

Evidence-based review of the use of the pulmonary artery catheter: impact data and complications

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Abstract

The pulmonary artery catheter (PAC) was introduced in 1971 for the assessment of heart function at the bedside. Since then it has generated much enthusiasm and controversy regarding the benefits and potential harms caused by this invasive form of hemodynamic monitoring. This review discusses all clinical studies conducted during the past 30 years, in intensive care unit settings or *post mortem*, on the impact of the PAC on outcomes and complications resulting from the procedure. Although most of the historical observational studies and randomized clinical trials also looked at PAC-related complications among their end-points, we opted to review the data under two main topics: the impact of PAC on clinical outcomes and cost-effectiveness, and the major complications related to the use of the PAC.

Introduction

No single monitoring device in the history of medicine has created as much enthusiasm and controversy as has the pulmonary artery catheter (PAC). Pulmonary artery (PA) catheterization was first performed in the mid-1940s under fluoroscopic guidance. With the application of distal tip balloon floatation, introduced by Ganz in the 1960, it became available to the bedside clinician. However, up until the early 1970s PACs were used almost exclusively for diagnostic purposes in catheterization laboratories to identify potential cardiac surgical cases. In 1971 Swan and colleagues [1] introduced the first commercially available balloon-tipped catheter that could be inserted at the bedside for assessment of cardiac pump function. The initial studies focused on the ability of PAC-derived data to identify patients whose natural history was different and in whom treatments would presumably also be different. Interestingly, no clinical trials were initially conducted to determine whether patient outcomes were altered by data derived from insertion of these catheters or the associated therapeutic interventions. In fact, PACs have been widely used in critically ill patients for diagnosis and therapeutic guidance, just because benefit was simply assumed. One estimate of the use of PAC monitoring in the USA [2] showed that, as of 2000, more than 1.2 million PACs were placed annually, with associated costs of over US$2 billion.

This review describes the evidence on the impact and complications of PAC use in critically ill patients. A summary of clinical studies using PAC along with the significant findings of each is brought in Table 1. We specifically exclude studies focusing on use of the PAC exclusively in the operating room, because operating room monitoring is often used to eliminate complications arising from surgery rather than to treat underlying conditions. Furthermore, any adverse intraoperative outcome is considered serious, whereas many trauma and septic shock patients often die despite aggressive and appropriate resuscitation. However, we do consider studies that include PAC monitoring as an overall package of management throughout the course of critical illness that also involves surgery.

Impact of PAC on patients outcome

Observational studies

During the 1980s two retrospective observational studies of patients with acute coronary syndromes questioned for the first time the benefit and safety of PAC monitoring, suggesting a higher mortality in patients undergoing PAC placement. Gore and coworkers [3] conducted a retrospective study in 3263 patients with acute myocardial infarction (MI). They found a consistent and significant increase in PAC use in patients with acute MI over time, from 7.2% in 1975 to 19.9% in 1984. They also found use of a PAC to be associated with increased length of hospital stay, irrespective of the development of acute clinical complications, without any long-term benefit. Zion and coworkers [4] analyzed the use of PAC in a registry including 5841 hospitalized patients with acute MI. A total of 371 patients underwent PAC

CHF = congestive heart failure; CI = cardiac index; CVP = central venous pressure; ICU = intensive care unit; LBBB = left bundle branch block; MI = myocardial infarction; OR = odds ratio; PA = pulmonary artery; PAC = pulmonary artery catheter; RBBB = right bundle branch block; RR = relative risk; TEV = thrombotic endocardial vegetation; To_2 = global oxygen transport; Vo_2 = oxygen consumption.

placement, and in-hospital mortality was found to be higher in patients with congestive heart failure (CHF) who received a PAC irrespective of the presence or absence of 'pump failure'. One may argue that PAC use is reserved for sicker patients, thus inappropriately skewing such data against PAC use. Further analysis supported this assumption that the PAC was used more frequently in sicker patients. However, on adjusting for the severity of CHF, no difference in mortality was found in patients with mild or moderate CHF. Therefore, Zion and coworkers concluded that although higher in-hospital mortality was found in patients receiving PAC, this excess was probably related to differences in severity of CHF. They assumed that it was unlikely that PAC increased mortality because severity-adjusted mortality rates were similar. The issue of adjustment for severity of illness when comparing groups recurs in later studies. Specifically, how does one adjust for differences in case mix? Severity scores were not calibrated to adjust for comparisons between heterogeneous groups.

In the 1990s more investigators became interested in addressing the relationship between survival and PAC use. However, those studies focused more on the potential harm of using PACs. In 1996 Connors and coworkers [5] conducted a retrospective observational study of patients with end-stage terminal disease who were expected to die within 12 months of enrollment, analyzing the subgroup of patients who required intensive care unit (ICU) admission separately. In all, 5735 critically ill patients from a 9105 SUPPORT (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments) patient cohort were retrospectively analyzed. Of this subset, 2184 (24%) patients underwent PAC placement; from this subgroup the investigators identified 1008 (11%) patients for whom matched non-PAC critical care patients were available for analysis. The data suggested that PAC use in the critically ill was associated with increased 30-day mortality (odds ratio [OR] 1.24), increased costs of care (mean difference in cost US$13,600), and increased length of ICU stay (mean difference 3 days), even after adjusting for some of the underlying risk factors for catheterization. Nevertheless, the matching criteria were based on demographic parameters such as sex, age, patient education and type of health care insurer, but not need for catecholamines. Thus, it is not clear whether the matching of patients was appropriate. Furthermore, as designed, the propensity score used in that study would be insensitive to a response to therapy within 24 hours. Thus, failure to respond to initial therapy could be an important missing covariate in this propensity score and could account for much of the increased mortality and use of resources associated with PAC use.

The latter study [5] raised many questions about the safety of PAC use, and so it is important to consider the flaws of that work. First, patients who did not respond to initial therapy were more likely to undergo PAC, as demonstrated by the TISS (Therapeutic Intervention Scoring System) score employed that study. Second, patients managed with a PAC were more likely to enter the study with multiple organ failure, acute respiratory failure, CHF and higher APACHE (Acute Physiology and Chronic Health Evaluation) III score - factors known to be associated with increased mortality. Third, the patients receiving a PAC had lower mean arterial pressures and baseline serum albumin concentration, which are two other factors associated with increased mortality. Thus, it is not clear that PAC use increased mortality, even in the SUPPORT cohort. Although the authors were unable to account for this apparent lack of benefit, they suggested that a randomized controlled trial of PAC use might clarify the result.

In 2000 another large retrospective observational study of 10,217 patients, conducted by Rapoport and coworkers [6], identified an independent association between PAC use and admission to a surgical ICU (a twofold increase), patient race (OR 1.38 for white patients), care delivered by an intensivist (a two-thirds reduction in the probability of catheter use), and having private insurance coverage (OR 1.33). Therefore, they suggested that studies measuring clinical and economic outcomes could help in developing policies for rational use of PACs. However, Murdoch and coworkers [7] conducted a similar study to that by Connors and coworkers described above. Considering 15 relevant variables in 4182 ICU patients (1849 with PAC use and 2333 without), they demonstrated a propensity score of 0.88, similar to that reported by Connors and colleagues (0.83), indicating good predictive value for insertion of a PAC, which was also found to be a strong predictor of death (OR 45, 95% confidence interval [CI] 34.7-58.3). However, use of a PAC was not predictive of death (OR 1.08, 95% CI 0.87-1.33) after correction for treatment bias using this propensity score. This analysis confirms the hypothesis tested, namely that mortality is greater for patients receiving a PAC, although the increased mortality is not related to the PAC itself.

To underscore the concept that patients who have a higher risk of dying are more likely to receive a PAC, Polanczyk and coworkers [8] reported a prospective observational study of 4059 patients undergoing major elective non-cardiac surgery. The purpose of the study was to evaluate the relationship between use of perioperative PAC and postoperative cardiac complication rates in patients undergoing major noncardiac surgery. Multivariate analysis identified a threefold increase in major postoperative cardiac events and a twofold increase in major noncardiac events in those patients treated with a PAC. They also suggested that randomized clinical trials should be conducted to evaluate the impact of this intervention on perioperative care.

Controversies over benefits of PAC: urge for clinical trials

In mid-1990, following the controversies regarding the safety of PAC use raised by the Connors study [5], Dalen and Bone [9] suggested that the US Food and Drug Administration

should impose a moratorium against use PAC until further studies were done. This caused a series of letters to the editors of various journals about disagreements among critical care physicians regarding the utility of and risks associated with PAC monitoring.

A survey of physician members of the Society of Critical Care Medicine in the USA was then conducted to evaluate physicians' attitudes toward and knowledge of the PAC and its use [10]. With a 22% return rate, the results of the survey were significant in that 95% of the respondents felt that a moratorium against PAC use was not warranted and that 75% of the respondents favored a prospective, randomized controlled trial involving PAC. The survey also showed that one-third of respondents incorrectly identified PA occlusion pressure on a clear tracing. This inability to identify one of the key hemodynamic variables available from PAC monitoring correctly raised another issue, namely that of the quality of training of ICU specialists in interpreting PAC findings. Subsequently, other studies were done to evaluate whether ICU physicians could predict the hemodynamic values generated by PAC monitoring prior to performing the procedure. If they could, then it was reasoned that they did not need to perform PAC placement. These small series studies found an average 50% rate of correct prediction of PAC values by physicians. Furthermore, 50% of PAC-derived variables in critically ill patients led to a change in management. Importantly, these changes tended to congregate among those patients with circulatory shock who were unresponsive to standard therapeutic measures [11-13]. Interestingly, these were the very patients originally suggested by Swan and coworkers [1] to be those who would benefit from PAC placement.

Other studies [14,15] compared the utility of PAC and CVP-only monitoring in managing the perioperative period in patients undergoing cardiac and vascular surgery. No differences in clinically relevant outcomes were seen between the two groups (including a specific subgroup analysis of the highest risk patients); these outcomes included length of ICU stay, occurrence of perioperative cardiac, pulmonary or renal morbidities, in-hospital mortality, major hemodynamic aberrations, and significant noncardiac systemic complications. The one statistically significant difference between groups was the professional fee charged for anesthetic care, which was higher for patients with PAC than for those with CVP catheters. These studies, along with other limited cost-effectiveness studies [2,16], suggested that there was a need for large multicenter randomized clinical trials and recommended that, until then, even high-risk cardiac and vascular surgical patients may safely be managed without routine PAC placement, which could result in important cost savings.

These controversies stimulated a series of small clinical trials; unfortunately, the discrepant results of those studies only exacerbated the uncertainty. Guyatt [17] reported a significant difference in favor of patients not receiving PAC, but Sandham and coworkers [18] found no benefit from therapy directed by PAC over standard care in high-risk surgical patients. At the same time, in an evaluation of all randomized clinical trials of PACs using a random effect model, Ivanov and coworkers [19] reported a relative risk ratio of 0.8 in favor of PAC, but they also showed serious deficiencies, including a lack of *a priori* sample size calculations, unclear definitions of concomitant therapy, inability to blind physicians and patients, and lack of blinded outcome assessments. Therefore, all of these studies collectively suggested that better designs and large, multicenter randomized clinical trials were needed.

Multicenter clinical trials

In 2003, Richard and coworkers [20] conducted a multicenter randomized clinical trial of early use of PAC versus no PAC in management of patients with shock, acute respiratory distress syndrome, or both. The treatment was left to the discretion of treating physicians. As with all previous prospective studies, those investigators found no significant impact of PAC on mortality (at 28 or 90 days) or morbidity (organ failure or ventilator dependence). Valentine [21] and Bender [22] and their groups independently found similar results in vascular surgery patients; they concluded that routine use of PACs for perioperative monitoring during aortic surgery is not beneficial and may even be associated with a higher rate of intraoperative complications.

Recently, the UK National Health Service sponsored study PAC-Man (Pulmonary Artery Catheters in Patient Management in Intensive Care) [23] reported results comparing PAC-based versus CVP-based management. As with all previous studies, the PAC-Man study found no difference in hospital mortality between patients managed with and those managed without a PAC. It also found that none of the complications associated with insertion of a PAC (<10%) was fatal. Therefore, no clear evidence of benefit or harm from managing critically ill patients with a PAC was found.

Finally, data from the ESCAPE (Evaluation Study of Congestive heart failure and Pulmonary artery catheter Effectiveness) trial [24] were recently published. In that trial it was found that basing the decision to administer vasodilator and diuretic therapy on PAC data plus clinical judgment was not superior to basing the decision on clinical judgment alone, in terms of decreasing mortality or length of hospital stay. The time to resolution of symptoms was faster with PAC data plus clinical judgment, but this did not translate into other tangible benefits. The authors did note that there was a trend toward better outcomes using PAC-guided therapy in centers admitting greater numbers of patients, and there was a consistent trend toward greater functional improvement following PAC-guided therapy, which could reflect the close relation between filling pressures and symptoms of CHF. That

both ESCAPE and PAC-Man found PAC to be safe suggests that previous retrospective reports of excess mortality with this monitoring device were confounded by the severity of the clinical settings in which the PAC was applied [5,23,24].

Use of PAC to guide treatment protocol

Based on the results of these retrospective and prospective clinical trials, there is level 1 evidence that nonspecific use of the PAC in the general management of critically ill patients is not associated with any change in mortality or morbidity. To a certain extent, these findings are comforting because they demonstrate that critical care physicians can use a highly invasive catheter with a series of potential complications (*infra vide*) without causing harm. However, these data do not address the fundamental issue regarding the utility of the PAC in patient management. Every study reported above merely compared the presence of a PAC with its absence. None of the studies used PAC-specific data to drive a treatment protocol that is known to improve outcome.

Presently, results with numerous resuscitation algorithm protocols have reflected a consistent theme of benefit or harm, depending on the timing and aggressiveness of that resuscitation. Resuscitation in shock can be divided into primary and secondary periods. The primary period is the time from initial evaluation through to the first round of resuscitation. The goals during this period are cardiopulmonary/cerebral resuscitation [25]. This encompasses establishment of an adequate airway and, if necessary, mechanical ventilation, restoration of productive cardiac rhythm and forward blood flow, and attainment of a mean arterial blood pressure above 60 mmHg [26]. Without achieving the latter initial goal, all other resuscitative goals are of questionable value and thus should not be considered alone. Once mean arterial blood pressure is sufficient to maintain cerebral and myocardial perfusion, then the secondary period of resuscitation begins. The goals during this period are establishment of an adequate organ perfusion pressure for all organs, establishment of adequate organ blood flow, and establishment of adequate oxygen transport to metabolically active tissues. The first two goals are achieved by utilizing volume expansion and vasoactive agents, often using data acquired by invasive hemodynamic monitoring via a PAC. The utility of the PAC must be assessed within this context, because no monitoring device can be expected to improve patient outcome if it is not coupled to a treatment that itself improves outcome.

In support of this is the recent, large, single-center clinical trial of early goal-directed therapy for the management of severe sepsis [27]. That study documented markedly improved outcomes when individuals were aggressively treated for circulatory shock in the emergency department during the initial 6 hours of hospitalization, rather than waiting for them to be transferred to the ICU for better monitoring. That study focused on rapidly achieving an adequate mean arterial pressure, CVP and urine output, as well as an adequate degree of tissue perfusion, as assessed by superior vena caval oxygen saturation. This study is in stark contrast to the negative findings of numerous large studies that aimed to improve survival in patients once they were transferred to the ICU using similar resuscitation end-points [28-31]. These negative studies do not mean that resuscitation is ineffective in supporting life in patients who are in shock. They merely demonstrate that there is no specific level of oxygen transport or mixed venous oxygen saturation that one must attain to ensure a good outcome once shock has induced tissue injury. Thus, the lack of documented benefit of PAC use in these clinical trials probably more reflects inadequate study design than inadequate utility [32].

Shoemaker and coworkers [33] conducted a prospective trial of supranormal oxygen delivery values in high-risk surgical patients before surgery and then during the operative interval. They then followed these patients during the postoperative period for development of acute lung injury, length of time of mechanical ventilation, mortality and total hospital costs. Following initial resuscitation (blood pressure >120/80 mmHg, hematocrit >34), patients were assigned to one of three treatment groups: PA control group ($n = 30$; goals: cardiac index [CI] 2.8-3.5 ml/min per m^2, global oxygen transport [To_2] 400-550 ml/min per m^2, and oxygen consumption [Vo_2] 120-140 ml/min); PA protocol group ($n = 28$; goals: CI >4.5 ml/min per m^2, To_2 >600 ml/min per m^2, and Vo_2 >170 ml/min); and CVP control group (no specific additional treatment goals). In each group the targeted levels of CI, To_2, and Vo_2 were achieved. The PA protocol group, as compared with the PA control group, had less time on the ventilator (2.3 versus 9.4 days), fewer postoperative deaths (1/28 versus 10/30), and fewer ICU days (10.2 days versus 15.8 days). Similarly, their hospital costs were the lowest of the three groups. The CVP group fared similarly to the PA control group. These data are in accordance with the large clinical trials reviewed above. When a PAC is present but not used to drive therapy, outcomes are no different than if the PAC is not present.

Interestingly, Lobo and coworkers [34] examined maximizing oxygen delivery in high-risk elderly surgical patients. They included 37 high-risk patients aged above 60 years. They compared a control resuscitation ($n = 18$; To_2 520-600 ml/min per m^2) versus a hyper-resuscitation protocol ($n = 19$; To_2 >600 ml/min per m^2). They observed that the To_2 goals were achieved in only 13 out of 37 patients (achievers). Importantly, there were more postoperative complications in the control group, including infections (12/18 in the control group versus 6/19 in the protocol group; relative risk [RR] 0.47, 95% CI 0.2-0.9) and cardiovascular dysfunction (RR 0.34, 95% CI 0.1-0.8). A mortality benefit was suggested but not demonstrated (mortality at 28 days: 33% in the control group versus 16% in the protocol group; RR 0.32, 95% CI 0.1-0.98). Importantly, these benefits also observed in the

'non-achiever' subgroup of the protocol group, suggesting that hyper-resuscitation prior to insult improves outcomes even if it does not increase the measured oxygen delivery.

Gattinoni and coworkers [29] studied 762 patients from 56 centers, all of whom had an Acute Physiology Score above 11. The population included patients undergoing high-risk surgery; those with massive blood loss, sepsis and respiratory failure; and trauma patients. However, the mean time from developing severe shock to enrollment in the study was 23 hours, making this study a late recovery protocol, not an early resuscitation protocol. The goals of therapy were separated into three treatment groups: CI 2.5-3.5 ml/min per m^2; CI >4.5 ml/min per m^2; and mixed venous oxygen saturation >70%. Unfortunately, the therapeutic goals were achieved in less than half of the second group. Importantly, the investigators found no difference in ICU or 6-month mortality for any diagnosis, even in the subgroup of patients in whom the targeted goals were achieved. This study concluded that therapy aimed at achieving supranormal CI or normal mixed venous oxygen saturation in patients with severe circulatory shock for more than 24 hours cannot be justified. In support of this lack of benefit, Hayes and coworkers [28] studied 100 critically ill patients with severe circulatory shock, assigning them to either aggressive supranormal oxygen delivery levels or normal oxygen delivery levels. They found markedly increased mortality in the treatment group compared with the control group (54% versus 34%; $P < 0.05$). Thus, aggressive therapy once tissue injury has occurred will not restore organ function but will carry its own increased risks. However, one can also conclude that early aggressive resuscitation before organ injury may be beneficial in high-risk patients, but is probably of marginal benefit in those who are less sick.

Recently, Shah and coworkers [35] conducted a meta-analysis of 5051 patients studied in 13 RCTs during the past 20 years, randomized to the use of PAC or no PAC. They found that there was a significantly higher rate of use of vasodilator and inotropic agents in PAC groups, but there was no difference in mortality between groups. The use of PAC did not improve survival or decrease the length of hospital stay. Importantly, none of the studies used PAC-derived variables to drive therapies of proven benefit. They merely noted the impact of having a PAC in place on outcome. They stated, as others have, that monitoring without linkage to therapies of proven benefit is unlikely to show benefit. All of these trials excluded patients in whom treating physicians thought a PAC was required for treatment, and so it is possible that patients outside the studied population – such as patients who are evaluated for heart and lung transplants – are in fact those who would benefit from PAC placement [35].

The NIH ARDSNet FACTT (Fluids and Catheters Treatment Trial) study, a multicenter clinical trial of PAC versus CVP, has just finished enrollment. It is study of 2 × 2 factorial design comparing liberal versus conservative fluid management with specific hemodynamic goals and treatment strategies, which involve use of fluids, inotropes, vasopressors, and diuretics as per protocols. This study is the only trial coupling a treatment protocol with use of PAC. Therefore, if it identifies any difference in outcomes between patients managed by PAC and those managed by CVP, then one can conclude that protocolized treatment guided by PAC is more or less effective, and so the study has more credibility and may justify a change to practice regarding use of PAC in the ICU. However, FACTT used PAC-derived filling pressures not to guide resuscitation but to limit it, considering the issue of whether limited resuscitation to avoid increasing pulmonary edema in acute respiratory distress syndrome can improve outcome. Thus, the results of this trial, although important, will not address the broader issue of PAC-guided therapy in the critically ill.

Summary: impact of PAC on outcome

The combined literature shows that the nonspecific placement of a PAC in a critically ill patient does not impair outcomes. However, no study has used PAC-derived variables to drive treatment protocols of proven benefit to determine whether PAC-specific data result in better outcomes than do data derived from less invasive devices, such as the central venous catheter and echocardiography. Such studies are needed, not only to validate use of the PAC or reject it, but also to validate or reject the use of any hemodynamic monitoring tool.

Complications

Pulmonary arterial catheterization is an invasive procedure. It requires the insertion of a central venous port and passage of a catheter across two heart values. Inflation of the catheter once in a PA may cause rupture of that vessel with disastrous consequences. Furthermore, the continual presence of a PAC increases the likelihood of catheter-related bloodstream infections and endocarditis.

The recently published PAC-Man [23] and ESCAPE [24] randomized clinical trials identified incidences of complications of 10% and 5%, respectively, in patients in whom PAC insertion was attempted. The most common complications in PAC-Man were site hematoma (4%), arterial puncture (3%), and arrhythmias needing treatment (3% with one cardiac arrest). In ESCAPE PAC-related infections occurred in 2.5%, catheter knotting and pulmonary infarction/hemorrhage in 1% each, and ventricular arrhythmia in 0.5%. None of the complications in either study led to death.

Boyd and coworkers [36] reported on 528 PAC insertions in 500 consecutive patients at the New York University Medical Center in the 1990s. They found that complications occurred in 126 out of 528 catheterizations. Serious complications occurred in only 23 of these 528 catheterizations (4.4%).

Table 1

Summary of clinical studies of PAC use

Ref.	Year	Number of cases	Study design	Clinical settings	Significant findings
[41]	1975	413	Case series	Autopsy reports	TEV with PAC was 4.25 times more frequent than with central lines; impact on mortality not studied
[38]	1979	116	Prospective case series	Critically ill patients with shock, pulmonary edema, and hemodynamic instability postoperatively	77% Arrhythmia without increased mortality or morbidity, 1.7% staphylococcal bacteremia, 1.7% subclavian DVT
[49]	1981	60	Incidence study	Critically ill patients	48% PVC and 33% VT with one death
[40]	1981	320 PAC in 219 patients	Prospective case series	Critically ill patients	3% Major complications; only one death
[36]	1983	528 PAC placements in 500 patients	Case series	All cases in one medical center	24% Complications, with 4.4% serious ones; no deaths related to complications
[42]	1983	36	Prospective case series	Autopsy	61% mural thrombosis; incidence increased with prolonged duration of catheter; no significant impact on clinical course
[46]	1984	55	Case series	Autopsy, patients with PAC within 1 month of death	53% RH endocardial lesions, 7% infective endocarditis, with pulmonic valve (56%) and pulmonary artery (5%) being the most and least common sites, respectively
[48]	1985	56	Prospective case series	ICU patents with shock, ARDS and preoperative	12.5% advanced ventricular arrhythmia; no treatment required
[37]	1985	141	Case series	Autopsy	PAC associated with higher rate of mural thrombi compared with central lines
[3]	1987	3263	Retrospective	Patients with acute myocardial infarction	Increased length of hospital stay associated with PAC use; no long-term benefit
[33]	1988	88 (30/28/30)	RCT (PAC control versus supranormal Do_2 versus CVP)	Preoperative high-risk surgical patients	PAC had no effect on outcome unless used to guide therapy
[47]	1989	279 PAC	Prospective	ICU patients	3% new RBBB
[14]	1989	1094 (537/557)	Controlled prospective cohort	Elective coronary artery bypass graft	No significant difference in outcome between PAC and CVP groups
[4]	1990	5841	Retrospective, analysis of PAC registry	Patients with acute myocardial infarction	Higher in-hospital mortality in CHF patients; thought to be related to use of PAC in sicker patients
[17]	1991	33 (16/17)	RCT (PAC versus no PAC)		Nonsignificant benefit in favor of not receiving PAC
[43]	1991	297	Prospective, incidence study	Medical/surgical ICU	22% local infection and 0.7% bacteremia; factors associated with high-risk catheter-related infection included skin colonization, IJ insertion, catheter placement >3 days and insertion in the OR
[28]	1994	100 (50/50)	RCT (supra-normal Do_2 versus normal Do_2)	Severe circulatory shock without response to fluid challenge	Increase mortality in treatment group

Table 1 (continued)

Summary of clinical studies of PAC use

Ref.	Year	Number of cases	Study design	Clinical settings	Significant findings
[29]	1995	762 (252/253/257)	RCT (control versus supranormal Do_2 versus minimal Svo_2)	Multicenter, high-risk surgical patients with hemorrhagic, septic ARDS and trauma	No difference in mortality, organ dysfunction, or length of stay
[45]	1995	32442	Retrospective chart review	OR and ICU	0.03% PA rupture with 70% mortality rate
[39]	1995	630 PAC placements in 118 patients	Retrospective analysis	Patients with aneurysmal subarachnoid hemorrhage	13% catheter related sepsis, 2% CHF, 1.2% DVT, 1% pneumothorax; no PA rupture
[5]	1996	2016 (1008/1008)	Prospective cohort, case matching analysis	Critically ill patients	Increased mortality, cost of care and length of ICU stay in PAC group
[22]	1997	104 (51/53)	RCT (routine PAC versus clinically indicated PAC)	Low-risk elective abdominal vascular surgery	Routine PAC had no benefit in mortality or morbidity
[21]	1998	120 (60/60)	RCT (PAC versus no PAC)	Surgical low-risk AAA repair	No benefit, possibly with higher intraoperative complications
[6]	2000	10,217	Retrospective database study	Nonoperative patients in medical and surgical ICU	Direct association of PAC use with admission in surgical ICU, white race, care given by nonintensivist, and having private insurance
[8]	2001	4059 (221/3838)	Prospective, observational cohort	Elective major noncardiac surgery	Increase in cardiac and noncardiac events with PAC
[18]	2003	1994 (997/997)	RCT (PAC versus no PAC)	High risk, >6-year-old surgical patients	No benefit in PAC group, higher PE in catheter group, survival rate favored non-PAC group
[20]	2003	676 (335/341)	RCT (PAC versus no PAC)	Multicenter; shock and ARDS patients	No impact of PAC on mortality or morbidity
[23]	2005	1041 (519/522)	RCT (PAC versus no PAC)	Multi-center, all adult ICUs	No evidence of benefit or hospital mortality, 10% complications but not fatal
[24]	2005	433 (215/218)	RCT (PAC versus no PAC)	Multicenter, severely symptomatic CHF patients	No evidence of benefit or overall mortality, 5% complications but none fatal

AAA, abdominal aortic aneurysm; ARDS, acute respiratory distress syndrome; CHF, congestive heart failure; CVP, central venous pressure; Do_2, oxygen delivery; DVT, deep venous thrombosis; ICU, intensive care unit; IJ, internal jugular; MI, myocardial infarction; OR, operating room; PA, pulmonary artery; PAC, pulmonary artery catheter; PE, pulmonary embolism; RHC, right heart catheterization; RH, right heart; RBBB, right bundle branch block; RCT, randomized clinical trial; Svo_2, mixed venous oxygen saturation; TEV, thrombotic endocardial vegetation; VT, ventricular tachycardia.

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These complications, although serious, did not contribute directly to any of the 31 deaths seen in these patients. PAC was reported by clinicians to have been of benefit in the management of 80% of the patients. The authors concluded that use of PAC is justified if it is likely that the catheter will contribute significantly to the management of the individual patient.

In a series of 141 consecutive autopsy cases in which a central catheter was present at the time of death [37], three deaths were attributable to catheter use and two to perforation. Furthermore, mural thrombi were present in 33 (33%) of 99 patients with PAC and in 12 (29%) of 42 patients with central venous catheters. The incidences of pulmonary emboli and bacteremia were no greater in patients with thrombi than in those without. The use of central catheters may thus be complicated by perforation or development of mural thrombi. Although the thrombi may embolize or may become infected, the incidence and clinical significance appear to be low. Importantly, complications of central vascular access define the primary complications of PAC, and thus are not diminished if the patient only has a central venous catheter placed.

In the following discussion we review studies that look into PAC-related complications and divide them into three major categories.

Catheter-related infections and thromboembolic events

Elliott and coworkers [38] evaluated the incidence and the significance of complications resulting from the use of PAC to monitor critically ill patients in a prospective study of 116 PAC insertions. In two cases (1.7%) staphylococcal bacteremia probably originated from the catheter. In addition, the PAC led to two cases (1.7%) of subclavian vein thrombosis. *Post mortem* examinations revealed perforations of the pulmonic valve in one case. Furthermore, in a retrospective analysis of 630 PAC placements in 184 patients with aneurysmal subarachnoid hemorrhage, Rosenwasser and coworkers [39] demonstrated a 13% incidence of catheter-related sepsis, a 2% incidence of congestive heart failure, and a 1.3% incidence of subclavian vein thrombosis. Sise and colleagues [40] reported similar findings. They prospectively studied the use of 320 catheters in 219 critically ill patients. Major complications (including six pneumothoraces and three arrhythmias requiring treatment, one of which was fatal) occurred in 3% of catheterizations, but only one subclavian vein thrombosis occurred. Site complications occurred more frequently in catheters maintained for longer than 72 hours.

Pace and coworkers [41] reported on an autopsy series of 413 patients over 2 years assessing the incidence of aseptic thrombotic endocardial vegetations (TEVs) after PAC use. They found five instances of aseptic TEV, three of which occurred in 88 patients with PACs, one in 120 patients with central venous catheters, and one in the 205 patients without central vascular catheters. They concluded that the incidence of TEV is increased by PAC placement. The impact of TEV on patient mortality, unfortunately, could not be ascertained.

Lange and coworkers [42] examined 36 hearts of patients who died with an indwelling PAC in place to assess the incidence and extent of localized lesions in the right side of the heart. Bland mural thrombosis in the superior vena cava, the right atrium, and the PA was found in 22 out of 36 cases (61%). Patients with catheter placement durations in excess of 2 days had a greater incidence and extent of bland mural thrombosis (79%) than did patients with short-term catheterization (41%; $P < 0.01$). Anticoagulation had no influence on bland mural thrombosis. Valvular hemorrhage occurred in 31% and TEV in 8% of the hearts. No case of infective endocarditis was identified. Four of 36 cases (11%) had evidence of pulmonary infarction that appeared to be unrelated to the lesions in the right side of the heart. Endocardial lesions were common complications of PAC but had no significant impact on clinical courses.

Mermel and coworkers [43] conducted a prospective clinical study of hospitalized adult medical and surgical patients undergoing PAC placement. Overall, 65 (22%) of 297 PACs exhibited local infection of the introducer (58 catheters) or the intravascular portion of the PAC (20 catheters); only two catheters (0.7%) caused bacteremia. Eighty per cent of infected PACs (the introducer or PAC) exhibited concordance with organisms cultured from skin of the insertion site, 17% with a contaminated hub, and 18% with organisms contaminating the extravascular PAC portion beneath the sleeve. Isolates from infected PACs were most likely to exhibit concordance with concomitantly infected introducers (71%). The risk for PAC-associated bacteremic infection with good sterile technique was about 1%. However, with heavy colonization of the insertion site, percutaneous insertion in the internal jugular vein rather than subclavian vein, catheterization for longer than 3 days, and insertion with less stringent barrier precautions significantly increased the risk for catheter-related infection.

In another case series study of 32 patients brought to autopsy with a right PAC in place, Connors and coworkers [44] identified thrombosis in 53% and intimal fibrin deposition in 66%. Ninety per cent of cases had either thrombosis or hemorrhage, or both, in this autopsy series, and the incidence of thrombosis was significantly higher if the catheter was in place for longer than 36 hours.

Pulmonary artery rupture and endocardial damage

Kearney and Shabot [45] conducted a retrospective chart review study of 32,442 inpatients requiring PAC monitoring in the operating rooms and ICUs of a large, private teaching hospital over a 17-year period. Ten patients suffered PA rupture (observed rupture rate 0.031%), seven of whom died

(70% mortality rate). All 20 patients had hemoptysis and five (50%) had pulmonary hypertension. Two patients (20%) had undergone anticoagulation at the time of rupture. Four of the six surgical patients were still in surgery at the first sign of rupture. Patients who underwent thoracotomy for PA rupture showed better survival than who did not.

Rowley and coworkers [46] studied the frequency and clinical importance of right-sided endocardial lesions in patients who received a PAC within 1 month of death. Of the 55 catheterized patients, 53% had one or more right-sided endocardial lesions; 22% had subendocardial hemorrhage, 20% sterile thrombus, 4% hemorrhage and thrombus, and 7% infective endocarditis. Fifty-six per cent of lesions were located on the pulmonic valve, 15% on the tricuspid valve, 15% in the right atrium, 10% in the right ventricle, and 5% in the main PA. All four patients with infective endocarditis had had positive *ante mortem* blood cultures while the catheter was in place, but in only one had the diagnosis of endocarditis been suspected clinically. The unusual locations of the infected vegetations (on the pulmonic valve in three and in the right atrium in one) and the similar location of the uninfected lesions suggest that the infective endocarditis was a consequence of catheter-induced endocardial damage with concurrent or subsequent bacteremia. Among the 87 non-catheterized patients, there were two subendocardial hemorrhages and one resolving right atrial thrombus. These authors concluded that endocardial damage from the PAC is common and that right-sided infective endocarditis should be suspected in all bacteremic catheterized patients.

Arrhythmias

Sprung and coworkers [47] tried to determine the incidence of new right bundle branch block (RBBB) and complete heart block during PAC insertion. They studied 293 patients undergoing 307 PAC insertions. They found that 3% were associated with the development of a new RBBB. None of the 14 patients with a pre-existing left bundle branch block (LBBB) developed complete heart block. The incidence of complete heart block during PA catheterization of patients with previous LBBB was not higher than the incidence of RBBB in patients without underlying conduction defects. Elliot and coworkers [38] found a 77% incidence rate of arrhythmias, including premature atrial or ventricular depolarizations, ventricular tachycardia, and transient RBBB in 116 patients undergoing PAC insertion, but this high rate was not associated with morbidity or mortality.

In another study, Iberti and colleagues [48] reported advanced ventricular arrhythmias (three or more consecutive premature ventricular contractions) in 25–68% of ICU patients undergoing PA catheterization. A group of 56 ICU patients who received a PAC were prospectively studied to determine the incidence of catheter-induced arrhythmias and the time required for catheterization. Advanced ventricular arrhythmias were observed in seven out of 56 (12.5%) patients, the longest duration of arrhythmia being seven consecutive premature ventricular contractions. No patient required treatment for their arrhythmias and all arrhythmias resolved with catheter movement. There was no statistical difference in catheterization times or incidence of arrhythmias between critically ill patients and preoperative patients.

Sprung and coworkers [49] revisited this issue by studying 60 sequential PAC insertions. Twenty-nine out of 60 catheterizations (48%) were associated with premature ventricular contractions and 20 (33%) were associated with ventricular tachycardia. Two patients required antiarrhythmic therapy or a precordial thump to convert ventricular tachycardia. One patient developed ventricular tachycardia and fibrillation and died. Based on these data the incidence of serious PAC-associated arrhythmias is very low and appears not to influence patient outcome.

Conclusion

One may conclude that PAC use is associated with increased risk for arrhythmias during insertion, infections and thrombotic complications during prolonged retention (>48 hours), and very rare PA rupture. Considering that the there are no benefits of PAC use that is not associated with a defined treatment protocol, this review supports the discontinuance of routine PAC insertion unless it is coupled to a defined treatment protocol of proven efficacy. Such protocols exist but they need to be followed in defined high-risk patient populations. Considering the dearth of actual clinical trials of the utility of PAC-derived data in driving effective treatment protocols other than those of pre-optimization, it is clear that appropriate prospective clinical trials of proven treatments using PAC-derived data are indicated if the PAC is to retain its place in monitoring critically ill patients.

Competing interests

MH declares no competing interests. MRP has received financial benefits from Arrow International, Edwards Lifesciences and LiDCO Ltd and holds shares in LiDCO Ltd. MRP holds US Patent 6.776.764 and has received NIH Grants HL67181, HL07820 and HL073190.

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