A Pilot Study of Pulse Contour Cardiac Output Monitoring in Patients With Septic Shock

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ABSTRACT

Objective: *To assess the relationship between PiCCO-derived signals and conventional measures of pre-load and gas exchange in patients with septic shock.*

Methods: *Prospective observational study of 23 patients with septic shock. Scheduled collection of clinical, conventional haemodynamic and PiCCO derived variables. Statistical analysis of correlations.*

Results: *Patients had a mean SAPS II score of 53.5 ± 14.5 with 78.3% on mechanical ventilation at PiCCO insertion. PiCCO monitoring lasted a mean of 4.3 ± 2.9 days. SAPS II predicted 28-day mortality was 54.2%, while actual mortality was 39.1%. At PiCCO insertion, there was an inverse correlation between cardiac (CI) and extravascular lung water index (EVLWI) ($r = -0.442$; $p < 0.05$). During treatment, the most significant correlation was between the PiCCO-derived global end-diastolic volume index (GEDVI) and PaO_2/F_IO_2 ratio ($r = 0.386$; $p < 0.01$). There was also a correlation between changes in GEDVI and changes in CI ($r = 0.329$; $p < 0.01$). Increases in EVLWI correlated with decreases in PaO_2/F_IO_2 ratio ($r = -0.332$; $p < 0.01$).*

Conclusions: *PiCCO-derived pre-load and extravascular lung water signals show logical associations with conventional indirect indicators of haemodynamic and fluid status suggesting physiological and clinical relevance.* (**Critical Care and Resuscitation 2005; 7: 160-165**)

Key words: Pulse contours cardiac output, transpulmonary thermodilution, septic shock, global end-diastolic volume index, extravascular lung water index, fluid balance, mortality

The management of septic shock remains a major challenge.[1-4] A particularly challenging component of its management relates to haemodynamic support and fluid resuscitation, especially where septic shock is complicated by other conditions such as suspected cardiogenic shock, ARDS, acute pulmonary oedema and fluid overload. Thermodilution (TD)-derived cardiac output monitoring through a pulmonary artery catheter (PAC) has been used extensively to assist with such management.[5,6]

More recently, the technology of transpulmonary thermodilution with pulse contours continuous cardiac output (PiCCO) has been introduced.[7-9] Such technique requires a central venous catheter and a 5 French (Fr) femoral arterial catheter.

This technique provides continuous information on cardiac output, but also offers several derived signals of volume status such as the extravascular lung water index (EVLWI) and the global end-diastolic volume index (GEDVI). These new indices might help intensivists adjust fluid therapy, if shown to have some physiological and/or clinical relevance. The validity of the transpulmonary thermodilution technique has been demonstrated in several previous studies.[7-16] However, the relationship between PiCCO-derived signals of volume status and more conventional, clinically used measures of vascular filling, fluid status and gas exchange in septic shock patients has not been studied. Accordingly, we studied PiCCO-based monitoring in a series of complex septic shock patients and assessed the

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relationship of PiCCO-derived indices of intravascular and extravascular fluid status with other indirect and more conventional measures.

METHODS

This was an observational study of current practice in a tertiary intensive care unit (ICU). Over a twelve month period, a total of twenty three patients received extended haemodynamic monitoring according to clinician judgement using PiCCO catheters because of the clinical diagnosis of septic shock and the perceived need to monitor cardiac output. As this was an observational study of current practice, the need for informed consent was waived by the Institutional Ethics committee.

Patients

Patients who fulfilled consensus criteria for septic shock were included in the study. In many of these patients, significant complicating factors were also present or suspected (suspected left ventricular dysfunction, ARDS, acute pulmonary oedema or fluid overload). For all patients, demographic and clinical information was obtained at admission. In all patients, PiCCO thermodilution measurements were obtained at least every 8 hours or more frequently, if clinically indicated, to calculate derived indices and calibrate the continuous cardiac output measurements. The measurements obtained during the 0800 hr thermodilution studies were recorded in a database for subsequent analysis. Conventional haemodynamic information, fluid balance information and oxygenation data were also obtained in the period surrounding these PiCCO measurements and this information was also entered in the database for subsequent analysis.

Study Protocol

The recording of all variables ceased at day seven after PiCCO insertion. Complications and reason for PiCCO removal were also recorded. Patients' ICU outcome and hospital outcome were recorded.

Statistical Analysis

Statistical analysis was performed using a commercial statistical package (Staview, Abacus Inc, CA). Descriptive statistical analysis was performed. Results were expressed as means ± SD. The correlations between study variables were assessed using Spearman's correlation test. A $p<0.05$ was considered statistically significant.

RESULTS

Of the twenty-three patients, fourteen were male and nine female. All were monitored because of septic shock with or without complicating factors (Table 1). There were no complications in relation to PiCCO insertion or monitoring.

Table 1. Clinical diagnosis at PiCCO insertion

Suspected diagnosis	*PiCCO group number (%)*
Septic shock	11 (47.8)
Septic shock + suspected CGS	7 (30.4)
Septic shock + FO/APO	1 (4.3)
Septic shock + suspected CGS + APO	3 (13.0)
Septic shock + ARDS + FO/APO	1 (4.3)

CGS = cardiogenic shock, FO = fluid overload, APO = acute pulmonary oedema, ARDS = acute respiratory distress syndrome

The age range was 36 to 87 years (mean age of 69 ± 12). The mean SAPS II score was 53.5 ± 14.5. All patients received noradrenaline infusions to keep their MAP > 70 mmHg. The mean noradrenaline dose at catheter insertion was 22.6 ± 22.7 μg/min. Of these patients, 73.9% (17) received mechanical ventilation and 95.7% (22) had an elevated serum creatinine at PiCCO insertion. Ten (43.5%) subsequently received renal replacement therapy (RRT). Other initial pathophysiological findings are shown in table 2.

Table 2. Variables at PiCCO insertion

	Patients use Picco with sepsis
HR (bpm)	106 ± 19
MAP (mmHg)	74.4 ± 6.7
CVP (mmHg)	12.6 ± 3.8
CI ($L/m^2/min$)	3.4 ± 0.9
ITBVI (mL/m^2)	1062.3 ± 341.9
EVLWI (mL/kg)	8.1 ± 2.6
GEDVI (mL/m^2)	849.8 ± 273.5
PaO_2/F_IO_2	208 ± 96
Urea (mmol/L)	15.6 ± 6.7
Creatinine (μmol/L)	229.8 ± 144.8
Mechanical ventilation rate (%)	78.3
Renal replacement therapy rate (%)	21.7
Insertion day fluid balance (mL)	424 ± 2401

Insertion day fluid balance = fluid balance calculated from the PiCCO catheter insertion till that day midnight, Hr = heart rate, MAP = mean arterial pressure, CVP = central venous ptressure, CI = cardiac index, ITBVI = intrathoracic blood volume index, EVLWI = extravascular lung water index, GEDVI = globe end diastolic volume index, PBVI = pulmonary blood volume index.

The mean fluid balance was negative beginning from day 1 and the overall mean fluid balance was -94.4 ± 1910.3 mL (mean ± SD) during the 99 PiCCO monitoring days (Figure 1).

The first measurement after PiCCO insertion showed that the EVLWI was inversely correlated with the CI ($p < 0.05$, R = -0.442) and with norepinephrine infusion dose ($p < 0.05$, R = -0.494) (Table 3).

Subsequently, a significant correlation was demonstrated for the PiCCO derived pre-load signal of global end diastolic volume (GEDVI) and the patients' oxygenation status (PaO_2/F_IO_2 ratio) ($p < 0.01$, R = 0.386). The EVLWI and PaO_2/F_IO_2 ratio also showed correlation ($p < 0.05$, R = 0.207, n = 95) (See table 4 and figures 2-4).

We studied 24-hourly changes in the values of the variables under investigation and their correlation. We found that a change in GEDVI (i.e. ΔGEDVI) showed a significant correlation with ΔCI ($p < 0.01$, R = 0.329)(Table 4).

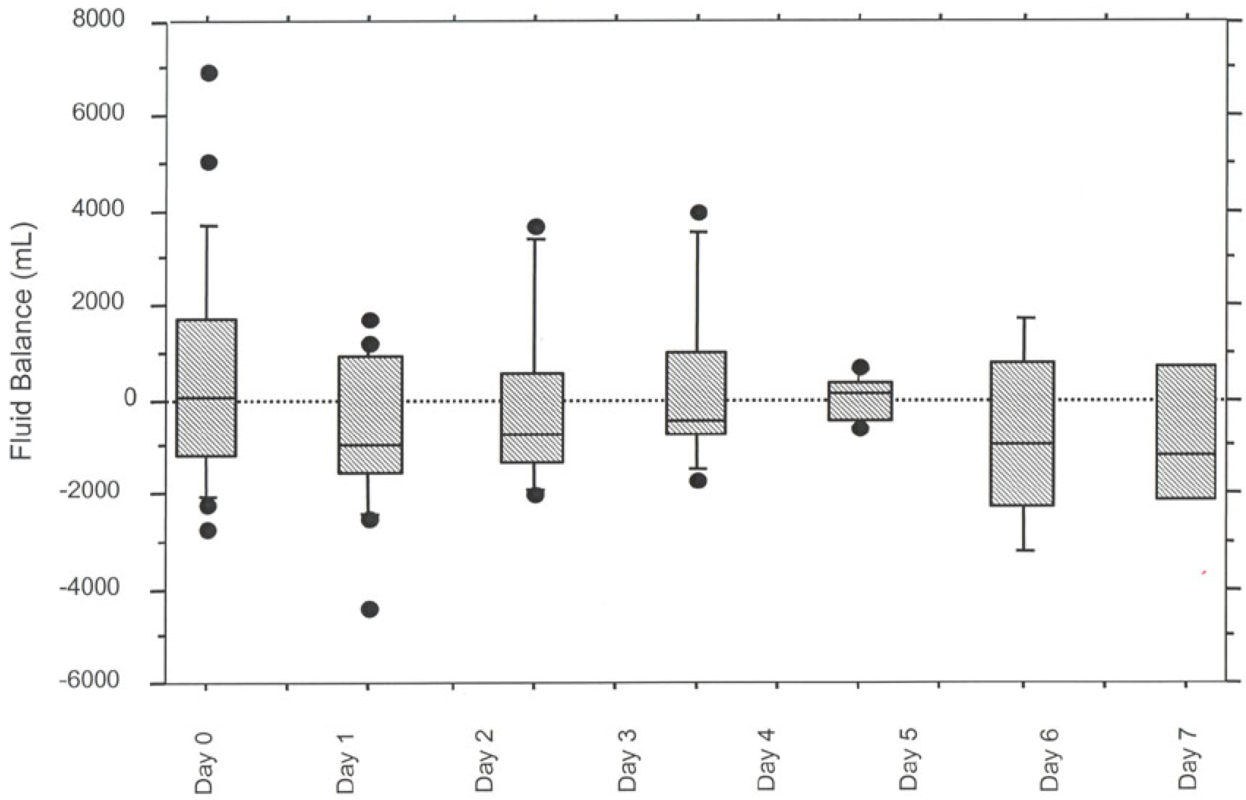

Figure 1. Mean fluid balance from day 0 to day 7.

Table 3. Correlation between physiological variables at PiCCO insertion

Parameters	*Correlation (r)*	*Measurement (n)*	*p value*
CI vs EVLWI	-0.442	21	< 0.05
CI vs EVLWI	0.471	21	< 0.05
CI vs serum creatinine level	-0.486	23	< 0.05
EVLWI vs NAD dose	-0.494	21	< 0.05
Heart rate vs NAD dose	0.534	23	< 0.01
Fluid balance vs NAD dose	-0.450	20	< 0.05

CI = cardiac index, EVLWI = extravascular lung water index, NAD = noradrenaline.

Table 4. Correlation between changes in physiological variables during PiCCO monitoring

Parameters	*Correlation (r)*	*Measurement (n)*	*p value*
ΔCI vs ΔCVP	0.254	74	< 0.05
ΔGEDVI vs ΔCI	0.329	73	< 0.01
ΔCVP vs ΔNAD dose	0.262	74	< 0.05
ΔGEDVI vs Δurea	-0.250	73	< 0.05
ΔEVLWI vs $\Delta PaO_2/F_IO_2$	-0.332	73	< 0.01
Fluid balance vs $\Delta PaO_2/F_IO_2$	-0.253	74	< 0.05

ΔCI = change in cardiac index between two continuous measuring days, ΔCVP = change in central venous pressure between two continuous measuring days, ΔEVLWI = change in extravascular lung water index between two continuous measuring days, ΔGEDVI = change in globe end diastolic volume index between two continuous measuring days, $\Delta PaO_2/F_IO_2$ = change in PaO_2/F_IO_2 ratio between two continuous measuring days.

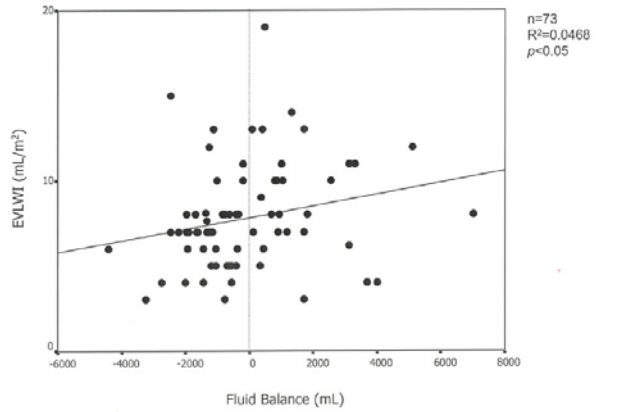

Figure 2. Correlation between EVLWI and daily fluid balance from day 0 - 7.

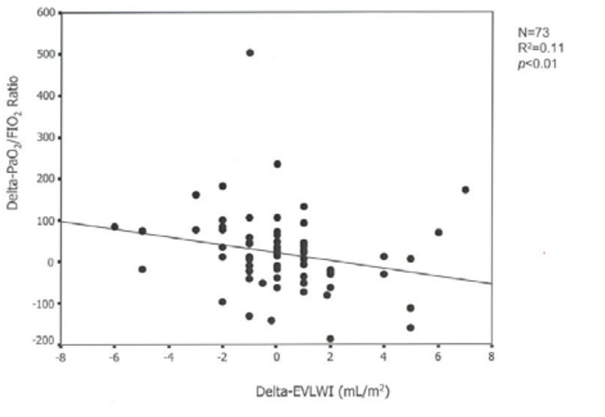

Figure 3. Correlation between ΔEVLWI and $\Delta PaO_2/F_IO_2$ ratio from day 0 - 7.

Similarly and, as expected, the Δ EVLWI and Δ PaO_2/F_IO_2 ratio showed an inverse correlation ($p < 0.01$, R = -0.332) such that an increase in EVLWI predicted a lower PaO_2/F_IO_2 ratio. The Δ PaO_2/F_IO_2 ratio also correlated with daily fluid balance ($p < 0.05$, R = -0.253), with a negative fluid balance predicting an increase in oxygenation (Figure 3,4). The length of ICU and hospital stay was 7 ± 23 days and 10 ± 23 days respectively. Although the SAPS-II score was 53.5 ± 14.5 (mean ± SD) and the predicted 28-day mortality was 54.2%, the actual 28-day mortality was 39.1%. There were no complications of PiCCO insertion. Catheter dwell time was 4.3 ± 2.9 days and no episodes of catheter infection were recorded

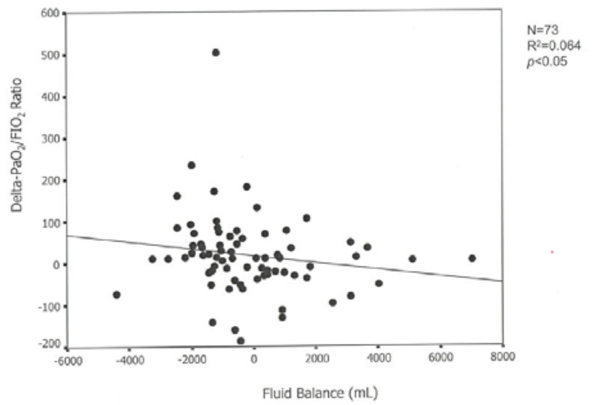

Figure 4. Correlation between $\Delta PaO_2/F_IO_2$ ratio and fluid balance from day 0 - 7.

DISCUSSION

In this study, we found that, at PiCCO insertion, septic shock patients had a high GEDVI and EVLWI, a low PaO_2/F_IO_2 ratio, needed vasopressor support and had an elevated serum creatinine indicating the presence of multiorgan dysfunction. In these patients, we found significant and logical correlations between PiCCO-derived indices of lung water and cardiac filling and more conventional measures such as cardiac index, central venous pressure, PaO_2/F_IO_2 ratio and fluid balance. Furthermore, we found that ΔGEDVI showed a significant correlation with Δ CI suggesting that GEDVI might be a clinically relevant preload signal. We also found that ΔEVLWI correlated to $\Delta PaO_2/F_IO_2$ ratio, suggesting that the extravascular lung water signal might be clinically relevant. To further support this notion, ΔEVLWI inversely correlated with fluid balance. All these observations are physiologically logical, recurrent and internally consistent suggesting that they might be clinically useful.

This study has several limitations. It is not randomised or controlled and does not focus on the effects of PiCCO on outcome. The findings are from a single center and the correlations demonstrated are not strong. Furthermore, these correlations are not with alternative, independent and scientifically accurate measures of either preload or lung water. These limitations of our study are important. However, to our knowledge, this is the first longitudinal study of the use of PiCCO in patients with complex septic shock and it compares patient outcomes to accepted illness severity-derived predictions. Furthermore, it relates PiCCO-derived indices to similarly imperfect but commonly obtained clinical indirect indicators or predictors of preload and lung water, thus making the observations clinically relevant. Finally, given the composite nature of such clinical indicators and the multiple confounding variables involved in their pathogenesis, it is not surprising that correlations with PiCCO-derived signals are not very strong.

Several studies of PiCCO technology have been performed focussing on the validity and accuracy of the values obtained for several variables.[10,11,15] They have, in general supported, the comparability and perhaps superiority of this device to other available technology.[12-14] However, in the area of septic shock, only 3 studies have been conducted in humans.[17-19] These studies have focussed on short-term issues of cardiac output signal reproducibility and accuracy[18] and the predictive ability of GEDV with regard to the effect of fluid loading on cardiac output.[17,19] These studies are very important because they establish the value of PiCCO-derived signals as markers of pre-load and the accuracy of cardiac output signals. However, they do no tackle the important issue of how such signals may be integrated into the clinical approach to patient management, where other imperfect signals are also commonly used (fluid balance, gas exchange, central venous pressure) to guide therapy. Our findings suggest that PiCCO-derived indices could be at least similarly used and might have particular usefulness in supporting clinical impressions derived using conventional markers or in challenging such impressions and demanding re-evaluation. In this regard, it might be desirable in the future to study the relationship between GEDVI and pulmonary artery catheter derived right ventricular end diastolic volume. In the aggregate, our observations support the view that PiCCO-derived indices such as GEDVI and EVLWI are physiologically and clinically relevant. We believe that, as the PiCCO-derived signals of preload and lung water are recurrently shown to be physiologically and clinically relevant, outcome studies should represent the next step in the development of our understanding of when and how this technology should be used.

In conclusion, we applied the PiCCO technique to the management of critically ill patients with septic shock and multiorgan failure and found it to be complication-free. Furthermore, in this very ill and haemodynamically compromised group of patients, PiCCO-derived signals showed a degree of correlations with conventional markers of preload or pulmonary function. In their aggregate, these observations suggest that PiCCO-derived indices have clinical as well as physiological relevance. These initial observations require confirmation in a larger cohort of patients and in a multicentre setting.

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REFERENCES

1. Dellinger RP, Carlet JM, Masur H, et al. Surviving Sepsis Campaign Management Guidelines Committee. Surviving sepsis campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004;32:858-873.
2. Holmes CL, Walley KR. The evaluation and management of shock. Clin Chest Med 2003;24:775-789.
3. Sharma S, Kumar A. Septic shock, multiple organ failure, and acute respiratory distress syndrome. Curr Opin Pulm Med 2003;9:199-209.
4. Dellinger RP. Cardiovascular management of septic shock. Crit Care Med 2003;31:946-955.
5. Ginosar Y, Sprung CL. The Swan-Ganz catheter: Twenty-five years of monitoring. Crit Care Clin 1996;12:771-776.
6. American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Anesthesiology 2003;99:988-1014.
7. Wesseling KH, Purschke R, Smith NT, Wust HJ, de Wit B, Weber HA. A computer module for the continuous monitoring of cardiac output in the operating theatre and the ICU. Acta Anaesthesiol Belg 1976;27 suppl:327-341.
8. Jansen JR. Wesseling KH, Settels JJ, Schreuder JJ. Continuous cardiac output by pulse contour during cardiac surgery. Eur Heart J 1990;11 Suppl I:26-32.
9. Irlbeck M, Forst H, Briegel J, Haller M, Peter K. Continuous measurement of cardiac output with pulse contour analysis. Anaesthesist 1995;44:493-500.

10. Tannenbaum GA, Matheus D, Weissman C. Pulse contour cardiac output in surgical intensive care unit patients. J Clin Anaesth 1993;5:471-478.
11. Goedje O, Hoeke K, Lichtwarck-Aschoff M, Faltchauser A, Lamm P, Reichart B. Continuous cardiac output by femoral arterial thermodilution calibrated pulse contour analysis: comparison with pulmonary arterial thermodilution. Crit Care Med 1999;27:2407-2412.
12. Buhre W, Weyland A, Kazmaier S, et el. Comparison of cardiac output assessed by pulse-contour analysis and thermodilution in patients undergoing minimally invasive direct coronary artery bypass grafting. J Cardiothorac Vasc Anesth 1999;13:437-440.
13. Mielck F, Buhre W, Hanekop G, Tirilomis T, Hilgers R, Sonntag H. Comparison of continuous cardiac output measurements in patients after cardiac surgery. J Cardiothorac Vasc Anesth 2003;17:211-216.
14. Rodig G, Prasser C, Keyl C, Liebold A, Hobbhahn J. Continuous cardiac output measurement: pulse contour analysis vs thermodilution technique in cardiac surgical patients. Br J Anaesth 1999;82:525-530.
15. Mahajan A, Shabanie A, Turner J, Sopher MJ, Marijic J. Pulse contour analysis for cardiac output monitoring in cardiac surgery for congenital heart disease. Anesth Analg 2003;97:1283-1288.
16. Della Rocca G, Costa GM, Coccia C, Pompei L, Di Marco P, Pietropaoli P. Preload Index: Pulmonary artery occlusion pressure versus intrathoracic blood volume monitoring during lung transplantation. Anesth Analg 2002;95:835-843.
17. Marx G, Cope T, Mc Crossan L, et al. Assessing fluid responsiveness by stroke volume variation in mechanically ventilated patients with severe sepsis. Eur J Anaesthesiol 2004;21:132-138.
18. Sakka SG, Reinhart K, Meier-Hellmann A. Comparison of pulmonary artery and arterial thermodilution cardiac output in critically ill patients. Intensive Care Med 1999;25:843-846.
19. Michard F, Alaya S, Zarka V, Bahloul M, Richard C, Teboul JL. Global end-diastolic volume as an indicator of cardiac preload in patients with septic shock. Chest 2003;124:1900-1908.