Cardiovascular monitoring in sepsis: why pulmonary artery catheters should not be used

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ABSTRACT

The pulmonary artery catheter (PAC) has been used extensively to guide treatment of severe sepsis. However, it has some risk of complications, and limitations in knowledge of its proper use may lead to inaccurate data. In 1996, an observational cohort study found that use of a PAC in the first 24 hours of intensive care was associated with increased 30-day mortality, length of stay and cost. This prompted prospective randomised studies. Six such studies have been published, four of which included significant numbers of patients with sepsis. All have found that, although there was no increase in deaths with PAC use, neither was there benefit in mortality in the intensive care unit, hospital or up to 90 days, nor any difference in ICU or hospital length of stay, and no reduction in organ failures or need for organ support. The PAC-Man study, a pragmatic study of 1014 patients, found no benefit compared to usual treatment, which in 80% of cases was allowed to include alternative measures of cardiac output. The recent Fluid And Catheter Treatment Trial (FACTT) of 1000 patients had similar findings when the control group used central venous pressure and clinical assessment of adequacy of cardiac output. Functional rather than static measures of pressure better predict fluid responsiveness. Furthermore, whether measuring cardiac output using any method can improve outcome is unknown. In the treatment of patients with severe sepsis as a whole, the PAC offers no benefit and some risk. Subgroups with specific benefit or harm may exist.

Crit Care Resusc 2006; 8: 256–259

No other form of patient monitoring has been subject to as much controversy as the balloon-tipped flow-directed pulmonary artery catheter (PAC). It was introduced into clinical practice in the 1970s,[1,2] and enthusiastically taken up by intensive care physicians who assumed that the direct measurements and derived values it provided would help direct therapy in a way that would improve patient outcome. However, until recently, this hypothesis had never been tested in prospective randomised clinical trials.

The use of the PAC grew rapidly (particularly in health systems where its use attracted additional provider reimbursement[3]) so that, by the late 1980s, it was estimated that US$4 billion was spent annually on its use worldwide.[4] At the same time, there was increasing evidence of morbidity and mortality attributable to PAC use. Complications were reported in 10%–53% of patients (including pulmonary artery thrombosis or embolus, pulmonary haemorrhage or infarction, right atrial thrombosis, internal jugular stenosis or thrombosis, atrial and ventricular dysrhythmias, electromechanical dissociation, right heart valvular damage or infection, and systemic sepsis). These complications were fatal in 0–4%.[5-9] Another significant issue was poor knowledge of the technical aspects of PAC use among doctors and nurses.[10-12] Although there was no evidence that this led to inappropriate treatment or worse outcomes, it was unlikely to improve outcomes. In addition, two observational studies in patients with acute coronary syndromes suggested a higher mortality for those receiving a PAC.[13,14] One early attempt in 1991 at a randomised controlled trial failed,[15] as only 33 of 148 eligible patients were actually enrolled.

As a result of these findings, there were early calls for a moratorium on use of the PAC.[16] However, the issue of its clinical effectiveness and safety came to a head in 1996 with the publication of a large, prospective, observational cohort study of mixed medical and surgical patients,[17] which found that use of a PAC in the first 24 hours of intensive care was associated with increases in 30-day mortality, length of stay and cost. This study was criticised as, although a propensity score was used for risk adjustment, there may have been unknown and unmeasured sources of bias which led to the decision to place a PAC in patients who were more severely ill. However, the study led to much stronger calls for prospective randomised studies to be performed,[18] and the development of consensus statements on PAC use,[19] in which the ability of the PAC to improve outcome in sepsis and septic shock was considered uncertain. At the same time, two meta-analyses found that a proposed benefit of the PAC — to facilitate the maximisation of oxygen delivery — could not be proven to be of value in patients with acute critical illness.[20,21]

The scene was therefore set for prospective randomised trials of the PAC in critically ill patients, with several conducted over the past 10 years. A single-centre study in a general intensive care unit in the United Kingdom found that there was no difference in 28-day mortality in 201

patients with shock, respiratory failure or early renal dysfunction randomised to treatment with or without a PAC.[22] A subsequent French multicentre study of 676 patients with shock and/or acute respiratory distress syndrome (ARDS) in 36 ICUs also found no difference in mortality up to 90 days after randomisation to treatment with or without a PAC.[23] There was also no difference in the use of renal replacement or vasoactive agents, or in the duration of mechanical ventilation, ICU or hospital length of stay.

The largest prospective, randomised controlled trial of the PAC in critically ill patients is the PAC-Man (Pulmonary Artery Catheters in Management of patients in intensive care) study,[24] published in 2005. This pragmatic study enrolled 1041 patients in 65 ICUs, who were considered by their treating clinician as patients who should be managed with a PAC. Only 6% were elective surgical cases; most were medical (66%), and the remainder were emergency surgery (28%). Two thirds of patients had multiorgan dysfunction, and 57% were considered likely to have infection. The main reason for considering a PAC was the need to guide the use of vasoactive agents. Randomisation to treatment with or without a PAC was in two strata (a priori self-selection by ICU): in one stratum no alternative cardiac output (CO) monitoring used (21% of patients), and in the other it was permitted (79% of patients). All other clinical treatment was at the discretion of the treating clinician. There was some crossover, with 5% of the control group receiving a PAC, while 7% of the intervention group did not receive one. Changes in therapy attributed to the information gained from the PAC were reported in 80% of cases, most often additional fluid (42%), significant changes in vasoactive drug doses (43%), or initiation of vasoactive drug(s). However, on an intention-to-treat analysis, no differences were found in hospital, 28-day or ICU mortality, duration of organ support, or ICU or hospital length of stay. Unfortunately, no data have yet been published on the frequency of use of other CO measures (although a post-hoc analysis is planned), and so the conclusion from this study is limited to PAC use being no better (or worse) than current practice that includes alternative CO measurement. There were too few patients in the no-CO measurement group of stratum A ($n = 107$) to draw any firm conclusion, but, as the two control groups had identical mortality, it suggests either that there was a very low use of alternative CO measurement or that having such measures confers no benefit.

The most recent study, the Fluid And Catheter Treatment Trial (FACTT), is a 2×2 factorial design study from the ARDSNet group, comparing protocolised treatment of patients with acute lung injury or ARDS with PAC versus a central venous catheter (CVC) alone, and a conservative versus liberal fluid strategy.[25,26] Although enrolment required acute lung injury to be present, primary pulmonary infection or sepsis from another site was the aetiology in 70% of the 1000 patients. Randomisation occurred on the second ICU day, so that only a minority of patients (33%) had shock. Crossover was minimal (2.3% in the PAC group, 1.4% in the CVC group), and there was high protocol adherence and excellent follow-up. Fluid, vasopressor and inotrope therapy were based on mean arterial pressure and urine output in both groups, with pulmonary artery occlusion pressure (PAOP) and thermodilution cardiac output used in the PAC group, and central venous pressure and clinical signs of an effective circulation in the CVC group. The study found no difference in 60-day mortality for all patients or for the subgroup with shock, no difference in ventilation-free or ICU-free days in the first 28 days, and no difference in organ failure-free days for cardiovascular, neurological, coagulation, hepatic or renal systems.

Similar results have been reported in other patient groups without sepsis. The Canadian Critical Care Trials Group compared goal-directed therapy guided by a PAC with standard care without a PAC in mainly elective high-risk surgical patients.[27] They found no difference in survival up to 12 months or in morbidity, except that the PAC group had a higher incidence of pulmonary embolism. The ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial[28] compared patients with significant heart failure treated with or without the use of a PAC. This study found no difference in the number of days alive and out of hospital during the first 6 months, and a significant increase in adverse events in the PAC group.

What are we make of this accumulated evidence, especially with regard to the treatment of patients with sepsis? There are now at least six prospective, randomised controlled trials of PAC use, including four with a significant proportion of patients with sepsis, none of which found benefit (or significant harm). A 2005 meta-analysis also concluded that PAC use did not alter mortality or length of hospitalisation.[29] There is some evidence that use of the PAC does lead to changes in therapy, but this does not translate into changes in outcome. The reason appears to be that the measures obtained from the PAC (right atrial pressure, PAOP, and thermodilution CO) do not add to those obtained by less invasive means. There is good evidence that these filling pressures are inaccurate measures of ventricular volumes or preload, and in particular do not predict the capacity of the heart to increase stroke volume with volume expansion.[30] Techniques that determine thoracic or ventricular volumes also do not reliably predict preload responsiveness.[31,32] The ability of the heart to increase CO in response to volume expansion may be best determined by functional rather than static assess-

ment.[33] Similarly, PAOP is inaccurate in predicting the development of pulmonary oedema.[34]

The value of CO estimates in guiding therapy so as to improve outcome from sepsis remains unproven. The PAC studies suggest no benefit, but there are no prospective randomised studies of less invasive methods compared with clinical assessment alone. In my department's practice, the frequency of use of the PAC in patients with severe sepsis has steadily declined over the past 15 years virtually to zero, without being replaced by alternative CO measurement, but with a falling mortality over this time.

Use of a PAC can also provide knowledge of mixed venous oxygenation, but using this and other variables to guide treatment to produce supranormal values of cardiac index or oxygen delivery has been found to be of no value.[20,21] A more recent study of early goal-directed therapy in sepsis indicated that there may be benefit in protocolised resuscitation using central venous oxygen saturation as an end-point.[35] However, this was a single-centre study with high mortality in the control group, and requires further validation. Also, which elements in such a protocol might be essential remains unclear, and the results may reflect the "Hawthorne effect" related to increased monitoring in the intervention arm. Perhaps the best intervention we can provide is a sound clinician at the bedside.

A number of new cardiovascular monitoring technologies have become available in recent years, which provide intermittent or continuous estimates of CO, as well as other indices, such as intrathoracic blood volume and extravascular lung water. Although these are minimally invasive technologies, and thus unlikely to produce direct harm, we must ensure that they undergo rigorous evaluation in studies with patient-centred outcome measures, lest we repeat the saga of the PAC over the past 30 years.

In summary, in the monitoring of the cardiovascular system in sepsis, the PAC can, when used by well-trained medical and nursing staff, accurately provide a number of physiological measurements and derived variables. Unfortunately, this information is unable to influence therapy in a way that improves patient outcome, and thus, as it is associated with a small but measurable risk of harm, the PAC should not be used in sepsis. Alternative approaches to cardiovascular measurement should also be examined to determine whether they are able to guide treatment and improve patient outcomes beyond the guidance provided by good clinical assessment.

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References

1 Swan H, Ganz W, Forrester J, et al. Catheterisation of the heart in man with the use of a flow-directed balloon-tipped catheter. *N Engl J Med* 1970; 283:447-51.
2 Ganz W, Donoso R, Marcus H, et al. A new technique for measurement of cardiac output by thermodilution in man. *Am J Cardiol* 1971; 27: 392.
3 Rapoport J, Teres D, Steingrub J, et al. Patient characteristics and ICU organisational factors that influence frequency of pulmonary artery catheterisation. *JAMA* 2000; 283: 2559-67.
4 Shoemaker W. Use and abuse of the balloon-tipped pulmonary artery (Swan-Ganz) catheter: are patients getting their money's worth. *Crit Care Med* 1990; 18: 1294-5.
5 Elliott C, Zimmerman G, Clemmer T. Complications of pulmonary artery catheterisation in the care of critically ill patients: a prospective study. *Chest* 1979; 76: 647-52.
6 Sprung C, Jacobs L, Caralis P, Karpf M. Ventricular arrhythmias during Swan-Ganz catheterisation of the critically ill. *Chest* 1981; 79: 413-5.
7 Chastre J, Cornud F, Bouchama A, et al. Thrombosis as a complication of pulmonary artery catheterisation via the internal jugular vein: prospective evaluation by phlebography. *N Engl J Med* 1982; 306: 278-81.
8 Boyd KD, Thomas SJ, Gold J, et al. A prospective study of complications of pulmonary artery catheters in 500 consecutive patients. *Chest* 1983; 84: 245-9.
9 Connors AF Jr, Castele RJ, Farhat NZ, et al. Complications of right heart catheterization. A prospective autopsy study. *Chest* 1985; 88: 567-72.
10 Iberti TJ, Daily EK, Leibowitz AB, et al. Assessment of critical care nurses' knowledge of the pulmonary artery catheter. The Pulmonary Artery Catheter Study Group. *Crit Care Med* 1994; 22: 1674-8.
11 Iberti TJ, Fischer EP, Leibowitz AB, et al. A multicenter study of physicians' knowledge of the pulmonary artery catheter. Pulmonary Artery Catheter Study Group. *JAMA* 1990; 264: 2928-32.
12 Gnaegi A, Fehi F, Perret C. Intensive care physicians' insufficient knowledge of right heart catheterisation at the bedside: time to act? *Crit Care Med* 1997; 25: 213-20.
13 Gore JM, Goldberg RJ, Spodick DH, et al. A community-wide assessment of the use of pulmonary artery catheters in patients with acute myocardial infarction: a prospective autopsy study. *Chest* 1985; 88: 567-72.
14 Zion MM, Balkin J, Rosenmann D, et al. Use of pulmonary artery catheters in patients with acute myocardial infarction. *Chest* 1990; 98: 1331-5.
15 Guyatt G. A randomised controlled trial of right heart catheterisation in critically ill patients. Ontario Intensive Care Study Group. *J Intensive Care Med* 1991; 6: 91-5.
16 Robin ED. Death by pulmonary-artery flow-directed catheter: time for a moratorium? *Chest* 1987; 92: 727-31.
17 Conners AF, Speroff TS, Dawson NV, et al; for the SUPPORT Investigators. The effectiveness of right heart catheterisation in the initial care of critically ill patients. *JAMA* 1996; 276: 889-97.
18 Dalen J, Bone R. Is it time to pull the pulmonary artery catheter? *JAMA* 1996; 276: 916-8.
19 Pulmonary Artery Catheter Consensus Conference: consensus statement. *Crit Care Med* 1997; 25: 910-25.
20 Hayland DK, Cook DJ, King D, et al. Maximising oxygen delivery in critically ill patients: a methodological appraisal of the evidence. *Crit Care Med* 1996; 24: 517-24.
21 Ivanov RJ, Allen J, Sandham JD, Calvin JE. Pulmonary artery catheterisation: a narrative and systematic critique of randomised

controlled trials and recommendations for the future. *New Horiz* 1997; 5: 268-76.

22 Rhodes A, Cusack RJ, Newman PJ, et al. A randomised, controlled trial of the pulmonary artery catheter in critically ill patients. *Intensive Care Med* 2002; 28: 256-64.

23 Richard C, Warszawski J, Anguel N, et al. Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome. *JAMA* 2003; 290: 2713-20.

24 Harvey S, Harrison DA, Singer M, et al; PAC-Man study collaboration. Assessment of the clinical effectiveness of pulmonary artery catheters in intensive care (PAC-Man): a randomised controlled trial. *Lancet* 2005; 366: 472-7.

25 The National Heart, Lung and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Pulmonary-artery versus central venous catheter to guide the treatment of acute lung injury. *N Engl J Med* 2006; 354: 2213-24.

26 The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network; Wiedemann HP, Wheeler AP, Bernard GR, et al. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 2006; 354: 2564-75.

27 Sandham SD, Hull RD, Brant FR, et al, for the Canadian Critical Care Trials Group. A randomised, controlled trial of the use of pulmonary artery catheters in high-risk surgical patients. *N Engl J Med* 2003; 348: 5-14.

28 Binanay C, Califf RM, Hasselblad V, et al and the ESCAPE investigators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA* 2005; 294: 1625-33.

29 Shah MR, Hasselblad V, Stevenson LW, et al. Impact of the pulmonary artery catheter in critically ill patients. Meta-analysis of the randomised clinical trials. *JAMA* 2005; 294: 1664-70.

30 Michard F, Boussat S, Chemla D, et al. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. *Am J Respir Crit Care Med* 2000; 162: 134-8.

31 Lichtwarck-Aschoff M, Zeravik J, Pfeiffer UJ. Intrathoracic blood volume accurately reflects circulatory volume status in critically ill patients with mechanical ventilation. *Intensive Care Med* 1992; 18: 137-8.

32 Michard F, Alaya S, Zarka V, et al. Global end-diastolic volume as a predictor of cardiac preload in patients with septic shock. *Chest* 2003; 124: 1900-8.

33 Pinsky MR. Functional haemodynamic monitoring. *Intensive Care Med* 2002; 28: 386-8.

34 Levy M. Pulmonary capillary pressure and tissue perfusion: clinical implications during resuscitation from shock. *New Horiz* 1996; 4: 504-18.

35 Rivers E, Nguyen B, Havstad S, et al. Early goal directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345: 1368-77. ❑