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Assessment of three minimally invasive continuous cardiac output measurement methods in critically ill patients and a review of the literature

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Abstract

Background. In this study we compared the accuracy of three continuous cardiac output (CCO) measurement methods, with intermittent transcardiopulmonary thermodilution (TPTD-CO) as the gold standard. The three studied CCO measurement methods were: uncalibrated peripheral pulse contour measurement (FCCO), calibrated central pulse contour measurement (PCCO), and CCO obtained by indirect Fick principle (NCCO).

Methods. We performed an observational study in 23 critically ill patients. Statistical analysis was done using Pearson's correlation and Bland-Altman analysis. A review of the relevant medical literature was performed.

Results. Only PCCO showed good correlation (R = 0.9) and agreement with a bias of 0.0 ± 0.8 L min^{-1} and percentage error of 24.5% when compared to TPTD-CO. In patients with normal systemic vascular resistance index (SVRI > 1,700 dyne sec cm^{-5} m^{-2}), NCCO (R = 0.8 and bias 0.4 ± 1.3 L min^{-1}) and FCCO (R = 0.8 and bias 0.1 ± 1 L min^{-1}) also produced reliable results.

Conclusion. These results indicate that in our patient population, CCO can be most reliably monitored by calibrated central pulse contour measurements. All other methods appeared less accurate, especially in situations of low SVRI.

Key words: haemodynamic monitoring, cardiac output, pulse contour, thermodilution

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Every day, important decisions regarding the management of critically ill patients are guided by cardiac output (CO) measurements obtained by different techniques. Since the 1970s, the gold standard for CO measurement in the clinical setting has been the pulmonary artery catheter (PAC). More recently, transcardiopulmonary thermodilution cardiac output (TPTD-CO) measurement has been extensively validated as a less invasive alternative to PAC monitoring [1, 2, 3, 4]. However, both PAC and TPTD-CO have the significant disadvantage of being non-continuous, and are also somewhat labour-intensive and complex. In recent years, new and easier to use methods have been developed, providing continuous CO measurements with or without calibration.

The aim of this observational study was to compare the accuracy of three of these CCO-monitoring devices (Vigileo-FCCO, PiCCO-PCCO and NICO-NCCO) to the gold standard (TPTD-CO) in critically ill patients on high doses of vasopressors and inotropics. The basic characteristics of the three tested techniques and the gold standard technique are summarised in Table 1.

METHODS

The study was conducted in accordance with the Intensive Care Unit (ICU) protocol, the Declaration of Helsinki, and applicable regulatory requirements as approved by the institutional review board and the local institutional ethics

Table 1. Characteristics of the CCO devices

Method	Device	Calibration	Input	Method	Validation
FCCO	Flotrac/Vigileo Edwards Lifesciences, Software version 1.03 and 1.04 Irvine, CA, USA	No	Radial arterial line	Pulse contour analysis	Reasonable results after version 1.07
NCCO	NICO Philips Respironics, Murrysville, PA, USA	No	Capnograph, pulse oxymeter	Indirect Fick principle [8]	Few validation studies [9]
PCCO and TPTD-CO	PICCO Pulsion Medical Systems, Munich, Germany	Yes, by TPTD-CO	Femoral arterial line	Pulse contour analysis	Extensively validated [1–4]

CO — cardiac output; FCCO — FloTrac continuous cardiac output; NCCO — NICO continuous cardiac output; PCCO — PiCCO continuous cardiac output; TPTD-CO — transcardiopulmonary thermodilution cardiac output

committee (approval number 3789, 11 May 2011). In view of the nature of the study being purely observational and not demanding any deviation from standard clinical ICU care, informed consent from the patient or next of kin was not deemed essential. We merely retrospectively analysed the existing situation and did nothing to influence events. Only treating ICU physicians accessed the medical records. All data was pseudonymised before analysis.

The files of all patients treated in the intensive care units of the Ziekenhuis Netwerk Antwerpen (ZNA) campus Stuivenberg, between February 2004 and December 2006, were examined. During this period, mechanically ventilated patients were monitored with NCCO, while in patients who remained haemodynamically unstable in spite of fluid resuscitation, monitoring was frequently escalated to TPTD-CO. In addition, some of our referred patients were being monitored with FCCO on admission. This implies that some of our patients had multiple CO-monitoring devices installed simultaneously.

For inclusion in this data analysis, patients had to fulfill the following criteria:

1. mechanical ventilation,
2. FCCO or NCCO already in place,
3. persistent haemodynamic instability, after initial fluid resuscitation with clinical need to escalate to TPTD-CO monitoring with PCCO.

Data collection from the files of included patients was carried out as follows: first, we collected TPTD-CO measurements from the analogue patient files and/or TPTD-CO monitor digital data files. Second, three values from the CCO-device that was installed alongside the TPTD-CO monitor were obtained from the analogue patient files and/or CCO monitor digital data files. These three values were obtained during the five minutes before each TPTD-CO measurement. When more than three CCO values were found within this time window, those closest to the moment of TPTD-CO measurement were selected. Subsequently, the average of each trio of CCO measurements was taken to form a paired measurement with their corresponding TPTD-CO measurement. These paired measurements were then used to perform Bland and Altman analysis and to calculate Pearson correlation coefficients.

Statistical analysis was done using SPSS software version 13 (SPSS Inc., Chicago, IL, USA). We performed Bland and Altman analysis as previously described [5] and computed Pearson correlation coefficients [6] to analyse the agreement between different methods of CO measurement. Two methods are considered equal and may be used interchangeably if R^2 (R — Pearson's correlation coefficient) is > 0.6, if the differences within bias ± 1.96 SD (limits of agreement, LA) are not clinically important, if the precision of the new technique is comparable to the reference technique, and if the percentage error is less than 30%. Because different numbers of repeated measurements were performed in the patients, the appropriate analyses of co-variance were performed as suggested by Bland and Altman to look for intra- and inter-subject variability. We also performed subanalysis according to systemic vascular resistance index (SVRI). A low SVRI was defined as less than or equal to 1,700 dyne sec cm^{-5} m^{-2}.

RESULTS

Overall, 23 patients could be included. The patient demographics and haemodynamics at inclusion are listed in Tables 2 and 3. Patients were severely ill with a mean APACHE II and SAPS II score of 20.8 ± 7.5 and 52.4 ± 14.6 respectively. The largest group of patients were admitted to the ICU for sepsis (n = 11).

In total, 450 TPTD-CO measurements with 450 corresponding triple CCO data sets could be extracted from the patients' files: 210 paired PCCO/TPTD-CO, 125 paired FCCO/TPTD-CO, and 115 paired NCCO/TPTD-CO measurements. Mean TPTD-CO recorded during the study period was 6.9 ± 1.8 L min^{-1}.

CCO VS. TPTD-CO IN THE GLOBAL STUDY POPULATION

The Pearson correlation coefficient comparing TPTD-CO to various CCO techniques was best for PCCO (R = 0.9), followed by NCCO (R = 0.6) and then FCCO (R = 0.4). Bland and Altman analysis comparing TPTD-CO to CCO revealed

Table 2. Patient demographics on admission

Patients (n)	23
Measurements (n)	450
n/patient	19.5
Age (years)	63.7 ± 14.6
BMI (kg m^{-2})	27 ± 4.2
ICU stay (days)	20.8 ± 16.3
ICU mortality (%)	5 (21.7%)
Gender (M/F)	13/10
SAPS II score	52.4 ± 14.6
APACHE II score	20.8 ± 7.5
SOFA score	7.8 ± 3.9
Acute kidney injury	1
Abdominal sepsis	4
Respiratory sepsis	7
Polytrauma — neurotrauma	4
Intracerebral bleeding	2
Post CPR	2
Gastro-intestinal bleeding	1
Cardiogenic shock	2

BMI — body mass index; ICU — intensive care unit; M/F — male/female; SOFA — sequential organ failure assessment; CPR — cardiopulmonary resuscitation; other abbreviations see Table 1

Table 3. Patient haemodynamics at inclusion

Parameter	Mean ± SD
HR (bpm)	82.2 ± 20
MAP (mm Hg)	83.8 ± 17.9
GEF (%)	26.9 ± 6.7
SVV (%)	10.4 ± 5.4
PPV (%)	9.7 ± 5.9
CVP (mm Hg)	10.1 ± 3
GEDVI (mL m^{-2})	662 ± 109
EVLWI (mL kg^{-1})	8.3 ± 3
SVRI (dyne sec cm^{-5} m^{-2})	1,818 ± 922
TPTD-CO (L min^{-1})	6.9 ± 1.8
PCCO (L min^{-1})	6.9 ± 2.1
FCCO (L min^{-1})	5.9 ± 1.5
NCCO (L min^{-1})	6 ± 2
Noradrenaline (µg kg^{-1} min^{-1})	0.5 ± 0.2
Dobutamine (µg kg^{-1} min^{-1})	12.5 ± 4.5

HR — heart rate; MAP — mean arterial pressure; GEF — global ejection fraction; SVV — stroke volume variation; PPV — pulse pressure variation; CVP — central venous pressure; GEDVI — global end-diastolic volume index; EVLWI — extravascular lung water index; SVRI — systemic vascular resistance index; other abbreviations see Table 1, 2

Table 4. Pearson correlation and Bland and Altman analysis for the different comparisons

Correlation	n	mean CO (L min^{-1})	range	R	COVA (%)	*P*-value	Bias (L min^{-1})	Precision (L min^{-1})	LLA (L min^{-1})	ULA (L min^{-1})	%error (%)
TPTD-CO vs. PCCO	210	6.9 ± 1.9	1.9–12.7	0.9	27.6	< 0.0001	0.0	0.8	–1.7	1.7	24.5
TPTD-CO vs. FCCO	125	6.3 ± 1.3	3.1–10.5	0.4	20.2	< 0.0001	0.9	1.6	–2.4	4.2	52.0
TPTD-CO vs. NCCO	115	6.7 ± 1.6	3.8–11.0	0.6	24.6	< 0.0001	1.3	1.7	–2.1	4.7	50.8
PCCO vs. FCCO	125	6.3 ± 1.4	3.5–10.3	0.4	28.8	< 0.0001	0.9	1.8	–2.8	4.5	57.6
PCCO vs. NCCO	115	6.7 ± 1.8	3.6–11.3	0.6	26.7	< 0.0001	1.5	2.0	–2.5	5.5	59.0
FCCO vs. NCCO	57	5.9 ± 2.0	1.5–10.4	0.7	33.3	< 0.0001	0.2	1.9	–3.6	4.0	64.2

COVA — coefficient of variance, defined as SD divided by mean CO; LA — limits of agreements, defined as 2 x precision; LLA — lower limits of agreement, defined as bias minus LA; % error — percentage error, defined as LA divided by mean CO; R — Pearson correlation coefficient; ULA — upper limits of agreement, defined as bias plus LA; other abbreviations see Table 1, 2, 3

a mean bias ± 1.96 SD (LA) of 0.0 ± 1.6 L min^{-1} (PCCO), vs. 0.9 ± 3.2 L min^{-1} (FCCO) and 1.3 ± 3.4 L min^{-1} (NCCO). This is summarised in Table 4. Figure 1 (panels A to C) shows the correlation of CCO vs. TPTD-CO in the global study population for the different techniques, while the Bland and Altman plots are shown in Figure 2 (panels A to C). We found no difference with regard to the FCCO software version 1.03 compared to 1.04.

CCO VS. TPTD-CO ACCORDING TO SVRI

Subgroup analysis was performed comparing patients with low SVRI (defined as SVRI ≤ 1,700 dyne sec cm^{-5} m^{-2}) to those with normal SVRI (> 1,700 dyne sec cm^{-5} m^{-2}). Table 5 lists the haemodynamic parameters in both groups. Pearson correlation coefficients and Bland and Altman analysis comparing TPTD-CO with PCCO, FCCO and NCCO stratified to patients with low or normal SVRI are given in Table 6. In patients with a low SVRI, only PCCO showed a good correlation with TPTD-CO (R = 0.9) with a mean bias ± LA of 0 ± 2 L min^{-1} while there was no good TPTD-CO/FCCO or TPTD-CO/NCCO correlation. In patients with a normal SVRI, PCCO remains the most reliable monitoring device (R = 0.9, bias ± LA of –0.1 ± 1.4 L min^{-1}) although both FCCO (R = 0.8, bias ± LA of 0.1 ± 2.0 L min^{-1}) and NCCO (R = 0.8, bias ± LA of

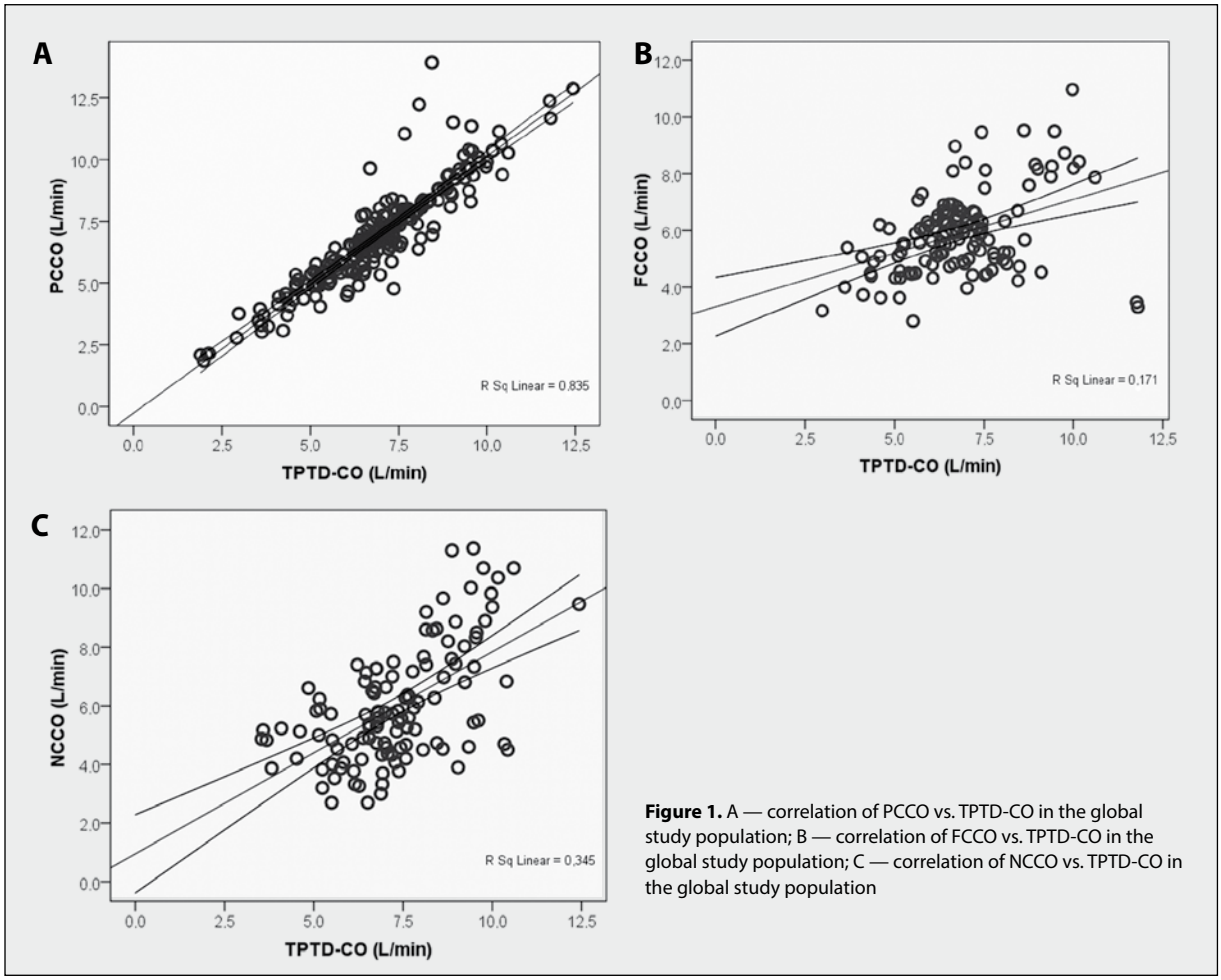

Figure 1. A — correlation of PCCO vs. TPTD-CO in the global study population; B — correlation of FCCO vs. TPTD-CO in the global study population; C — correlation of NCCO vs. TPTD-CO in the global study population

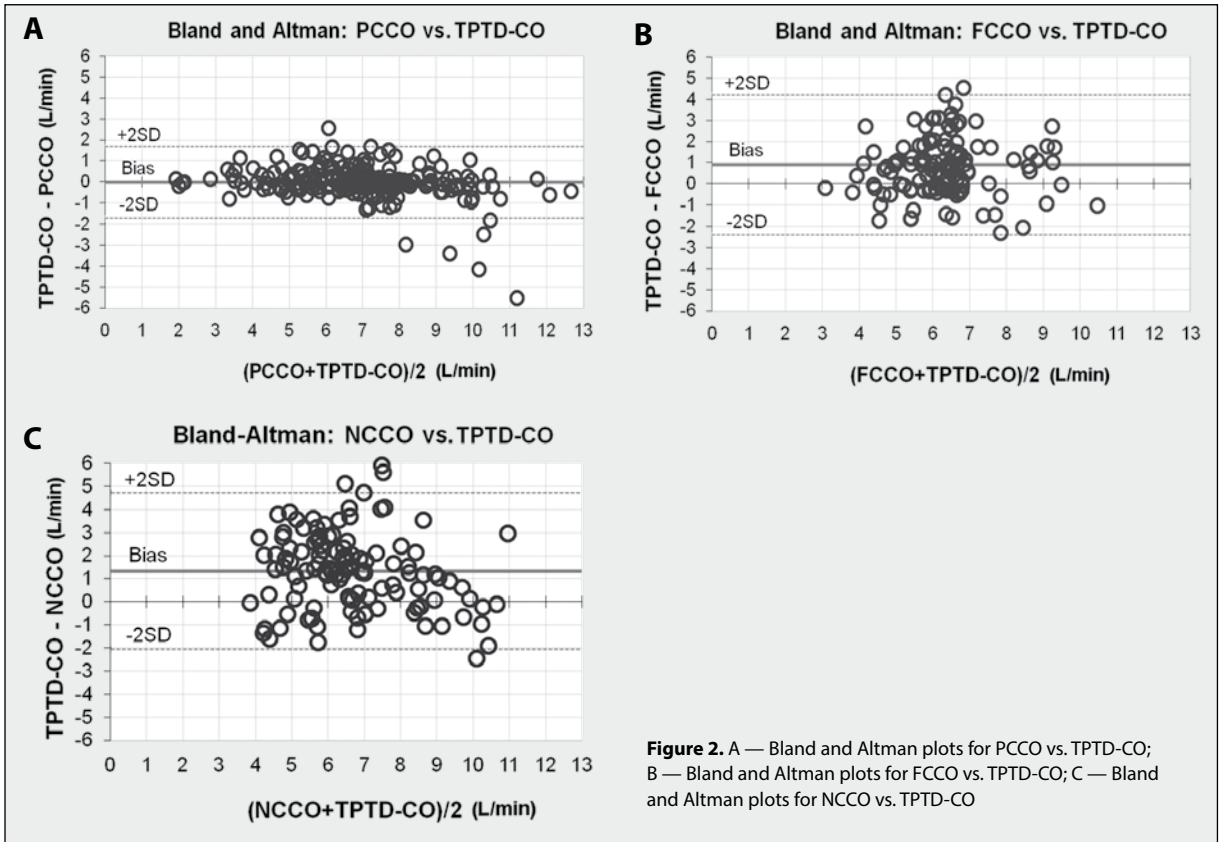

Figure 2. A — Bland and Altman plots for PCCO vs. TPTD-CO; B — Bland and Altman plots for FCCO vs. TPTD-CO; C — Bland and Altman plots for NCCO vs. TPTD-CO

Table 5. Subgroup analysis according to systemic vascular resistance (SVRI)

	Low SVRI	Normal SVRI	*P*-value
Patients (n)	10	13	
Measurements (n)	112	98	
HR (bpm)	86 ± 17.6	77.8 ± 21.6	0.003
MAP (mm Hg)	74.4 ± 13.4	94.5 ± 16.4	< 0.0001
GEF (%)	27.4 ± 4.9	26.4 ± 8.3	NS
SVV (%)	10.6 ± 4.7	10.3 ± 6.1	NS
PPV (%)	9.7 ± 5	9.7 ± 6.8	NS
CVP (mm Hg)	10.4 ± 3.1	9.8 ± 3	NS
GEDVI (mL m^{-2})	678 ± 104	645 ± 113	0.04
EVLWI (mL kg^{-1})	8.5 ± 3.2	8.1 ± 2.8	NS
SVRI (dyne sec cm^{-5} m^{-2})	1,330 ± 208	2,375 ± 1,092	< 0.0001
TPTD-CO (L min^{-1})	7.6 ± 1.5	6.1 ± 1.9	< 0.0001
PCCO (L min^{-1})	7.6 ± 1.9	6.2 ± 2	< 0.0002
FCCO (L min^{-1})	5.9 ± 1.4	5.9 ± 1.5	NS
NCCO (L min^{-1})	5.9 ± 2.2	6.2 ± 1.8	NS

Abbreviations see Table 1, 2, 3, 4

Table 6. Regression and Bland and Altman analysis according to low versus normal systemic vascular resistance (SVRI)

TPTD-CO vs.	PCCO		FCCO		NCCO	
SVRI	Low	Normal	Low	Normal	Low	Normal
Data points (n)	112	98	66	59	59	56
R	0.9	0.9	0.2	0.8	0.6	0.8
P-value	< 0.0001	< 0.0001	NS	< 0.0001	< 0.0001	< 0.0001
Mean CO (L min^{-1})	7.6 ± 1.6	6.1 ± 1.9	6.7 ± 1	5.9 ± 1.4	6.9 ± 1.6	6.4 ± 1.7
Range (L min^{-1})	3.3–12.7	1.9–10	4.9–9.5	3.1–10.5	4.1–11	2.5–9.9
Bias ± precision (L min^{-1})	0 ± 1	–0.1 ± 0.7	1.6 ± 1.8	0.1 ± 1	2.1 ± 1.7	0.4 ± 1.4
LLA (L min^{-1})	–1.9	–1.4	–1.9	–1.9	–1.3	–2.4
ULA (L min^{-1})	2.0	1.3	5.2	2.1	5.6	3.1
% error (%)	25.8	21.8	52.4	34.4	49.4	43.4

Abbreviations see Table 1, 2, 3, 4, 5

0.4 ± 2.8 L min^{-1}) also showed to be reliable in this specific patient group.

DISCUSSION

This study was designed to compare the accuracy of different CCO measurement methods (FCCO, NCCO and PCCO) to the gold standard TPTD-CO in critically ill patients.

We found that PCCO could reliably monitor CCO. Only the PCCO method showed good agreement with TPTD-CO independent of SVRI, although the PCCO measurements appeared to be slightly more accurate in patients with normal SVRI, it needs to be emphasised that CCO measurements were taken prior to recalibration. These findings are in line with current literature. Performing an extensive literature search on validation studies comparing PCCO to TPTD-CO or other gold standard CO measurements, we found an average bias ± LA of 0.0 ± 1.7 L min^{-1} with a percentage error of 28.6 ± 7% (3,992 paired measurements in 587 patients) and a Pearson R^2 of 0.74 ± 0.2 (range 0.16 to 0.91). Table 7 lists some of the most important validation studies for PCCO. Indeed, PCCO is the most invasive of all the CCO monitoring systems tested. However, the fact that the PCCO method uses calibration through intermittent TPTD-CO to adjust for the unique mechanical properties of each patient's arterial tree appears to be the feature that enables this method to accurately monitor CO in unstable haemodynamic conditions with changing preload, afterload or contractility.

FCCO did not show a good correlation with TPTD-CO in the overall study population nor in the subgroup of patients with low SVRI. A fair to good CO correlation was found in the subgroup with normal SVRI. The unacceptably high LA can partially be explained by the software version of

Table 7. Summaries of findings on validation studies for PCCO

Authors	Year	Study population	Gold standard	Patients (n)	Data points (n)	Mean CO (L/min)	Bias (L/min)	Precision (L/min)	LA (L/min)	LLA (L/min)	ULA (L/min)	%Error ° (%)	R^2
Haller et al. [10]	1995	Mixed ICU	PAC	14	168	NA	–0.4	0.5	1.0	–1.4	0.7	NA	0.91
Goedje et al. [11]	1998	Cardiac surgery	PAC	30	270	NA	0.1	0.6	1.2	–1.1	1.3	NA	0.91
Goedje et al. [12]	1999	OPCABG	PAC	20	NA	NA	–0.1	0.5	1.0	–1.1	0.9	NA	0.82
Goedje et al. [13]	1999	SICU	PAC	24	216	NA	0.1	0.7	1.4	–1.3	1.5	NA	0.85
Buhre et al. [14]	1999	CABG	PAC	12	36	4.7	0.0	0.6	1.3	–1.3	1.3	26.8	0.90
Zöllner et al. [15]	2000	Cardiac ICU	PAC	19	NA	NA	–0.3	1.3	2.5	–2.8	2.2	NA	0.77
Goedje et al. [16]	2001	Cardiac surgery	PAC	24	517	NA	–0.2	1.2	2.4	–2.6	2.2	NA	0.77
Kuntscher et al. [17]	2002	Burns	PAC	14	113	NA	–0.2	0.7	1.5	–1.7	1.3	NA	0.81
Della Rocca et al. [18]	2002	Liver transplant	PAC	62	186	7.6	0.0	0.9	1.7	–1.7	1.7	22.2	0.88
Della Rocca et al. [19]	2003	Lung transplant	PAC	58	NA	NA	0.1	0.7	1.4	–1.4	1.5	NA	NA
Mielck et al. [20]	2003	CABG	PAC	22	96	6.6	0.4	1.3	2.6	–2.2	3.0	35.0	NA
López-Herce et al. [21]	2006	Pigs	TPTD CO	51	209	1.7	0.0	0.3	0.6	–0.6	0.5	31.8	0.40
Halvorsen et al. [22]*	2006	OPCABG	PAC	30	107	5.0	–0.1	0.9	1.8	–1.9	1.6	33.5	NA
Bajorat et al. [23]	2006	Pigs	AFP	9	366	4.5	–1.2	0.7	1.4	–2.6	0.2	31.1	0.90
Fakler et al. [24]	2007	Cardiac surgery	TPTD CO	24	168	NA	0.1	0.8	1.5	–1.4	1.6	NA	0.86
Spöhr et al. [25]	2007	SICU	PAC CCO	14	182	8.8	0.1	1.4	2.7	–2.6	2.8	30.7	0.71
De Wilde et al. [26]	2007	Cardiac surgery	PAC	24	199	4.8	0.1	0.9	1.7	–1.6	1.9	36.2	NA
Chakravarthy et al. [27]	2007	OPCABG	PAC	15	438	NA	0.1	1.1	2.2	–2.1	2.4	20.0	0.16
Breukers et al. [28]	2009	Cardiac surgery (valvular)	PAC CCO	8	48	5.8	0.9	0.7	1.5	–0.5	2.4	25.5	0.64
Breukers et al. [28]	2009	CABG	PAC CCO	8	48	6.9	1.0	0.9	1.9	–0.9	2.9	27.2	0.81
Mutoh et al. [29]	2009	SAH	PAC	16	179	6.8	0.2	0.6	1.3	–1.1	1.5	18.3	0.64
Hofer et al. [30]	2010	Cardiac (OR/ICU)	PAC	26	156	5.0	–0.3	1.1	2.2	–2.5	1.9	44.0	NA
Monnet et al. [31]*	2010	Sepsis (ICU)	TPTD CO	40	80	6.3	0.1	0.7	1.4	–1.2	1.5	21.6	0.53
Present study	2012	Mixed ICU	TPTD CO	23	210	6.9	0.0	0.9	1.7	–1.7	1.7	24.5	0.81
Total				587	3,992								
Mean				24.5 ± 14.8	190.1 ± 124	5.8 ± 1.7	0 ± 0.4	0.8 ± 0.3	1.7 ± 0.5	–1.6 ± 0.7	1.7 ± 0.7	28.6 ± 7	0.74 ± 0.2
Range				8 to 62	36 to 517	1.7 to 8.8	–1.2 to 1	0.3 to 1.4	0.6 to 2.7	–2.8 to –0.5	0.2 to 3	18.3 to 44	0.16 to 0.91

*values were given for CI; to obtain CO, CI was multiplied by 1.9 (= average BSA for 175 cm and 75 kg adult); °%error was only given for Mielck, Halvorsen, Monnet and present study; it was retrospectively calculated in other studies based on LA and mean CO data given (%error = 100*LA/mean CO); AFP — aortic flow probe; CABG — coronary artery bypass graft; ICU — intensive care unit; NA — not available; OPCABG — off pump CABG; OR — operating room; PAC — pulmonary artery catheter; other abbreviations see Table 1, 2, 3, 4, 5, 6

Table 8. Summaries of findings on validation studies for FCCO

Author	Year	Study population	Reference method	Version	Patients (n)	Data points (n)	mean CO (L/min)	CI*/ CO	Bias (L/min)	Precision (L/min)	LA (L/min)	LLA (L/min)	ULA (L/min)	%Error ° (%)	R^2
Opdam et al. [32]	2007	Cardiac (ICU)	PAC	1.03	6	218	NA	CI*	0.02	1.14	2.28	−2.26	2.3	NA	0.27
Opdam et al. [32]	2007	Cardiac (ICU)	PAC (cont)	1.03		218	NA	CI*	0.46	0.93	1.86	−1.41	2.32	NA	0.06
Sander et al. [33]	2006	Cardiac (OR/ICU)	PAC	1.03	30	108	4.8	CO	−0.2	1.4	2.8	−3	2.6	54	0.05
Breukers et al. [34]	2006	Cardiac (ICU)	PAC		20	56	5.5	CO	−0.14	1	2	−2.14	1.86	31	0.55
De Waal et al.[35]**	2007	Cardiac (OR/ICU)	PAC		22	185	5.3	CO	0	0.87	1.74	−1.74	1.74	33	0.56
De Waal et al. [35]**	2007	Cardiac (OR/ICU)	TPTD			140	5.4	CO	−0.01	1.09	2.17	−2.18	2.16	40	0.36
McGee et al. [36]	2007	Mixed (ICU)	PAC		84	561	6.2	CO	−0.2	1.28	2.55	−2.75	2.35	43	NA
Manecke et al. [37]	2007	Cardiac (ICU)	PAC		50	295	NA	CO	−0.55	0.98	1.96	−2.51	1.41	NA	NA
Manecke et al. [37]	2007	Cardiac (ICU)	PAC (cont)			295	NA	CO	−0.6	1.05	2.1	−2.7	1.5	NA	NA
Mayer et al. [38]**	2007	Cardiac (OR/ICU)	PAC	1.03	40	244	4.8	CI*	−0.87	1.09	2.19	−3.06	1.31	46	0.28
Button et al. [39]	2007	Cardiac (OR/ICU)	PAC	1.07	31	150	5.2	CO	−0.25	1.14	2.27	−2.52	2.02	54	NA
Cannesson et al. [40]**	2007	Cardiac (OR/ICU)	PAC		11	166	4.6	CO	0	0.87	1.74	−1.74	1.74	38	0.43
Sakka et al. [41]	2007	Sepsis (ICU)	TPTD		24	72	6.7	CO	0.5	2.3	4.6	−4.1	5.1	68.7	0.26
Lorsomradee et al. [42]***	2007	Cardiac (OR)	PAC (cont)		52	NA	4.9	CO	0	1.37	2.74	−2.74	2.74	56	0.03
Lorsomradee et al. [42]***	2007	Cardiac (OR)	PAC (cont)			NA	4.9	CO	0	1.23	2.45	−2.45	2.45	50	0.03
Chakravarthy et al. [27]	2007	Cardiac (OR)	PAC		15	438	NA	CO	0.15	0.33	0.66	−0.51	0.81	NA	0.24
Prasser et al. [43]**	2007	Cardiac (ICU)	PAC		20	158	6.1	CO	0.01	0.82	1.63	−1.62	1.64	26.9	NA
Zimmermann et al. [44]	2008	Cardiac (OR/ICU)	PAC		30	192	NA	CO	−0.1	1.45	2.9	−3	2.8	NA	0.31
Biais et al. [45]	2008	LTX	PAC		20	400	NA	CO	0.8	1.33	2.65	−1.8	3.5	43	0.55
Mehta et al. [46]**	2008	Cardiac (OR)	PAC		12	96	4.3	CO	0.26	0.63	1.25	−0.99	1.51	29	NA
Staier et al. [47]	2008	Cardiac (OR)	PAC		30	120	4.6	CO	−0.02	0.52	1.03	−1.05	1.01	44	NA
Compton et al. [48]**	2008	Medical ICU	TPTD	1.1	25	324	5.3	CI*	1.29	1.57	3.13	−1.84	4.42	58.8	NA
Mayer et al. [49]	2008	Cardiac (OR/ICU)	PAC		40	282	4.8	CI*	−0.36	0.57	1.14	−1.5	0.78	24.6	NA
Senn et al. [50]**	2009	Cardiac (ICU)	TPTD		50	200	5.5	CO	0.15	0.8	1.6	−1.45	1.75	29	NA
Zimmermann et al. [51]**	2009	Cardiac (ICU)	PAC	1.1	24	138	5	CO	−0.04	1.07	2.13	−2.17	2.09	43	0.32

Table 8 (cont.). Summaries of findings on validation studies for FCCO

Author	Year	Study population	Reference method	Version	Patients (n)	Data points (n)	mean CO (L/min)	CI*/ CO	Bias (L/min)	Precision (L/min)	LA (L/min)	LLA (L/min)	ULA (L/min)	%Error ° (%)	R^2
Marque et al. [52]***	2009	Cardiac (OR)	PAC (cont)		29	12,099	4.9	CO	–0.01	0.81	1.62	–1.63	1.61	33.3	0.48
Mayer et al. [53]	2009	Cardiac (OR)	PAC		38	262	4.6	CI*	–0.36	0.63	1.25	–1.62	0.89	26.6	0.61
Biancofiore et al. [54]	2009	LTX	PAC	1.1	29	290	5.2	CO	–1.3	1.43	2.85	–1.5	4.1	45	NA
Ostergaard et al. [55]	2009	Cardiac (OR/ICU)	PAC	1.0	25	50	4.2	CO	–0.51	0.94	1.87	–2.38	1.36	48	NA
Chakravarthy et al. [56]***	2009	Cardiac (ICU)	PAC (cont)		20	140	4.9	CI*	0.04	0.87	1.75	–1.71	1.79	35.4	NA
Concha et al. [57]	2009	Colon surgery	TEE		10	88	4.8	CO	1.17	1.01	2.02	–0.85	3.19	40	NA
De Wilde et al. [58]	2009	Cardiac (ICU)	PAC		13	104	5.3	CO	–0.33	1.23	2.46	–2.79	2.13	34	NA
Eleftheriadis [59]***	2009	Cardiac (OR)	PAC		16	112	5	CO	–0.4	0.85	1.7	–2.1	1.3	34	0.4
Mutoh et al. [29]	2009	SAH	TPTD	1.14	16	179	6.8	CO	–0.57	0.44	0.88	–1.45	0.31	24.8	0.67
Hofer et al. [30]***	2010	Cardiac (OR)	PAC		26	156	5	CO	–0.2	1.05	2.1	–2.3	1.9	42	NA
Schramm et al. [60]**	2010	Cardiac (OR)	PAC		20	78	4.9	CO	0.35	1.88	3.76	–3.41	4.11	76	NA
Slagt et al. [61]**	2010	Sepsis (ICU)	PAC	1.07	4	86	6.7	CO	–1.6	1.6	3.2	–4.8	1.6	48	0.1
Slagt et al. [61]**	2010	Sepsis (ICU)	PAC	1.1	5	73	6.9	CO	–1.2	1.1	2.2	–3.4	1	32	0.81
Böttger et al. [62]	2010	Sepsis (ICU)	TPTD		19	55	6.4	CO	0.72	1.45	2.89	–2.17	3.61	49.1	NA
Jeong et al. [63]	2010	OPCABG	PAC (cont)		28	234	4	CO	0.23	1.13	2.27	–2.04	2.5	57	NA
Krejci et al. [64]**	2010	LTX	PAC		19	97	7.7	CI*	3.38	2.63	5.26	–1.88	8.65	68.5	0.2
Vetrugno et al. [65]**	2010	CABG	PAC		20	360	4.6	CO	–0.5	0.86	1.72	–2.22	1.22	37	0.49
Monnet et al. [31]**(*)	2010	Sepsis (ICU)	TPTD	1.1	40	80	5.9	CI*	–0.19	1.79	3.57	–3.76	3.38	61	0.03
Saraceni et al. [66]	2011	Mixed (ICU)	PAC	1.07 – 1.10	21	140	NA	CI*	–0.18	2.36	4.72	–4.9	4.54	NA	0.62
Biancofiore et al. [67]	2011	LTX	PAC	3.02	21	210	NA	CI*	0.4	NA	NA	NA	NA	52	0.67
Present study	2012	Mixed (ICU)	TPTD	1.03 – 1.04	12	125	6.3	CO	0.9	1.65	3.3	–2.4	4.2	52	0.17
Total					1,067	15,837									
Mean					25.4 ± 14.9	456.2 ± 1,799.5	5.4 ± 0.9		0 ± 0.8	1.2 ± 0.5	2.3 ± 1	–2.3 ± 0.9	2.4 ± 1.5	43.8 ± 12.8	0.35 ± 0.23
Range					4 to 84	50 to 12,099	4 to 7.7		–1.6 to 3.4	0.3 to 2.6	0.7 to 5.3	–4.9 to –0.5	0.3 to 8.7	24.6 to 76	0.03 to 0.81

*values were given for CI; to obtain CO, CI was multiplied by 1.9 (= average BSA for 175 cm and 75 kg adult); **mean CO was retrospectively calculated based on LA and %error data given (CO = 100 LA %error^{-1})
***%error was retrospectively calculated in other studies based on LA and mean CO data given (%error = 100 LA meanCO^{-1}); LTX — liver transplant; PAC — pulmonary artery catheter with intermittent thermodilution; PAC (cont) — pulmonary artery catheter with continuous CO; R^2 — square of Pearson regression coefficient; SAH — subarachnoid haemorrhage; TEE — transoesophageal echocardiography; TPTD — transcardiopulmonary thermodilution with PiCCO; other abbreviations see Table 1, 2, 3, 4, 5, 6, 7

Table 9. Summaries of findings on validation studies for NCCO

Author	Year	Study population	Reference method	Patients (n)	Data points (n)	mean CO (L/min)	Bias (L/min)	Precision (L/min)	LA (L/min)	LLA (L/min)	ULA (L/min)	% error (%)	R^2
de Abreu et al. [68]	1997	ARDS sheep	PAC	20	NA	NA	1.69	0.95	1.9	–0.21	3.59	NA	0.54
Kuck K et al. [69]	1998	Cardiac surgery	PAC	36	NA	NA	NA	NA	NA	NA	NA	NA	0.84
Guzzi et al. [70]	1998	CABG	PAC	27	NA	NA	–0.01	0.31	0.62	–0.63	0.61	NA	0.72
Jopling MW [71]	1998	Unknown	PAC	48	NA	NA	–1.75	1.14	2.28	–4.03	0.53	NA	NA
Watt et al. [72]	1998	Cardiac surgery	PAC	5	NA	NA	0.2	0.35	0.7	–0.5	0.9	NA	NA
Loeb et al. [73]	1999	Cardiac surgery	PAC	12	NA	NA	–1.19	0.58	1.16	–2.35	–0.03	NA	NA
Kuck et al. [74]	1999	CABG	PAC	134	NA	NA	0.69	0.47	0.94	–0.25	1.63	NA	0.6
Hayardi et al. [75]	2000	Dogs	PAC	6	246	5.1	0.07	0.7	1.4	–1.33	1.47	27.5	0.86
Van Heerden et al. [76]	2000	Post cardiac surgery	PAC	12	42	NA	NA	NA	NA	NA	NA	NA	0.69
Jin et al. [77]°	2000	Pigs Haemorragic	PAC	16	NA	NA	–1.1	1.35	2.7	–3.8	1.6	NA	0.69
Jin et al. [77]°	2001	Pigs Septic	AFP			2.5	1.3	1	2	–0.7	3.3	81.3	0.42
Jin et al. [77]°	2002	Pigs cardiogenic	AFP			4.9	0.1	0.6	1.2	–1.1	1.3	24.3	0.67
Maxwell et al. [78]**	2001	Pigs trauma	PAC	11	129	3.4	0.01	0.35	0.69	–0.68	0.7	20.3	0.54
Nilsson et al. [79]	2001	Cardiac surgery	PAC	30		4.4	0.2	0.9	1.8	–1.6	2	NA	NA
Odensted et al. [80]	2002	ICU (n = 3) Surgery (n = 12)	PAC	15	125	NA	0.04	0.86	1.72	–1.68	1.76	NA	0.96
Murias et al. [81]*	2002	General ICU	PAC	22	79	6	–0.18	1.39	2.78	–2.96	2.6	46	0.71
Kotake et al. [82]	2003	Aortic reconstruction surgery	PAC	28	112	NA	0.58	0.9	1.8	–1.22	2.38	NA	0.64
Mielck et al. [20]	2003	CABG	PAC	22	33	6.7	0.17	1.45	2.9	–2.73	3.07	44	NA
Gunkel et al. [83]°	2004	Dogs	LIDCO	6	47	3.6	0.22	0.84	1.68	–1.46	1.9	46.9	0.77
Botero et al. [84]	2004	CABG	AFP	68	NA	NA	0.04	1.07	2.14	–2.1	2.18	44.8	NA
Rocco et al. [85]**	2004	ICU non postoperative	PAC	12	36	7.3	1.2	0.75	1.5	–0.3	2.7	20.6	0.79
Bajorat et al. [23]**	2006	Pigs	AFP	9	366	3.3	–0.19	0.89	1.77	–1.96	1.58	54.5	0.59
Gueret et al. [86]**	2006	CABG	PAC	22	4,372	4.2	–0.1	1.15	2.3	–2.4	2.2	54.8	0.48
Ng et al. [8]**	2007	Thoracic surgery	PAC	12	76	4.7	0.29	0.78	1.56	–1.27	1.85	33.5	NA
Kotake et al. [87]	2009	Aortic reconstruction surgery	PAC	42	376	4.8	–0.18	0.81	1.62	–1.8	1.44	33.4	0.65
Present study	2012	Mixed ICU	TPTD	12	115	6.7	1.3	1.7	3.39	–2.09	4.69	50.8	0.34
Total				627	6,154								
Mean				26.1 ± 27.4	439.6 ± 1,137.5	4.8 ± 1.4	0.1 ± 0.8	0.9 ± 0.4	1.8 ± 0.7	–1.6 ± 1.1	1.9 ± 1.1	41.6 ± 16.6	0.66 ± 0.15
Range				5 to 134	33 to 4,372	2.5 to 7.3	–1.8 to 1.7	0.3 to 1.7	0.6 to 3.4	–4 to –0.2	0 to 4.7	20.3 to 81.3	0.34 to 0.96

°CO was calculated as 156 mL kg^{-1} min^{-1} based on an average weight of 23 kg, bias = 9.3 mL kg^{-1} min^{-1} and LA = 70.5; *mean CO was retrospectively calculated based on LA and %error data given (CO = 100 LA) $\%error^{-1}$ **%error was retrospectively calculated based on LA and mean CO data given (%error = 100 LA $meanCO^{-1}$); ARDS — acute respiratory distress syndrome; LIDCO — lithium dilution CO; other abbreviations see Table 1, 2, 3, 4, 5, 6, 7, 8

the device (version 1.03 and 1.04) we used. This is in line with the findings of other authors. Recently a review and meta-analysis published by Mayer et al. [7] also concluded that the FCCO method is unreliable using software versions earlier than 1.07. The results of the literature search on studies validating FCCO are listed in Table 8. On average, they show a bias ± LA of 0.0 ± 2.3 L min^{-1} with a percentage error of 43.8 ± 12.8% (15,837 paired measurements in 1,067 patients) and a Pearson R^2 of 0.35 ± 0.23 (range 0.03 to 0.81). In patients with normal SVRI, our results demonstrate that even the older software we used produced acceptable results (R = 0.8 and bias ± LA = 0.1 ± 2). So it seems that FCCO measurements are only unreliable in septic patients (with vasoplegia).

The NCCO method also produced unacceptably high limits of agreement with TPTD-CO in the general study population. As with FCCO, in the subgroup of patients with normal SVRI, NCCO produced more reliable results (bias ± 2SD = 0.4 ± 2.75 L min^{-1}. R = 0.8). Other studies have shown better results for NICO in the past. Table 9 lists the most important validation studies for NCCO currently available. On average, they show a bias ± LA of 0.1 ± 1.8 L min^{-1} with a percentage error of 41.6 ± 16.6% (6,154 paired measurements in 627 patients) and a Pearson R^2 of 0.66 ± 0.15 (range 0.34 to 0.96). We suspect the reason for the underperformance of NCCO in our study is related to the fact that it was performed in the ICU setting in unstable haemodynamic conditions, while most of the listed studies were performed in more stable post-surgical patients.

Subgroup analysis for SVRI showed, as expected, a lower mean arterial pressure and a higher heart rate in the low SVRI group. As we also expected, TPTD-CO was significantly higher in the low SVRI group, which consisted of hyperdynamic, septic patients. Further analysis showed a negative effect of low SVRI on the accuracy of FCCO and NCCO measurements. This is illustrated in Table 5 where only PCCO and TPTD-CO were able to detect the significantly higher CO in hyperdynamic, low SVRI states as seen in sepsis. In Table 6 one can appreciate that only PCCO has significant agreement with TPTD-CO in low SVRI states. This may be attributable to the fact that patients with low SVRI are generally more unstable and have a more rapidly changing haemodynamic situation. This reflects profound and dynamic changes in vascular resistance and compliance in these low SVRI patients, sometimes exacerbated by the use of vasopressive agents. Vascular resistance and compliance values are derived from standard demographic datasets in the uncalibrated CCO devices. Only PCCO is calibrated (by TPTD-CO), hence improving its accuracy in conditions of changing vascular compliance and resistance. This might be the reason why the performance of PCCO was not affected by SVRI.

CONCLUSION

We conclude that CCO was most reliably monitored by PCCO, particularly in unstable patients with low SVRI, where reliable information about haemodynamics is most critical. In situations of normal SVRI, NCCO and FCCO also showed acceptable accuracy.

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