

Continuous and intermittent cardiac output measurement: pulmonary artery catheter *versus* aortic transpulmonary technique

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Background. Cardiac output (CO) can be measured intermittently by bolus thermodilution methods in the pulmonary artery (CO_{pa}) or in the aorta (CO_{art}). A continuous thermodilution method (CCO) and a method for continuous estimation using the arterial pulse wave (PCCO) are also available.

Methods. We compared two methods of intermittent CO measurements in patients during liver transplantation: CO_{pa}, regarded as the current clinical standard, and an aortic transpulmonary thermodilution technique (CO_{art}) performed with the PiCCO system. We also compared CCO and PCCO. Measurements were made in 62 patients at three stages: after the induction of anaesthesia, after caval clamping phase, and at the end of surgery. We used Bland–Altman and correlation analysis.

Results. We found close agreement between the techniques. Mean bias between CO_{art} and CO_{pa} and PCCO and CCO was 0.15 (2SD of differences between methods=1.74) litre min⁻¹ and -0.03 (1.75) litre min⁻¹, respectively. Mean bias between CCO and CO_{pa} and PCCO and CO_{pa} was 0.02 (1.48) litre min⁻¹ and 0.04 (1.69) litre min⁻¹, respectively.

Conclusions. Measurement with the aortic transpulmonary thermodilution technique gives continuous and intermittent values that agree with the pulmonary thermodilution method.

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Cardiac output (CO) and invasive cardiovascular measurements are often used during liver transplantation because instability is common during the procedure.¹ CO is commonly measured by the bolus thermodilution technique (CO_{pa}) with a pulmonary artery catheter (PAC). This could miss transient changes in CO during the procedure. A nearly continuous thermodilution method (CCO) uses small quantities of heat and a modified PAC^{2–4} with a clinically acceptable accuracy comparable with the intermittent bolus technique (Intellicath for CCO and SvO₂, Baxter Healthcare Corp., Irvine, CA).^{3,5} Recently a method of pulse contour analysis (PiCCO system, Pulsion Medical System, Munich, Germany), which is less invasive than continuous CO monitoring, has been used to give beat-by-beat measurement of continuous CO from the arterial pulse contour analysis (PCCO).^{6,7} We compared two methods of intermittent measurement, CO_{art} and CO_{pa}, and two methods of continuous measurement, PCCO and CCO (Table 1).

Patients and methods

Patients

We obtained approval from the ethics committee and written informed consent from 62 patients (48 male and 14 female) who were about to undergo liver transplantation. We excluded patients with pre-existing pulmonary or cardiac diseases, apart from end-stage liver dysfunction.⁸

Anaesthesia and mechanical ventilation

We applied a lead II/V5 ECG to measure the heart rate and a pulse oximeter and placed a radial artery catheter to measure arterial pressure (AP) (PCM SpaceLabs, Inc., Redmond, WA USA). Anaesthetic management was standardized.

Intermittent positive-pressure ventilation and analysis of inspired gases and end-tidal CO₂ were done with a

Table 1 Methods used and their abbreviations

Method	Abbreviation
Bolus pulmonary artery thermodilution	COpa
Transpulmonary thermodilution	COart
Arterial pulse contour analysis	PCCO
Continuous pulmonary thermodilution	CCO

volumetric anaesthesia ventilator (CATO, Dräger Werk HG, Lübeck, Germany). Liver transplantation was done without veno-venous bypass, using the Piggy-back technique. Catecholamines were used, if needed, to stabilize the circulation during graft reperfusion. Body temperature was controlled to avoid hypothermia, using a warming blanket (Gaymar Meditherm, Orchard Park, NY, USA) and warm intravenous fluids (HOT LINE, SIMS Medical System, Graseby Ltd, UK).

PiCCO monitoring

In all patients, a 4-French gauge thermistor-tipped catheter (Pulsioath PV2014L, Pulsion Medical System, Munich, Germany) was placed via a 5-French gauge introducer (Adam Spence Europe Ltd, Abbeytown, Boyle, CR, Ireland) through the right femoral artery, and connected to the PiCCO System (version 4.1) for clinical monitoring of AP, PCCO measurements derived from the AP wave, and COart.

Cardiopulmonary monitoring

A modified 7.5-French gauge PAC for SvO_2 and CCO was inserted via an introducer (8.5Fr Baxter Edwards Laboratories, Irvine, CA, USA) into the right internal jugular vein using the Seldinger technique and connected to the Vigilance system (Baxter Edwards Laboratories, Irvine, CA, USA) for COpa and CCO monitoring.

Experimental procedure

COart was calculated from the thermodilution curves using the Stewart–Hamilton principle. The pulse contour device was calibrated after induction of anaesthesia by the mean values of three consecutive COart measurements randomized within the respiratory cycle. These were performed by injection of 15 ml cold saline solution, at a temperature lower than 10°C, via a central venous catheter with subsequent detection by the thermistor embedded into the wall of the arterial catheter. An enhanced version of the Wesseling algorithm, not yet published by the manufacturer, was used to analyse the pulse contour, with a correction factor to reduce the effects of mean AP on arterial impedance as described elsewhere.^{6,9,10} PCCO was calculated by multiplying stroke volume by heart rate and presented on the monitor as a moving average of the preceding 12 s. We passed the modified PAC into the

pulmonary artery by monitoring the pressure waveform from the distal port of the catheter. Intermittent CO measurements were done by manual injection of 10 ml cold saline solution into the superior vena cava through the atrial port. Three consecutive boluses were injected without regard to the phase of respiratory cycle, over a 2-min period. To avoid variation between operators, the injection was always performed by the same person. The plot of the washout curve was examined for stable baseline temperature, undisturbed rapid upstroke, and exponential decay without signs of early recirculation. If an injection had to be rejected, more injections were made to obtain three measurements after rejecting the lowest and the highest. The setting of the ventilator remained the same during the measurements. Intracardiac and pulmonary AP were monitored continuously to ensure that the catheter was in the correct position. Other intravenous fluids were infused at a constant slow rate during the measurements.

After the induction of anaesthesia and achievement of stable cardiovascular conditions, calibration of the pulse contour analysis system was done before induction of anaesthesia. Intermittent CO measurements were then obtained at specific times during the study period: after induction of anaesthesia (T1), after caval clamping phase (T2) and at the end of surgery (T3). Each set of measurements was made in a steady-state period, that is, at least 15 min after change in dosage of catecholamine or sedatives, infusion rate, or ventilator settings. At each time a single set of haemodynamic measurements was collected when the cardiovascular system was stable. The CO data (bolus and continuous) obtained for calibration and immediately following the calibration are not included in the analysis of PCCO results. At each time, PCCO and CCO were measured immediately before and after intermittent CO measurements and the mean of these PCCO and CCO data pairs recorded. To assess the influence of haemodynamic status on bias, two sets of data pairs were considered according to CO (<8 and >8 litre min⁻¹).

Statistical analysis

All results are expressed as mean (SD) unless indicated otherwise. Statistical analysis used the method described by Bland and Altman.¹¹ Bias between the methods was calculated as the mean difference between COart and COpa, PCCO and COpa, CCO and COpa, and CCO and PCCO. The upper and the lower limits of agreement were calculated as bias (2SD), and defined the range in which 95% of the differences between the methods were expected to lie. The precision of the bias analysis and limits of agreement was assessed using 95% confidence intervals. This analysis was done for all data obtained at T1, T2 and T3.

Bias between COpa–COart, COpa–CCO, and COpa–PCCO at each stage (T1, T2, T3) was analysed using the paired Student *t* test. CO, mean AP and systemic vascular resistance index (SVRI) were analysed using ANOVA for

Table 2 Patients characteristics and presenting conditions of study population. HCV, hepatitis C virus; HBV, hepatitis B virus

Characteristic	Mean (SD)	Range
Age (yr)	48 (10)	24–66
Body surface area (m ²)	1.8 (0.2)	1.42–2.15
Male/female	48/14	
Underlying disease		
HCV cirrhosis	22	
HBV cirrhosis	11	
Neoplastic cirrhosis	10	
Alcoholic cirrhosis	8	
HCV + HBV cirrhosis	3	
Cryptogenetic cirrhosis	3	
Hepatic angioma	2	
Other		
Child classification (A/B/C)	15/36/12	
Cold ischaemia time (h)	8.1 (2.1)	5.5–13
Anaesthesia time (h)	10 (1.7)	5.7–14

repeated measurements and the paired Student *t* test with Bonferroni correction. All statistical analysis was computed by SPSS for Windows (Version 8.0, 1997, SPSS Inc., Chicago, IL). Statistical significance was considered to be at $P < 0.05$.

Results

Patient characteristics and the diseases leading to transplant are reported in Table 2. Sixty-two patients were enrolled. PCCO was obtained at each time in all patients. No data were rejected. CO measurements had a range of 3.2–13.7 litre min⁻¹ for COart and of 3.3–13.5 litre min⁻¹ for COpa. There were 186 pairs of comparative measurements performed between PCCO and CCO. The CO range was 3–13 litre min⁻¹ for PCCO and 3–13.8 litre min⁻¹ for CCO. CO, mean AP and SVRI measured for the different sample times are reported in Table 3.

The results of the analysis of agreement and the distribution of the observed differences are shown in Table 4 and in Figure 1. Bias was not significantly related to the level of CO but the bias was greater at larger values of CO, without statistical significance (Table 5).

The level of agreement and precision for COart and COpa, PCCO and COpa, CCO and COpa, and CCO and PCCO remained constant throughout the study period. Bias and coefficient of correlation during the predefined analysed steps are reported in Table 6 and Figures 2–4. Correlation between changes in values with each technique in COpa, COart, CCO and PCCO are reported in Table 7.

No adverse effects related to either the PiCCO catheter or the Vigilance SvO₂/CCO catheter were observed.

Discussion

Thorough cardiovascular measurements are necessary during anaesthesia for liver transplantation. CO is usually

Table 3 Measurements made after induction of anaesthesia (T1), during the anhepatic phase (T2) and at the end of surgery (T3). Data are mean (SD). AP, arterial pressure; SVRI, systemic vascular resistance index; other abbreviations are given in Table 1. *Significant changes within the study period (analysis of variance); †significantly different from T2 and T1 ($P < 0.05$); ‡significantly different from the previous phase ($P \leq 0.001$)

	T1	T2	T3
Mean AP (mm Hg)	75 (16)	78 (12)	81 (13)
Range	45–119	61–108	52–116
SVRI (dyne s cm ⁵ m ²)	1310 (307)	1512 (378) [‡]	1220 (379) [‡]
Range	1014–2558	1074–2489	1006–2430
COart (litre min ⁻¹)*	7.6 (2.2)	7.0 (1.9)	8.8 (2.2) [†]
Range	3.7–13.7	3.2–11.8	4.3–13.3
COpa (litre min ⁻¹)*	7.5 (2.1)	6.7 (1.8)	8.6 (2.2) [†]
Range	3.6–13.4	3.3–10.6	4.7–13.5
PCCO (litre min ⁻¹)*	7.5 (2.3)	6.8 (1.8)	8.7 (2.3) [†]
Range	4.0–13.0	3.0–11.8	5.0–13.2
CCO (litre min ⁻¹)*	7.4 (2.3)	6.9 (1.8)	8.7 (2.1) [†]
Range	3.8–13.8	3.0–11.4	5.0–13.2

Table 4 Mean difference between COart–COpa, CCO–COpa, PCCO–COpa, (bias), and lower and upper limits of agreement (bias ± 2SD) and coefficient of correlation between the measurements during the procedure. Abbreviations as Table 1. * $P < 0.0001$

	Bias (litre min ⁻¹)	95% limits of agreement	r ²
COart vs COpa	0.15	-1.59 to 1.89	0.86*
PCCO vs COpa	0.04	-1.65 to 1.73	0.86*
CCO vs COpa	0.02	-1.46 to 1.50	0.88*
PCCO vs CCO	-0.03	-1.78 to 1.72	0.85*

measured intermittently but continuous measurement would be preferable. Methods for continuous or semicontinuous measurement with transoesophageal echocardiography or electrical impedance have been investigated during liver transplantation.^{12,13}

To our knowledge, this is the first study that compares continuous and intermittent CO measurement obtained with two different devices, the PiCCO System and a modified PAC (Intellicath) in patients undergoing liver transplantation. We confirmed that COart and PCCO measurements agree with COpa, the current clinical standard, and that PCCO agreed well with CCO, showing that measurements of continuous CO can be made successfully by PCCO during transplant surgery. In this study we used the COpa technique as the reference method for all comparisons because it is the current clinical standard.

Previous studies in critically ill patients have reported a small mean difference (bias) and limit of agreement (bias ± 2SD), considered clinically acceptable, between CCO, based on the pulsed warm thermodilution technique, and COpa measurements.^{2,14,15} Our results support the findings of others.³ Bottiger and colleagues report a bias of 0.24 and a degree of precision of 1.789 litre min⁻¹. In the early phase of transplantation, after inferior vena cava clamping and after graft reperfusion, the accuracy (bias

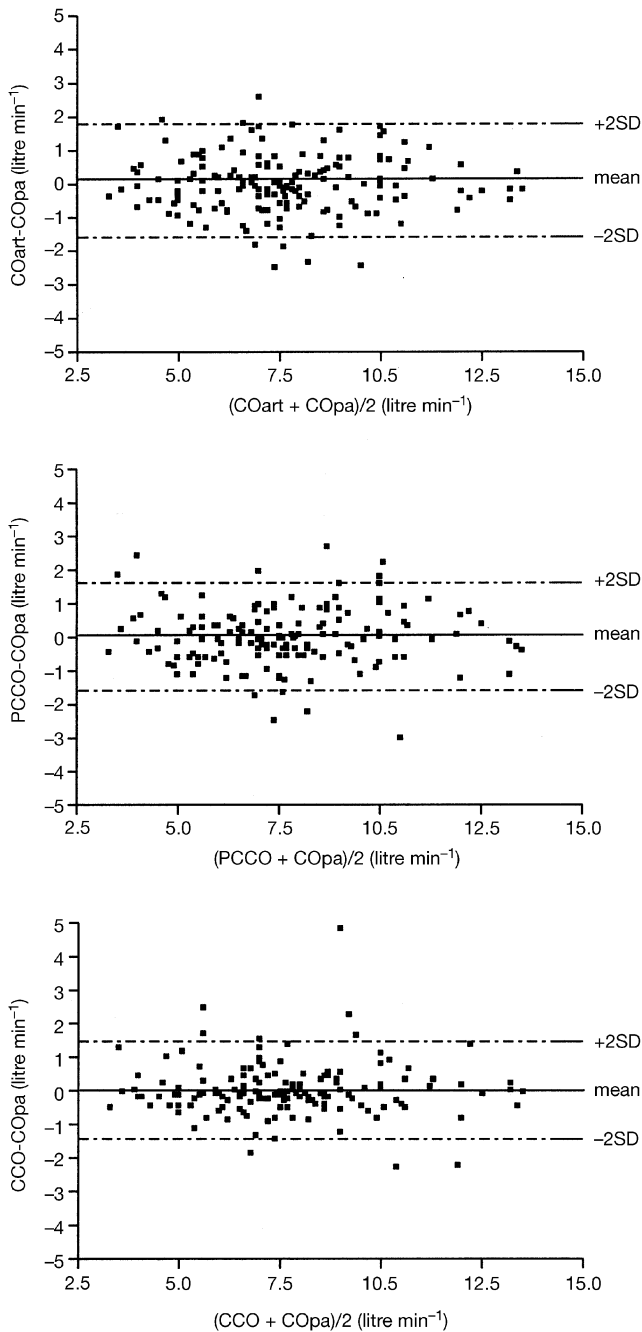


Fig 1 Bland and Altman plots between (from top to bottom) COart and COpa (0.15 [1.74] litre min⁻¹), PCCO and COpa (0.04 [1.69] litre min⁻¹), and CCO and COpa (0.02 [1.48] litre min⁻¹) for all measurements. The unbroken lines show the mean difference and the dotted lines show the 2SD limits of agreement.

0.78 litre min⁻¹) and precision (4.3 litre min⁻¹) were markedly decreased.³ When we compared CCO and COpa after caval clamping phase we found a bias (2SD) of 0.12 (1.43) litre min⁻¹ (Table 6). These differences could be because we do not usually use drug support during inferior vena cava cross-clamping and we carefully avoid hypothermia during liver transplantation so that hypothermia before and immediately after graft reperfusion is prevented.

Table 5 Mean difference between COart–COpa, PCCO–COpa, CCO–COpa (bias), and lower and upper limits of agreement (bias±2SD) at different values of CO. Abbreviations as Table 1

	Cardiac output (litre min ⁻¹)	Number of observations	Bias (litre min ⁻¹)	95% limits of agreement
COart vs COpa	<8	115	0.01	-1.73 to 1.75
	≥8	71	0.16	-1.62 to 1.47
PCCO vs COpa	<8	115	-0.11	-1.63 to 1.41
	≥8	71	0.18	-1.37 to 1.73
CCO vs COpa	<8	115	-0.03	-1.29 to 1.23
	≥8	71	0.19	-1.98 to 2.36

Table 6 Mean difference between COart–COpa, PCCO–COpa, CCO–COpa (bias), and lower and upper limits of agreement (bias±2SD) together with coefficient of correlation at sample times. Abbreviations as Table 1. T1, after anaesthesia induction; T2, during anhepatic phase; T3, end of surgery. **P*<0.0001

	Phase	Bias (litre min ⁻¹)	95% limits of agreement	<i>r</i> ²
COart vs COpa	T1	0.04	-1.62 to 1.70	0.86*
PCCO vs COpa	T1	-0.02	-1.46 to 1.50	0.89*
CCO vs COpa	T1	-0.11	-1.84 to 1.63	0.85*
COart vs COpa	T2	0.22	-1.72 to 2.16	0.75*
PCCO vs COpa	T2	0.09	-1.90 to 2.08	0.72*
CCO vs COpa	T2	0.12	-1.31 to 1.55	0.85*
COart vs COpa	T3	0.19	-1.35 to 1.73	0.87*
PCCO vs COpa	T3	0.07	-1.54 to 1.68	0.87*
CCO vs COpa	T3	0.06	-1.32 to 1.44	0.90*

Nowadays the transpulmonary indicator thermodilution technique allows intermittent CO measurement without the need to use a PAC. Animal experiments^{16–18} and clinical studies^{7, 19–21} found a good correlation between pulmonary thermodilution and the transpulmonary thermodilution technique. However, COpa is a measure of right ventricular output whereas COart also measures left ventricular output. Previous studies have found that transpulmonary CO is greater than the corresponding COpa. There may be loss of the cold, and right heart CO may be less than left heart CO because heart rate can be reduced by the cold injection. Approximately 3–4% of the indicator could be lost during passage in the pulmonary circulation, with overestimation of COart.^{17, 18} Lewis and co-workers²² described a 9% loss of the injected thermal indicator before femoral detection. Since other studies did not find an indicator loss,^{23, 24} the transient reduction in heart rate by the cold injection, which has less influence on the COart because of the longer appearance time, is more likely to be responsible for the somewhat lower values of COpa.²⁵ In the present study COart was higher than COpa, which supports results from other authors.^{22–25} Which CO is the true CO cannot be detected by this study. In any case a good agreement between the different techniques was observed. Our results comparing the two intermittent techniques (bias 0.15 [–1.59 to 1.89] litre min⁻¹) are similar to those reported by Gødje and co-workers who studied patients undergoing coronary

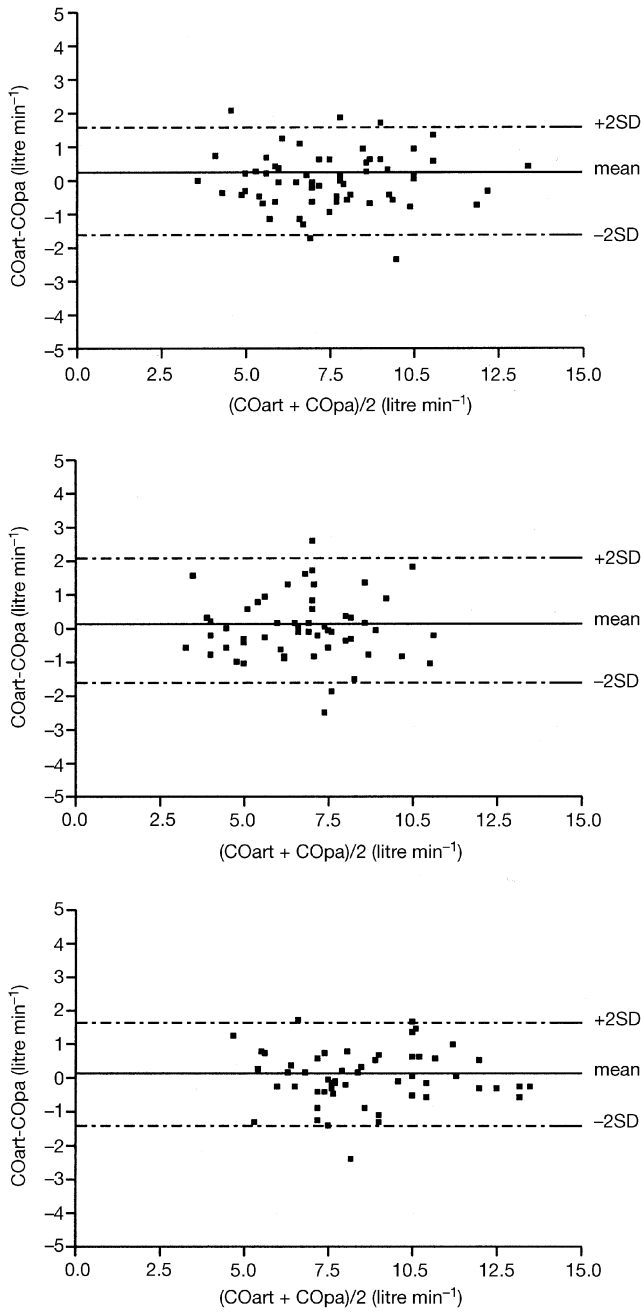


Fig 2 Bland and Altman plots between COart and COpa at specific times: T1 (top; 0.04 [1.66] litre min⁻¹); T2 (middle; 0.22 [1.94] litre min⁻¹); and T3 (bottom; 0.19 [1.54] litre min⁻¹). The unbroken lines show the mean difference and the dotted lines show the 2SD limits of agreement.

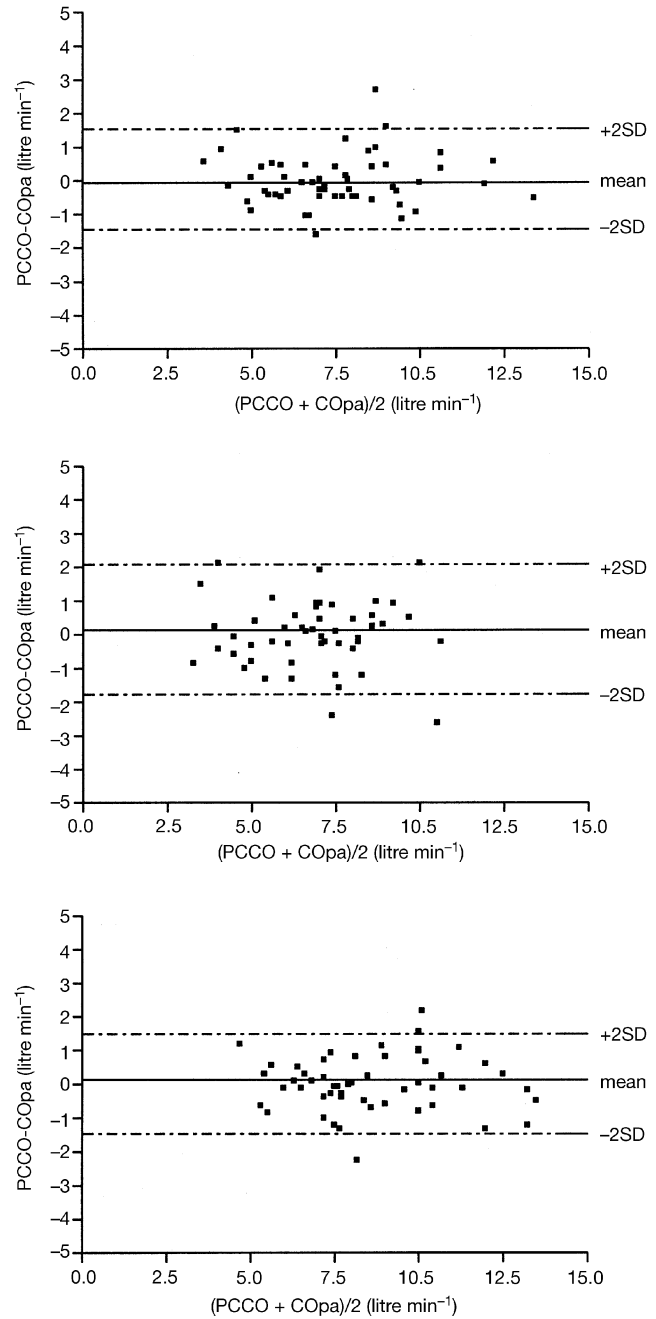


Fig 3 Bland and Altman plots between PCCO and COpa at specific times: T1 (top; -0.02 [1.48] litre min⁻¹); T2 (middle; 0.09 [1.99] litre min⁻¹); and T3 (bottom; 0.07 [1.61] litre min⁻¹). The unbroken lines show the mean difference and the dotted lines show the 2SD limits of agreement.

artery bypass grafting (bias -0.29 [-1.60 to 1.02] litre min⁻¹).⁷ In the present study we found a mean difference of 0.04 litre min⁻¹ with a level of agreement of 1.69 litre min⁻¹ between PCCO and COpa, similar to the results reported by Gödje and colleagues (bias [2SD] 0.07 [1.40] litre min⁻¹ and 0.10 [0.42] litre min⁻¹).^{7,26} Excellent results (0.003 [1.26] litre min⁻¹) were obtained during cardiac surgery in 12 patients.²⁷

Rödig and co-workers showed that changes in vascular tone of approximately 20% did not affect the pulse contour method but large changes in AP may affect PCCO measurements, and re-calibration of the PCCO device may be necessary.⁶ The finding that moderate changes in SVR did not necessarily affect the accuracy of PCCO support a study by Irlbeck and colleagues.²⁸ These authors studied PCCO and COpa in patients in the intensive care

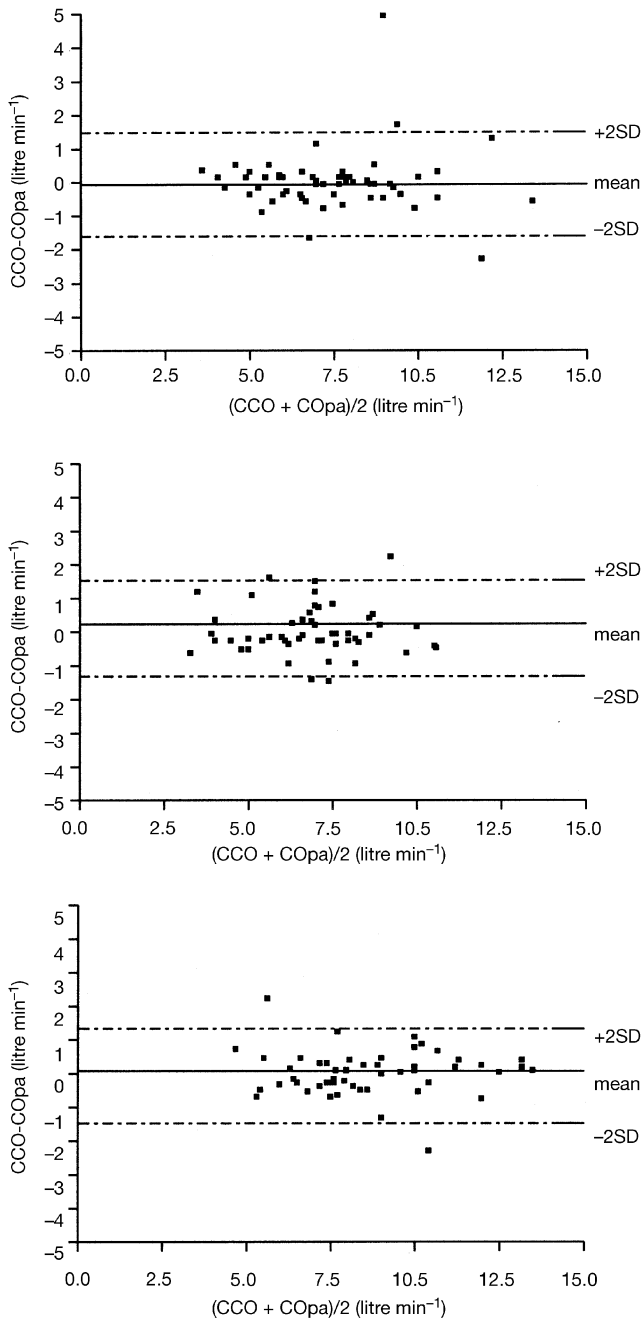


Fig 4 Bland and Altman plots between CCO and COpa at specific times: T1 (top; -0.11 [1.74] litre min^{-1}); T2 (middle; 0.12 [1.43] litre min^{-1}); and T3 (bottom; 0.06 [1.38] litre min^{-1}). The unbroken lines show the mean difference and the dotted lines show the 2SD limits of agreement.

unit and concluded that PCCO is valid for clinical purposes only if the initial calibration is repeated every 4 h.²⁸ We found no evidence that PCCO was not accurate even with substantial changes in SVR. The changes in vascular tone in our patients were probably less and had no effect on the pulse contour method. The site of pulse contour detection may be important. The pressure in peripheral arteries (such as the radial artery) may be influenced by the reflection of pulse waves and greater transit time, which can interfere

Table 7 Bias between COpa–COart, COpa–PCCO, COpa–CCO changes (Δ), and lower and upper limits of agreement (bias \pm 2SD) together with coefficient of correlation. Abbreviations as Table 1. Δ_1 =T2–T1; Δ_2 =T3–T2. * P <0.0001

		Bias (litre min^{-1})	95% limits of agreement	r^2
COpa vs COart	Δ_1	-0.10	-2.53 to 2.33	0.64*
COpa vs PCCO	Δ_1	0.04	-2.50 to 2.58	0.64*
COpa vs CCO	Δ_1	-0.12	-2.23 to 1.99	0.75*
COpa vs COart	Δ_2	-0.04	-1.91 to 1.83	0.76*
COpa vs PCCO	Δ_2	-0.01	-2.02 to 2.00	0.74*
COpa vs CCO	Δ_2	0.02	-1.59 to 1.63	0.82*

with the calculation of PCCO. In this study, PCCO was always measured with a catheter in the abdominal aorta, passed from the femoral artery. Problems with arterial catheters in the radial or brachial artery during periods of low CO were avoided. We did not observe a decrease in PCCO and/or CCO after injection of cold saline at any time during the procedures, despite giving large volumes of fluids that could affect the reliability of the continuous thermodilution CO measurements.³ At greater values of CO (>8 litre min^{-1}) the limits of agreement between PCCO–COpa and between CCO–COpa were -1.37 to 1.73 litre min^{-1} and -1.98 to 2.36 litre min^{-1} , respectively (Table 5).²⁹ Clinically the response to haemodynamic changes is more accurate with PCCO based on AP waveform than CCO because the latter method requires measurement over 3 min, being a semicontinuous method.

The risks of PAC have been recently discussed.³⁰ The transpulmonary thermodilution method performed with the PiCCO or COLD system requires a central venous cannula to inject cold saline, and a femoral arterial cannula, and avoids the use of a PAC.^{9 21 22 27} Given the closer correlation between the methods, the pulse contour method for determination of CO can be calibrated and made using COart, which would avoid unnecessary insertion of a PAC.^{7 26 27} A central venous cannula is necessary in most surgical patients anyway, and femoral artery catheterization, which allows continuous haemodynamic monitoring and blood sampling, is safe in critically ill patients.³¹

In conclusion, PAC insertion seems to be justified only when continuous measurement of SvO_2 is needed, or in patients with pulmonary hypertension. The PiCCO system is very useful in high-risk patients if less invasive monitoring is required.

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