

Early Use of the Pulmonary Artery Catheter and Outcomes in Patients with Shock and Acute Respiratory Distress Syndrome

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Question/Hypothesis

- Does early insertion of a PAC reduce morbidity and mortality in patients with septic shock or ARDS



Design

- Prospective
- Randomized
- Unblinded
- Multi-center
- Controlled trial



Setting

- In what environment was the study carried out?
- 36 ICUs in France



Methodology



Methodology

- Who was enrolled and what were the criteria?
- Inclusion criteria:
- Criteria for ARDS >24 hours
- Shock < 12 hours



Methodology

- Who was not and what were the criteria?
- Exclusion criteria
- <18 years
- Hemorrhagic shock
- Myocardial infarction / cardiogenic shock,
- Moribund / refused consent



Randomization

- If the study was randomized, how was this achieved?
- Telephone randomization – permuted block algorithm



Statistical Analysis

- Did the authors perform a power analysis?
- Yes – 1100 patients required to detect a 10% difference in mortality
- How was the data analyzed?



Interventions

- PAC inserted
- No specific directions to the use of the PAC



Standardization

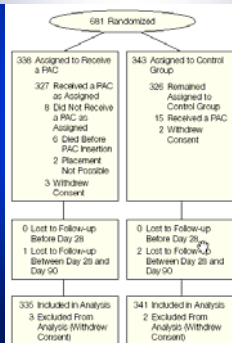


Table 1. Patient Admission and Baseline Characteristics*

Characteristics	PAC Group (n=256)	Control Group (n=261)
Age, mean (SD), y	62.2 (15.4)	62.2 (14.8)
Men	224 (88.3)	228 (88.6)
Mechanic and Jackson classification		
I	211 (82.8)	220 (85.6)
II	42 (16.7)	100 (39.7)
III	10 (4.0)	16 (6.4)
Score, mean (SD)		
SOFA†	54.1 (21.9)	54.8 (22.7)
SCRA	10.0 (4.6)	9.9 (4.4)
SIR	4.5 (1.7)	4.3 (1.7)
Bleeds	2.7 (1.3)	2.7 (1.3)
No. of patients included	252 (97.4)	270 (100)
Scheduled surgical	0 (0)	25 (9.3)
Unscheduled surgical	0 (0)	17 (6.3)
Admission before inclusion‡	137 (50.8)	139 (50.5)
Mechanical ventilation		
Required	222 (86.7)	200 (77.1)
Score, mean (SD)		
SOFA†	53.3 (15.3)	52.7 (13.9)
SCRA	9.9 (3.1)	9.9 (2.9)
SIR	2.4 (1.1)	2.3 (1.0)
Bleeds	2.5 (1.3)	2.6 (1.3)
Organ failure		
Cardiorespirator	276 (82.0)	286 (84.1)
Pulmonary	279 (83.3)	285 (83.5)
Renal	147 (44.1)	146 (42.9)
Hepatic	63 (24.8)	40 (24.5)
Hematologic	75 (22.7)	70 (21.2)
Central nervous system	26 (7.9)	23 (6.9)
Shock at inclusion§	266 (100)	266 (100)
Sepsis	251 (81.8)	228 (81.8)
Hypotensive shock	12 (4.4)	13 (4.8)
Cardiogenic shock	13 (4.4)	10 (3.7)
Anaphylaxis	1 (0.3)	1 (0.3)
Shock not defined	148 (44.3)	167 (48.0)
SIRS‖	67 (25.9)	76 (22.9)
Shock and SIRS	120 (38.9)	96 (29.0)
Shock for <12 hours at inclusion¶	226 (70.5)	225 (80.8)
APACHE II		
At inclusion	187 (59.9)	174 (63.0)
Primary	126 (39.3)	128 (45.1)
For <24 hours at inclusion¶	126 (39.3)	117 (38.6)
Secondary	61 (19.1)	46 (16.4)
Reoperative surgery	26 (8.0)	37 (12.0)

- Medical patients
- 80% shock
- 20% ARDS



Critical Appraisal of the Methodology



Appraisal of Methodology

- Were the patients properly randomized?
 - Yes
- Were the groups comparable?
 - Yes
- Was the outcome assessment "blind"?
 - No
- Was the study large enough?
 - No



Appraisal of Methodology

- Was the study length sufficient?
 - questionable
- Was it stopped after an interval evaluation?
 - No – stopped after a specified period of time – 30 months
- Was the follow up complete – were all the patients who entered the trial accounted for at its conclusion?
 - Yes
- And were they analyzed in the groups into which they were randomized?
 - Yes



Results



Results - Mortality

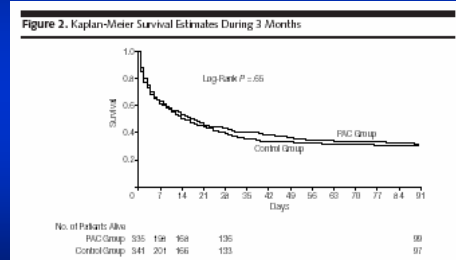
Table 2. Estimates of the Relative Risk of Mortality in Patients With a PAC at Day 28*

Group	No. of Patients	Mortality, No. (%)		Relative Risk (95% Confidence Interval)	P Value
		PAC (n = 235)	Control (n = 241)		
Total	676	120 (58.4)	208 (81.0)	0.97 (0.85-1.10)	.87
At inclusion†					
Shock exclusively	313	86 (58.0)	105 (62.9)	0.94 (0.78-1.12)	.47
ARDS exclusively	143	31 (46.2)	36 (47.4)	0.98 (0.60-1.30)	.00
Shock and ARDS	218	81 (67.5)	87 (68.4)	0.93 (0.62-1.10)	.69
Allergic shock	422	146 (64.0)	150 (69.4)	0.97 (0.85-1.11)	.60
Day 1 echocardiography					
Yes	346	62 (62.0)	124 (62.2)	1.00 (0.85-1.18)	.05
No	327	106 (67.0)	84 (59.6)	0.99 (0.80-1.15)	.84
Day 1 central venous catheter					
Yes	503	148 (62.2)	166 (62.6)	0.99 (0.87-1.14)	.02
No	169	40 (61.6)	41 (65.4)	0.93 (0.70-1.23)	.62
SAPS II (inserte)					
<44	174	33 (35.0)	35 (42.7)	0.84 (0.58-1.21)	.38
44-53	186	45 (55.6)	63 (60.0)	0.93 (0.72-1.19)	.54
54-61	145	51 (66.2)	48 (70.6)	0.94 (0.75-1.17)	.57
>=61	165	60 (62.1)	82 (78.5)	1.07 (0.92-1.25)	.29

Abbreviations: ARDS, acute respiratory distress syndrome; PAC, pulmonary artery catheter; SAPS II, Simplified Acute Physiology Score II.
*P values were obtained by Pearson χ^2 test; SAPS II scores were recorded at inclusion. †Echocardiography and central venous catheter were recorded during the first hours following inclusion (day 1).
†Without the removal of blood.

Did the use of Echocardiography Prejudice the Results?

3 Month Survival



Secondary Endpoints

Table 3. Secondary End Points According to the Intention-to-Treat Analysis*

End Point	PAC Group (n = 235)	Control Group (n = 241)	P Value
Mortality, No. (%)			
Day 14	167 (49.0)	175 (51.3)	.70
Day 90	236 (70.7)	244 (72.0)	.71
Duration of stay, d			
Intensive care unit	11.6 (10.1)	11.9 (10.0)	.72
Hospital	14.0 (11.6)	14.4 (11.3)	.67
Day 28 No. of free days			
Hospital	0.9 (3.6)	0.9 (3.3)	.05
Intensive care unit	3.4 (6.8)	3.3 (6.0)	.88
Ventilation	5.2 (8.5)	5.0 (8.5)	.72
Day 14 No. of free days			
Organ support	2.3 (3.6)	2.4 (3.5)	.72
Renal support	7.4 (6.0)	7.5 (6.3)	.08
Vasoactive agents	3.8 (4.8)	3.9 (4.5)	.78

Abbreviations: PAC, pulmonary artery catheter.
*Data are presented as mean (SD) unless otherwise specified. †Vital status was obtained for all patients until day 28 and for all except 3 patients at day 90. P values were obtained by Pearson χ^2 test for comparison of percentages or t test for comparison of means. For details of the calculation of free days, see "Methods" section.

28 day mortality was related to severity of illness

Table 4. Cox Proportional Hazards Regression Models of Predictors of Day 28 Mortality*

Predictor	Adjusted Hazard Ratio (95% Confidence Interval)	P Value
PAC vs control		
PAC	0.97 (0.79-1.20)	.78
Control	1.00	
Sex		
Male	1.23 (0.98-1.55)	.07
Female	1.00	
Age per 1 y	1.00 (0.99-1.01)	.76
At inclusion†		
Shock and ARDS	1.47 (1.04-2.08)	.03
Shock exclusively	1.10 (0.76-1.58)	
ARDS exclusively	1.00	
Method of inclusion vs surgical		
Medical	1.35 (0.98-1.87)	.07
Surgical	1.00	
SAPS II		
<44	2.84 (1.90-4.43)	<.001
44-53	2.50 (1.63-3.83)	
44-53	1.40 (0.92-2.03)	
>=61	1.00	
Day 1 central venous catheter		
Yes	0.83 (0.63-1.09)	.18
No	1.00	
Day 1 echocardiography		
Yes	1.06 (0.85-1.33)	.61
No	1.00	

Abbreviations: ARDS, acute respiratory distress syndrome; PAC, pulmonary artery catheter; SAPS II, Simplified Acute Physiology Score II.
*Cox proportional hazards regression model also stratified by hospital centers.
†Without the removal of blood.

Questions about results

- Study was underpowered
- Study did not use standardized methodology for use of PACs
- Authors' conclusion is that PACs are safe – but do they miss the point?



The Onus of Proof is
ALWAYS on the intervention!



What these studies tell us is:

1. PAC is not a therapy
2. Without set goals or protocols, it is unlikely that PAC is of any additional benefit to patients



Comments



