Intensive Care Med (2002) 28:256–264
DOI 10.1007/s00134-002-1206-9

ORIGINAL

Andrew Rhodes
Rebecca J. Cusack
Philip J. Newman
R. Michael Grounds
E. David Bennett

A randomised, controlled trial of the pulmonary artery catheter in critically ill patients

Received: 23 January 2001
Accepted: 9 August 2001
Published online: 13 February 2002

A. Rhodes (✉) · R.J. Cusack
P.J. Newman · R.M. Grounds · E.D. Bennett
Department of Intensive Care,
St George's Hospital,
London SW17 0QT, UK
e-mail: arhodes@sghms.ac.uk
Tel.: +44-208-7250884
Fax: +44-208-7250879

Abstract *Objective:* To compare the survival and clinical outcomes of critically ill patients treated with the use of a pulmonary artery catheter (PAC) to those treated without the use of a PAC. *Design:* Prospective, randomised, controlled, clinical trial from October 1997 to February 1999. *Setting*: Adult intensive care unit at a large teaching hospital. *Patients*: Two hundred one critically ill patients were randomised either to a PAC group (n=95) or the control group (n=106). One patient in the control group was withdrawn from the study and five patients in the PAC group did not receive a PAC. All participants were available for follow-up. *Interventions*: Participants were assigned to be managed either with the use of a PAC (PAC group) or without the use of a PAC (control group). *Main outcome measures:* Survival to 28 days, intensive care and hospital length of stay and organ dysfunction were compared on an intention-to-treat basis and also on a subgroup basis for those participants who successfully received a PAC. *Results:* There was no significant difference in mortality between the PAC group [46/95 (47.9%)] and the control group [50/106 (47.6)] (95% confidence intervals for the difference –13 to 14%, p>0.99). The mortality for participants who had management decisions based on information derived from a PAC was 41/91 (45%, 95% confidence intervals –11 to 16%, p=0.77). The PAC group had significantly more fluids in the first 24 h (4953 (3140, 7000) versus 4292 (2535, 6049) ml) and an increased incidence of renal failure (35 versus 20% of patients at day 3 post randomisation p<0.05) and thrombocytopenia (p<0.03). *Conclusions:* These results suggest that the PAC is not associated with an increased mortality.

Keywords Critically ill patients · Pulmonary artery catheter · Intention-to-treat · No increased mortality

Introduction

The pulmonary artery catheter (PAC) (also known as Swan-Ganz catheter) has become a clinical tool that is commonly used by critical care practitioners around the world [1]. It is a widely held belief that the management of critically ill patients utilising information gained from the PAC leads to both better treatment decisions and an improvement in outcome [2]. The routine use of this method for establishing haemodynamic status, however, has come under scrutiny in recent years [3]. Due to clinicians' beliefs that the PAC is beneficial in the treatment of critically ill patients and concerns about the ethicality of a randomised, controlled trial (RCT) of the PAC in this patient group, there has been very little evidence published supporting its use [4]. Over recent years, however, there have been a few observational studies performed suggesting that the routine use of this technique

in critically ill patients may lead to an increase in mortality [3, 5, 6].

A number of studies have been published on the effects of PAC on patients being treated following acute myocardial infarction (AMI) [5, 6, 7, 8]. All of these studies were observational in nature and concluded that the use of the PAC leads to an increased mortality. Connors and colleagues published an observational retrospective study on the use of the PAC in a mixed group of critically ill patients [3]. They used a propensity score to achieve case matching and came up with similar conclusions to the studies assessing the effects of the PAC on AMI. It is clear from the observational studies, that there is potentially a problem with the PAC when used without protocolled treatment regimes to guide utilisation of the data gained from the PAC. To date only one randomised, controlled study designed to investigate these possible adverse affects has been published [9]. This study by Guyatt from the Ontario Intensive Care Study Group was published in 1991 and was designed to randomise critically ill patients either to receive a PAC or not. Of the first 148 potentially eligible patients, only 33 (22%) were actually randomised. Fifty-two of the patients not randomised were excluded because the attending clinicians thought that it was unethical to continue treating the patients without a PAC.

Following the Connors study there have been a number of calls for both a moratorium on the use of the PAC and for RCTs to be started to assess the indications and efficacy of the PAC in critically ill patients [1, 4, 10]. This study was therefore designed to assess the feasibility of performing a RCT of the PAC in critically ill patients in the current ethical climate. As there was no prospective data to perform a power analysis on, this study was pilot in nature with the aim of being able to complete a power analysis for future studies.

Materials and methods

Summary

Patients were randomly allocated to either a PAC or control limb of the study. Patients randomised to the control arm of the study had resuscitation and management decisions as normal except that PAC was not allowed. Patients in the PAC arm had a PAC inserted from which the information gained was utilised to guide clinical decision making. No formal management protocols were used in this study. Patients were then followed up for 28 days to assess mortality and morbidity end points.

Objectives

The aims of this study were to identify what effects the PAC has on morbidity and mortality in critically ill patients.

Patient selection

All patients admitted to the general Intensive Care Unit (ICU), St George's Hospital, London, England, during a 17month period from October 1997 to February 1999 were screened for entry into the study. Patients were enrolled into the study if they were identified as requiring a PAC. Indications that a patient required a PAC were: if they were critically ill and fulfilled one of the following (1) circulatory shock unresponsive to 500 ml fluid challenge as evidenced by either a heart rate greater than 100 beats/min or a systolic arterial blood pressure less than 100 mmHg, (2) oliguria of less than 0.5 ml/kg per h urine output despite 500 ml fluid challenge, (3) requirement of a vasoactive infusion, (4) acute respiratory failure necessitating mechanical ventilation. Patients were excluded from the study if they were under 18 years of age or were admitted to the ICU for elective high risk surgery for which the standard of practice at St George's Hospital is to supra-normalise their circulation peri-operatively with the use of a PAC [11]. Patients were then randomised into either a PAC or a control arm of the study (Fig. 1). Because the trial design of one of the study arms necessitated the insertion and use of a PAC, it was felt that the study could not be blinded from the investigators.

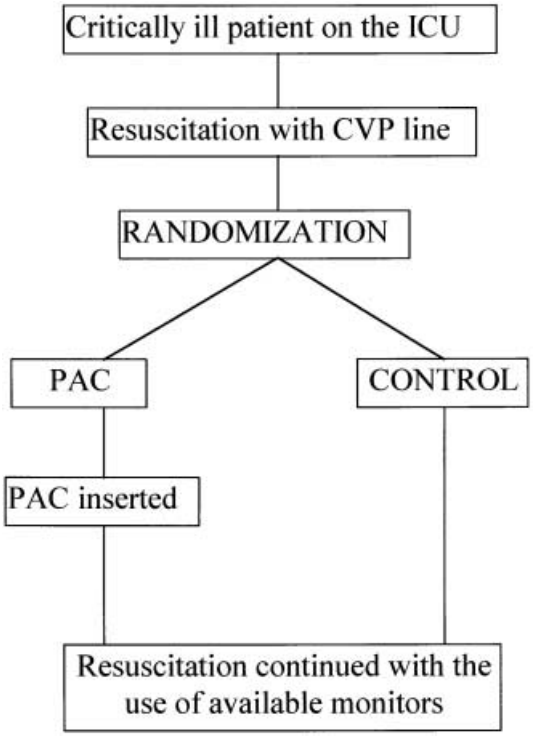

Fig. 1 Representation of trial design

Trial management

Institutional ethics committee approval was obtained prior to starting the study. Informed consent of the patients was obtained wherever possible. Assent of the relatives was sought when informed consent was not an option. All patients admitted to the ICU had resuscitation and treatment directed by the ICU clinicians. Resuscitation was aided in all patients by an intra-arterial catheter (Abbocath-T 20G, Abbott Laboratories, North Chicago, Ill.) that was inserted into either the radial or femoral artery and a central venous catheter that was inserted into either the internal jugular or femoral vein. The electrocardiogram, arterial and central venous waveforms were recorded continuously. Arterial blood gases, whole blood lactate, arterial and mixed venous oxygen saturation levels were all measured directly (ABL 625, Radiometer, Copen-

hagen). Data obtained from central venous pressure (CVP) measurements were available to clinicians treating in both groups throughout the study. In patients randomised to the PAC arm of the study, a continuous cardiac output PAC (Vigilance, Edwards Critical Care, Irvine, Calif.) was inserted into the pulmonary artery. Correct placement was checked by appropriate pressure traces and chest roentgenography. Pulmonary artery pressure waveforms were monitored continuously in these patients, as was cardiac output.

Formal treatment protocols for managing these patients were deliberately not made. Management decisions were thus left entirely to the ICU clinicians responsible for the patients' care. Patients in the PAC arm of the study had management decisions aided by information available from the PAC, whereas patients in the control arm were allowed no form of cardiac output monitoring throughout their stay in hospital. All information obtained from both treatment groups was analysed immediately and continuously acted upon. Formal measurements such as the pulmonary artery wedge pressure (PAWP) were made at least hourly in the initial stabilisation period, and more often if clinically indicated.

The first aim of resuscitation for patients in both groups included optimisation of circulating fluid volume. This was obtained by fluid challenges in order to obtain the optimum PAWP or CVP depending on the groups. In the PAC group the optimum PAWP was identified by giving fluid boluses until the cardiac index demonstrated no further increase. This was performed in all patients except for those with the acute respiratory distress syndrome (ARDS), where lower filling pressures were tolerated if other markers of tissue perfusion were satisfactory. In the control group the CVP was challenged with fluid boluses and fluid resuscitation directed by the responses seen in the CVP to the fluid challenge. Specific vasoactive agents were not protocolled, but were left to the discretion of clinicians who made their choice with the information allowed within the remits of the study. Vasoactive support was started when fluid balance was felt to be optimal and was directed at achieving a mean arterial blood pressure (MAP) of at least 60 mmHg, or higher if this was felt to be clinically indicated. Cardiac index was assessed in relation to other markers of tissue perfusion and manipulated only if it was felt to be inappropriately low for the clinical circumstances. No patient within the study had attempts at supra-normalising the circulation.

The PAC was removed when clinically appropriate. If it was still being used at 4 days post randomisation, it was exchanged for a new catheter.

Patient review

For the purposes of data collection, patients were reviewed at the following fixed time points: baseline, 1, 4, 6 h post randomisation and then daily until discharge from ICU. After the patient had been discharged from the hospital, the records were then reviewed to determine the length of time to discharge both from the ICU and the hospital and the number and types of co-morbidities (see below) involved. Survival to 28 days post randomisation was determined from hospital records or by direct contact with the patient.

Organ dysfunction definitions

Organ failure definitions were determined from the Systemic Organ Failure Assessment (SOFA) scoring system [12]. The SOFA score was calculated daily for each patient. APACHE II scores were calculated for the first 24 h for each patient [13]. ARDS was defined according to standard consensus criteria [14]. Acute renal failure was defined as either the requirement for renal replacement therapy, anuria or a creatinine concentration of greater than 300 µmol/l [12].

Study termination and statistical analysis

This study was intended to be a pilot study in order to assess the effects the PAC has on morbidity and mortality. There had previously been no prospectively performed trials studying the PAC in this patient group. Previous studies had mainly utilised case-matching techniques retrospectively to assess changes that could be attributable to the PAC. These studies have all elicited considerable controversy and the results are considered inconclusive. This study, therefore, intended to enrol 200 patients in a prospective fashion so that future trials could be appropriately powered.

Randomisation was achieved from computer-generated random numbers, which were then stored in sealed envelopes. The PAC and control groups were compared on an intention-to-treat basis. This means that every patient randomised to the PAC group was included in the analysis for that group irrespective of whether they actually received a PAC or not. A probability value less than 0.05 was considered significant in two-sided tests. Results are quoted as means (± SEM), median with 25–75th centiles or percentage as appropriate. Fisher's exact test was used to compare absolute data. Differences between the two groups over time were assessed using the repeated measures ANOVA test with Bonferroni's post hoc test. Individual differences between the groups for normally distributed data were analysed with Student's *t* test. Differences between the two groups for non-parametric data were analysed using the Mann Whitney U test and for paired samples by the Wilcoxon rank test. Differences between the two groups at baseline were assessed as having a significant effect on outcome by logistic regression analysis.

Results

A total of 201 patients were enrolled into the study and all were included in the data analysis that was performed on an intention-to-treat basis. No patients were refused entry into the study on ethical grounds. One patient, however, who was randomised to the control group, had to be withdrawn from the study on the insistence of the admitting physician who felt that it was unethical to withhold the use of a PAC from that patient. All other patients in the control group followed the protocol successfully. Five patients in the PAC group did not receive a PAC – two of whom died following randomisation but before insertion of the PAC and in the other three correct placement of the PAC was impossible.

As shown in Tables 1 and 2, randomisation resulted in two groups with no significant differences ($p>0.05$) in inclusion criteria, diagnostic category, demographics or organ dysfunction. Hundred one patients were entered into the study in septic shock, of which the majority had bronchopneumonia as the originating aetiology. Other aetiologies on entry into the study included cardiogenic shock (42 patients), haemorrhagic shock (17 patients) and postoperative multiple organ dysfunction syndrome (12 patients). As would be expected from the inclusion criteria, the patients entered into the study were elderly, the median age being 67 years (25th centile 51, 75th centile 74 years) and critically ill as evidenced by a high level of organ dysfunction and requirement for organ support. Sixty-eight (34%) patients at baseline needed

Table 1 Number of patients in inclusion criteria and diagnostic categories for the pulmonary artery catheter (*PAC*) and control groups

Inclusion Criteria (see text)	PAC	Control
Circulatory shock	56	63
Oliguria	37	40
Requirement for vasoactive infusion	46	40
Mechanical ventilation	30	44
Diagnostic category		
Septic shock		
Chest sepsis	30	30
Abdominal sepsis	13	16
Urinary sepsis	2	0
Intravascular line sepsis	2	1
Other sepsis	2	5
Cardiogenic shock	22	20
Haemorrhagic shock	4	13
Postoperative multiple organ dysfunction syndrome	6	6
Other	15	14

Table 2 Baseline characteristics of patients in the pulmonary artery catheter (*PAC*) and control groups (*MPR* mortality prediction ratio – derived from APACHE II equation)

n	PAC 96	Control 105
Median age (years)	67.5 (52, 74)	64 (49, 73)
Median admission SOFA score	7 (5, 10)	7 (5, 10)
Median APACHE II score	22.0 (17, 27)	19.0 (16, 26)
Median APACHE II MPR (%)	46.0 (28, 64)	34.5(24, 64)
Median base excess (mmol/l)	–5.1 (–1.5, –9.1)	–5.2 (–0.3, –8.9)
Median lactate (mmol/l)	2.2 (1.1, 4.3)	2.2 (1.2, 4.0)
Median PaO_2/FIO_2 ratio (kPa)	25 (16, 40)	23 (14, 39)
Renal failure, *n* (%)	13 (13.5)	12 (11.4)
ARDS, *n* (%)	7 (7.3)	9 (8.6)
Median bilirubin (μmol/l)	13 (8, 21)	14 (9, 20)
Median platelets ($\times 10^9$/l)	171 (113, 268)	174 (101, 248)
Adrenaline, *n* (%)	36 (37.5)	32 (30.4)
Dopexamine, *n* (%)	31 (33)	25 (23.8)

vasopressor or inotropic support, 74 (37%) mechanical ventilation and 25 (12.5%) renal replacement therapies. The median APACHE II score for the group was 21 (16, 26), which gave a median expected mortality for the population, as calculated from the APACHE II predictions, of 41% (24, 63). All other baseline characteristics were similar in the two groups ($p>0.05$).

Complications

There were no major complications directly attributable to the gaining of venous access in either of the two groups. Three patients in the PAC group had dysrhythmias whilst the PAC was floated through the right atrium, which were considered severe enough to prevent PAC insertion. No morbidity or mortality was thought to result directly from this cause. No other specific complication in the PAC group was thought to be directly attributable to any degree of morbidity or mortality.

Cardiorespiratory data

Table 3 describes the fluid replacement, the requirement of inotropic medication and acid base status of the two groups over the first 5 days post randomisation. The PAC group received significantly more fluid in the first 24 h of the study (4953 versus 4295 ml, $p=0.03$) than the control group. Fluid requirements for the rest of the study period were identical. There was a trend to a greater use of adrenaline infusions in the PAC group, although this did not reach statistical significance. There were no significant differences in acid base or lactate data between the two groups. Table 4 describes the haemodynamic variables for the two groups. As would be expected, there were no significant differences found between the two groups for heart rate, MAP or CVP ($p>0.05$). For the PAC group the median values of PAWP

Table 3 Fluid input, requirement of inotropic medication and acid base status for the two groups over the first 5 days post randomisation

		0	1	2	3	4	5
Adrenaline, *n* (%)	PAC	36 (37.5)	24 (28.2)	20 (24.4)	15 (19.2)	5 (7.4)	3 (4.5)
	Control	32 (30.4)	21 (23.6)	15 (18.3)	11 (13.2)	6 (9.1)	5 (7.3)
Median fluid input (ml)	PAC		4953* (3140, 7000)	3915 (2764, 5026)	3352 (2346, 4785)	3417 (2512, 4535)	2924 (2221, 4304)
	Control		4295 (2535, 6049)	4039 (2735, 5135)	3683 (2789, 4595)	3581 (2910, 4568)	3449 (2731, 4281)
Median lactate (mmol/l)	PAC	2.2 (1.1, 4.3)	1.3 (1.0, 2.0)	1.2 (1.0, 1.7)	1.3 (0.8, 1.7)	1.1 (0.9, 1.3)	1.1 (0.9, 1.4)
	Control	2.2 (1.2, 4.0)	1.4 (1.0, 2.3)	1.3 (0.9, 1.8)	1.3 (0.9, 1.8)	1.2 (0.9, 1.9)	1.3 (1.0, 1.9)
Median base excess (mmol/l)	PAC	–5.1 (–1.5, –9.1)	–3.0 (–5.4, 0.2)	–1.4 (–4.9, 2.9)	–0.3 (–4.7, 4.2)	0.6 (–3.2, 5.7)	1.3 (–3.3, 5.1)
	Control	–5.2 (–0.3, –8.9)	–1.9 (–5.7, 1.5)	–1.4 (–5.1, 3.0)	1.3 (–3.9, 3.7)	2.4 (–1.9, 5.3)	1.8 (–1.3, 4.9)

* implies $p=0.03$ for comparison between the two groups

Table 4 Haemodynamic data for the control and pulmonary artery catheter (*PAC*) groups over the first 5 days post randomisation

		Baseline	1 h	6 h	24 h	2 days	3 days	4 days	5 days
Heart rate	PAC	102 (2.3)	101 (2.2)	102 (2.2)	99 (2.0)	100 (2.7)	99 (2.7)	96 (2.6)	95 (3.3)
	Control	108 (2.7)	106 (2.3)	102 (2.3)	96 (2.3)	98 (2.8)	96 (26)	97 (2.7)	100 (3.5)
Mean arterial pressure	PAC	79 (2.3)	74 (1.8)	76 (1.4)	78 (1.7)	80 (2.0)	83 (2.4)	84 (2.7)	86 (2.4)
	Control	78 (1.8)	78 (1.7)	79 (1.7)	80 (1.8)	79 (2.1)	83 (2.6)	83 (2.6)	83 (2.6)
Central venous pressure	PAC	14 (0.9)	14 (0.6)	13 (0.5)	13 (0.6)	14 (0.7)	12 (0.6)	12 (0.7)	11 (0.8)
	Control	12 (0.8)	13 (0.6)	13 (0.5)	13 (0.5)	13 (0.7)	13 (0.6)	12 (0.7)	11 (0.7)
Mean pulmonary pressure	PAC		31 (1.0)	30 (1.1)	34 (1.3)	32 (1.1)	30 (1.3)	30 (1.5)	32 (1.7)
Pulmonary wedge pressure	PAC		17 (0.7)	16 (0.5)	18 (0.8)	17 (0.8)	15 (0.9)	15 (1.6)	16 (2.0)
Cardiac index	PAC		3.6 (0.4)	4.0 (0.3)	3.6 (0.2)	4.0 (0.2)	4.0 (0.2)	3.7 (0.4)	3.7 (0.6)
Systemic vascular resistance	PAC		944 (58)	887 (57)	874 (49)	831 (60)	904 (64)	878 (99)	747 (97)

Data are presented as means with a standard error

Table 5 Outcomes data

	PAC	Control	95% Confidence interval		*p*
			Lower	Upper	
28 day mortality rate, *n* (%)	46 (47.9)	50 (47.6)	–13%	–14%	>0.99
Median length of stay for all patients (days)					
ICU	5.7 (2, 12)	4 (2, 10)	–1.8%	4%	0.47
Hospital	13 (5, 32)	14 (3, 32)	–11.1%	8.7%	0.81
Median length of stay for survivors (days)					
ICU	10 (2, 14)	6 (2, 13)	–2.4%	7.5%	0.27
Hospital	29 (15, 54)	25 (15, 53)	–17%	18%	0.81

The 95% confidence intervals are calculated around the difference in outcomes between the two groups

were significantly higher than the CVP at all time points (p=0.008), however the correlation between these two variables was poor with an r^2 value of 0.30, demonstrating the poor ability of the CVP to predict left-sided pressures.

Clinical outcomes

The 28day mortality rate was 47.9% in the PAC group compared with 47.6% in the controls (p>0.99). This observed 0.3% difference in mortality has 95% CI of –13% to 14% for the difference between the two groups. Thus the 28day mortality rate may have been as much as 14% greater (a 29% relative risk increase) or as much as 13% less (a 27% relative risk reduction) in the PAC group compared with that in the control group [Table 5]. Although there were no significant differences between the two groups at baseline, the APACHE II score had a clinically relevant difference (22 versus 19, non-significant). Logistic regression analysis was performed to assess whether this difference at baseline might have an influence on the mortality for the two groups. The odds ratio unadjusted for the APACHE II score was 1.0 (95% CI: 0.6–1.8, p=0.9). After adjustment the odds ratio was 0.96 (95% CI 0.5–1.8, p=0.9). Hence there was no evidence of any treatment difference being masked by differences in the APACHE II score.

Since all-cause mortality in critically ill patients is unlikely to be influenced by a single intervention, other measures of morbidity were examined, including organ dysfunction scores (SOFA), individual organs performance and length of stay both in the ICU and hospital for all patients and survivors. Table 6 demonstrates the organ failure outcomes for the two groups. Both groups had a high level of organ dysfunction as evidenced by the SOFA score at baseline. There were subsequently no differences in SOFA scores between the two groups over the study period (p>0.05). There were no differences demonstrated in the number of patients developing ARDS, an abnormal PaO_2/FIO_2 ratio or hyperbilirubinaemia (p>0.05). Significant differences between the two groups were seen in the development of a low platelet count (p<0.03) in the PAC group and a greater incidence of acute renal failure by day 3 of the study for the PAC group (35 versus 19.5%, p<0.03) All patients achieving

Table 6 Organ dysfunction data for the control and pulmonary artery catheter (*PAC*) groups over the first 5 days post randomisation

		Baseline	24 h	2 days	3 days	4 days	5 days
Median SOFA score	PAC	7 (5, 10)	8 (5, 9)	7 (4, 10)	6 (4, 10)	5 (3, 8)	4 (2, 7)
	Control	7 (5, 10)	6 (4, 8)	6 (3, 9)	5 (3, 8)	4 (2, 8)	3 (1, 8)
Renal failure, *n* (%)	PAC	13 (13.5)	20 (24.1)	24 (30)	27 (35)	21 (30.4)	22 (32.8)
	Control	12 (11.4)	16 (17.9)	17 (20.7)	15 (19.5)[b]	14 (19.5)	12 (17.9)
ARDS, *n* (%)	PAC	7 (7.3)	8 (9.5)	10 (12.3)	11 (14.1)	9 (13.0)	8 (12.1)
	Control	9 (8.6)	12 (13.5)	13 (15.8)	12 (15.8)	12 (16.9)	10 (15.2)
Median PaO_2/FIO_2 ratio (kPa)	PAC	25 (16, 40)	29 (18, 39)	31 (18, 41)	32 (21, 38)	28 (22, 39)	31 (23, 39)
	Control	23 (14, 39)	29 (22, 37)	28 (18, 37)	29 (21, 36)	32 (22, 40)	30 (23, 40)
Median bilirubin (μmol/l)	PAC	13 (8, 21)	10 (7, 22)	15 (8, 21)	14 (8, 27)	15 (8, 22)	12 (9, 19)
	Control	14 (9, 20)	11 (7, 21)	12 (8, 23)	13 (8, 32)	12 (8, 35)	15 (9, 41)
Median platelet count ($\times 10^9$/l)	PAC	171 (113, 268)	140 (94, 241)	130 (83, 200)	131 (72, 167)	111 (70, 176)	135 (81, 190)
	Control[a]	174 (101, 248)	155 (84, 224)	148 (88, 222)	152 (80, 236)[c]	151 (99, 241)[c]	174 (112, 278)[c]

[a] $p<0.03$ between groups for all time points, tested by repeated measures ANOVA test

[b] $p=0.03$ between groups at that individual time point as determined by Fisher's exact test

[c] $p<0.05$ when compared to baseline, measured by the ANOVA test

the criteria of acute renal failure received renal support in terms of either haemofiltration or haemodialysis. There were no differences in the length of time patients stayed either in the ICU or hospital ($p>0.05$) [Table 5]. When stays are compared in those patients who survived, there were trends to shorter median ICU (10 versus 6 days) and hospital (29 versus 25 days) stays for the control patients, but these did not reach statistical significance.

These analyses were performed on an intention-to-treat basis; however, as noted, five patients included in these analyses as being randomised to the PAC group did not have a PAC inserted. These patients, therefore, cannot have had their outcomes influenced directly by the PAC. All of these patients subsequently died. If these patients are excluded from the outcome analysis, the 28day mortality rate for patients who had a PAC inserted is 45%. This would represent a 2.6% absolute reduction in mortality over the control group (95% CI –11% to 16%, $p=0.77$).

Discussion

In this study, critically ill patients were successfully managed with one of two treatment strategies based around the use of the PAC. Only one patient had to be withdrawn from the study due to external physician worries about the ethicality of treating that patient without a PAC. This demonstrates that despite previous concerns, it is possible to conduct a study on critically ill patients to determine the effects of specific monitoring devices such as the PAC [9]. The results of this study failed to demonstrate that the use of a PAC in critically ill patients was associated with a markedly worse outcome, contrary to previous observational reports [3, 5, 6]. There were no significant differences in the overall 28day mortality rate between patients managed with a PAC and those who were not. Patients managed with a PAC were more likely to be given more fluid in the first 24 h following insertion, develop acute renal failure and thrombocytopenia.

The lack of a significant treatment effect on mortality may reflect true equivalence, but may also result from the study's being under-powered. Table 5 lists 95% confidence intervals around the 28day mortality data. As expected, the 95% confidence intervals were wide. Using a 28day mortality rate of 47.6% in the control arm, we may have missed an increase in mortality to 67% (a relative risk increase of 141%) or a decrease in mortality to 19% (a relative risk reduction of 40%) using our sample size.

The study protocol was designed so as to separate patients into two distinct groups differing only in that one group had a PAC inserted. The aim of this study was to assess whether the insertion and use of the PAC had a detrimental effect on outcome. It was not the purpose to delineate how and when a PAC should be used. It is unclear from the literature, in all but a very few specific conditions [11], as to what management policies should be initiated from the use of the PAC. We therefore deliberately decided not to develop formal management protocols but to leave clinical decisions to the discretion of the clinician in charge of individual patients' care. By doing this we hoped to assess the effects of having a PAC on outcome, rather than assess the effects of individual management protocols. The downside to this approach, however, is that the way we use the PAC may not be the same as other intensive care units. Many factors interplay in the decision making process of whether to insert a PAC and these include such factors as severity of illness, age, diagnosis, race and reimbursement status [15]. Unless both the approach used by clinicians with PAC data and the

demographic characteristics influencing PAC insertion are similar, the extrapolation of our findings may not be valid. Much caution and further examination of these findings is therefore certainly warranted.

A negative study may have resulted from inappropriate patient selection. The inclusion criteria that we used for this study led to a heterogeneous group of very sick patients. It is possible that the mixing of different patient groups and severity of illnesses may have obscured any underlying effect that the PAC was having on outcome. Previous prospective studies utilising the PAC in specific patient groups have provided both positive [11, 16] and negative [17] impacts on outcome. This diversity of results in the literature made it very difficult to select a specific high risk group in which to assess a treatment effect with the PAC. Indeed, the previous observational study had aimed for the opposite, obtaining a broad heterogeneous group of patients [3]. We therefore decided on a broad and open set of inclusion criteria which would make patient accrual easier and allow both this and a future full study to be both feasible and the results more relevant to everyday practice. However, with the mixing of septic, cardiac and haemorrhagic causes of shock in our study we may have obscured any underlying effect.

To minimise the potential for selection bias, blinding of the randomisation process was used. Due to one group of the study having a PAC inserted, it was felt that double-blinding of the study was not feasible. The randomisation process, by a quirk of computer-generated random numbers, led to unequal numbers of patients being entered into each study arm. Despite this we feel that selection bias was unlikely, as the two groups were similar in respect of baseline diagnoses and characteristics.

Although the outcome analysis, on an intention-to-treat basis, demonstrated no differences in 28day mortality, several relevant points need to be discussed. Firstly, although there were no significant differences in baseline characteristics, the APACHE II-related mortality predictions are different for the two groups. By dividing the observed mortality by the predicted mortality a standardised mortality ratio (SMR) may be derived. Although SMRs have been criticised for comparing two different units' performances [18, 19], we feel that they may have a valid role for comparing two groups within one unit. The SMR for the group of patients managed with the use of the PAC in this study is 1.04 and the SMR for the control group is 1.38. This reduction in SMR for the protocol group suggests that the management of these patients with a PAC may have had a beneficial effect on outcome. Secondly, the aim of this study was to assess the effects of the PAC on outcome in critically ill patients. Five of the PAC group patients never had a PAC inserted. When these patients are excluded from the analysis, an improvement in outcome is seen for the PAC group (45% versus 47.6%) although this does not achieve statistical significance (p=0.77). If this data were used for future studies to assess the effects of the PAC in critically ill patients (attempting to detect a 5.4% reduction in mortality with the PAC from a control mortality of 47.6%) with a power (1-β) of 80% and a significance level (α) of 0.05, then 10,000 patients per study arm would be required.

The main significant differences between the two groups following the introduction of the PAC was that the PAC group received more fluid in the first 24 h of the study and developed an increased incidence of thrombocytopenia and renal failure. The association of thrombocytopenia and the use of the PAC has been reported previously and is thought to be due to an increased peripheral consumption of the platelets [20, 21]. The reasons for the increased incidence of renal dysfunction despite increase fluid volume are not so apparent. There are a number of possible explanations for this. First the PAC patients may have had a greater severity of illness at baseline and thus these finding may represent a continuation of their disease progression. Second, therapy started with the use of information obtained from the PAC may have been detrimental.

A number of observational studies are available in the literature that suggest an increased risk of death with the use of the PAC. These studies assessed the risk of death with PAC in the elderly [22], following AMI [5, 6, 7, 8] and in critically ill patients [3]. Gore was one of the first authors to suggest that the use of a PAC was associated with an increased mortality [5]. In a large study, 3263 patients, on AMI complicated by congestive cardiac failure (CCF), hypotension and shock they found an increased relative risk of death even after adjustment for age, sex, peak creatine phosphokinase and the occurrence of Q-wave infarction. These results were similar to those found by Zion [6], who analysed 5841 patients following AMI, of whom 371 (6.4%) had a PAC inserted. The in-hospital mortality rate of patients with CCF who received a PAC was 59.4% as compared to 33.5% who did not. The striking feature of both of these studies was that when patients who were in cardiogenic shock, and thus more relevant to our study patients, were analysed the mortality rates were essentially the same for the PAC patients and controls. Connors et al. presented similar data in 1996. From their large prospective cohort study they retrospectively analysed the outcomes of 5735 critically ill patients [3]. They assessed the severity of illness in all patients and compared the outcomes in those who received, and those who did not receive, a PAC in the first 24 h of care. They used a propensity scoring system to match patients with or without a PAC for severity of illness. They found that the PAC was associated with an increased mortality, increased length of ICU stay and increased costs. This increased mortality was especially evident in patients who underwent systematic "peri-operative" PAC insertion. This is of some interest as it may help to explain why our study, with no routine PAC in-

sertions in the peri-operative period, had no differences in outcome between the two groups.

There are two prospective interventional RCTs in the literature that have attempted to assess this problem. The first was by Shoemaker in 1988 [16] in a study on high risk surgical patients. In this study there were three groups; a PAC protocol group that underwent haemodynamic optimisation, a PAC control group and a CVP control group. They demonstrated that there were no differences in mortality between the two control groups but a markedly reduced mortality in the group of patients with a protocolled regimen for the use of the PAC. This reduction in mortality with the protocolled use of the PAC in high risk surgery is similar to results found by others [11]. The second study was by Guyatt and the Ontario Intensive Care Study Group [9]. They attempted to conduct a RCT on the PAC in critically ill patients. They randomised 33 patients into the study, but what was notable was the large number of patients excluded from the study (52) simply because attending clinicians felt that a PAC was ethically mandated. They not surprisingly were unable to demonstrate any differences between the two groups. Our study did not have the same problems of clinicians refusing patients entry into the study and this may reflect a changing perception as to the absolute usefulness of the PAC as a monitoring tool.

There are a number of studies in the literature that have utilised the PAC as part of a management strategy to augment oxygen delivery in order to improve outcome. This has led to a reduction in peri-operative mortality in high risk surgical patients [11, 23, 24] and an increased mortality in a mixed group of critically ill patients [17]. These findings have been confirmed by a meta-analysis of the available literature [25] and also backed up by recent review articles [26], which suggest that protocolled therapy utilising the PAC prior to a surgical insult may be useful whilst the same regimen in other groups of patients may be detrimental.

It is clear that the PAC is simply a monitor and thus is directly attributable to very little in the way of morbidity and mortality [1]. Any adverse effects associated with the PAC are likely, therefore, to be related to the therapeutic changes associated with the data obtained from that monitor. It is thus reliant on clinicians to interpret the data from the PAC [27, 28, 29, 30] and to utilise that data with relevant protocols. The literature is sadly lacking, however, and it is only a minority of patient groups where these protocols have been identified and tested [11, 21]. This study suggests that the PAC is not associated with an increase in mortality in critically ill patients. It may be, though, that the advantages of using the PAC in critically ill patients are small in terms of improved outcome without formal trial protocols directing therapy. Future studies need to take this into account or they risk randomising large numbers of patients with very little in the way of potential benefit.

References

1. Dalen JE, Bone RC (1996) Is it time to pull the pulmonary artery catheter? JAMA 276:916–918
2. Mimoz O, Rauss A, Rekik N, Brun-Buisson C, Lemaire F, Brochard L (1994) Pulmonary artery catheterization in critically ill patients: a prospective analysis of outcome changes associated with catheter-prompted changes in therapy. Crit Care Med 22:573–579
3. Connors AF Jr, Speroff T, Dawson NV, et al. (1996) The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. JAMA 276:889–897
4. Soni N (1996) Swan song for the Swan-Ganz catheter? BMJ 313:763–764
5. Gore JM, Goldberg RJ, Spodick DH, Alpert JS, Dalen JE (1987) A community-wide assessment of the use of pulmonary artery catheters in patients with acute myocardial infarction. Chest 92:721–727
6. Zion MM, Balkin J, Rosenmann D, et al. (1990) Use of pulmonary artery catheters in patients with acute myocardial infarction. Analysis of experience in 5,841 patients in the SPRINT Registry. SPRINT Study Group. Chest 98:1331–1335
7. Greenland P, Reicher-Reiss H, Goldbourt U, Behar S (1991) In-hospital and 1-year mortality in 1,524 women after myocardial infarction. Comparison with 4,315 men. Circulation 83:484–491
8. Blumberg MS, Binns GS (1994) Swan-Ganz catheter use and mortality of myocardial infarction patients. Health Care Financ Rev 15:91–103
9. Guyatt G (1991) A randomized control trial of right-heart catheterization in critically ill patients. Ontario Intensive Care Study Group. J Intensive Care Med 6:91–95
10. Bernard, GR, Sopko G, Cerra F, et al. (2000) Pulmonary artery catheterization and clinical outcomes: National Heart, Lung, and Blood Institute and Food and Drug Administration Workshop Report. Consensus Statement. JAMA 283:2568–2572
11. Boyd O, Grounds RM, Bennett ED (1993) A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. JAMA 270:2699–2707
12. Vincent JL, Moreno R, Takala J, et al. (1996) The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med 22:707–710
13. Knaus WA, Draper EA, Wagner DP, Zimmerman JE (1985) APACHE II: a severity of disease classification system. Crit Care Med 13:818–829
14. Bernard GR, Artigas A, Brigham KL, et al. (1994) The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes and clinical trial coordination. Am J Respir Crit Care Med 149:818–824

15. Rapoport J, Teres D, Steingrub J, Higgins T, McGee W, Lemeshow S (2000) Patient characteristics and ICU organizational factors that influence frequency of pulmonary artery catheterization. JAMA 283:2559–2567
16. Shoemaker WC, Appel PL, Kram HB, Waxman K, Lee TS (1988) Prospective trial of supranormal values of survivors as therapeutic goals in high-risk surgical patients. Chest 94:1176–1186
17. Hayes MA, Timmins AC, Yau EH, Palazzo M, Hinds CJ, Watson D (1994) Elevation of systemic oxygen delivery in the treatment of critically ill patients. New Engl J Med 330:1717–1722
18. Boyd O, Grounds RM (1993) Physiological scoring systems and audit. Lancet 341:1573–1574
19. Boyd O, Grounds M (1994) Can standardized mortality ratio be used to compare quality of intensive care unit performance? Crit Care Med 22:1706–1709
20. Vicente Rull JR, Loza Aguirre J, De la Puerta E, et al. (1984) Thrombocytopenia induced by pulmonary artery flotation catheters. A prospective study. Intensive Care Med 10:29–31
21. Bonfiglio MF, Traeger SM, Kier KL, Martin BR, Hulisz DT, Verbeck SR (1995) Thrombocytopenia in intensive care patients: a comprehensive analysis of risk factors in 314 patients. Ann Pharmacother 29:836–842
22. Wu AW, Rubin HR, Rosen MJ (1990) Are elderly people less responsive to intensive care? J Am Geriatr Soc 38:621–627
23. Wilson J, Woods I, Fawcett J, et al. (1999) Reducing the risk of major elective surgery: randomised controlled trial of preoperative optimisation of oxygen delivery. BMJ 318:1099–1103
24. Polonen P, Ruokonen E, Hippelainen M, Poyhonen M, Takala, J (2000) A prospective, randomized study of goal-oriented hemodynamic therapy in cardiac surgical patients. Anesth Analg 90:1052–1059
25. Heyland DK, Cook DJ, King D, Kernerman P, Brun-Buisson C (1996) Maximizing oxygen delivery in critically ill patients: a methodologic appraisal of the evidence. Crit Care Med 24:517–524
26. Boyd O, Hayes M (1999) The oxygen trail: the goal. Br Med Bull 55:125–139
27. Iberti TJ, Fischer EP, Leibowitz AB, Panacek EA, Silverstein JH, Albertson TE (1990) A multicenter study of physicians' knowledge of the pulmonary artery catheter. Pulmonary Artery Catheter Study Group. JAMA 264:2928–2932
28. Iberti TJ, Daily EK, Leibowitz AB, Schecter CB, Fischer EP, Silverstein JH (1994) Assessment of critical care nurses' knowledge of the pulmonary artery catheter. The Pulmonary Artery Catheter Study Group. Crit Care Med 22:1674–1678
29. Trottier SJ, Taylor RW (1997) Physicians' attitudes toward and knowledge of the pulmonary artery catheter: Society of Critical Care Medicine membership survey. New Horiz 5:201–206
30. Bernard GR, Sopko G, Cerra F, et al. (2000) Pulmonary artery catheterization and clinical outcomes. JAMA 283:2568–2572