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Comparison between pulse waveform analysis and thermodilution cardiac output determination in patients with severe pre-eclampsia

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Key points

- Cardiac output (CO) monitoring may be of value in patients with complicated severe pre-eclampsia.
- In view of potential risks of pulmonary artery catheter (PAC) insertion, thermodilution CO measurements were compared with values obtained from the minimally invasive LiDCO*plus* monitor.
- The comparison showed a statistically but not clinically significant bias after central venous calibration with lithium, and no significant bias after peripheral venous calibration.
- These findings support the use of LiDCO*plus* for haemodynamic monitoring in patients with complicated severe pre-eclampsia.

Background. This study compared cardiac output (CO) measurements derived from pulse waveform analysis with values obtained by thermodilution (TD), in patients with post-partum complications of severe pre-eclampsia.

Methods. Eighteen patients were recruited, 24–96 h post-delivery. After central venous calibration of the pulse waveform analysis monitor (LiDCO*plus*), CO readings were compared with those obtained by the TD method and repeated twice at 15 min intervals. The comparison was repeated after peripheral venous calibration. Further comparisons were made in eight patients at 120 and 240 min after peripheral venous calibration.

Results. Data were pooled for measurements at 0, 15, and 30 min after calibration. For the comparison between TD and LiDCO*plus* using central venous calibration, TD exhibited a significant positive bias of 0.58 litre min^{-1} [95% confidence interval (CI): 0.77 to 0.39]. After peripheral venous calibration, there was no significant bias [0.16 litre min^{-1} (95% CI: −0.37 to 0.06)]. The estimated limits of agreement for central and peripheral venous calibrations were −2.12 to 0.96 and −1.50 to 1.20 litre min^{-1}, respectively. When comparing LiDCO*plus* and TD, there was no time-based effect at 120 or 240 min post-peripheral calibration.

Conclusions. Central and peripheral venous calibrations of the LiDCO*plus* monitor were associated with clinically insignificant bias when compared with TD. Limits of agreement were within the recommendation of 30% for acceptance of a new CO technique when compared with current reference methods. This form of minimally invasive CO monitoring may have a valuable role in obstetric critical care.

Keywords: cardiac output; monitoring; pre-eclampsia

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The LiDCO*plus* system (LiDCO, Cambridge, UK) has been validated in a variety of clinical scenarios; however, there are no validation studies in the peripartum period. Indications for invasive monitoring in severe pre-eclampsia include pulmonary oedema, persistent oliguria, and hypovolaemic shock.[1 2] In such patients, the pulmonary artery catheter (PAC) provides valuable haemodynamic data, that is, pulmonary capillary wedge pressure, cardiac output (CO), systemic vascular resistance, and mixed venous oxygen saturation. Knowledge of these variables helps to guide management decisions on fluid, diuretic, and vasodilator therapy, which may influence morbidity and mortality. The insertion of the PAC is however an invasive procedure, with well-described complications, particularly in patients with thrombocytopaenia.[3] The use of a less invasive monitor of CO would be preferable in such high-risk cases. Therefore, a prospective validation study was undertaken in patients who had had a PAC placed for the management of complications of severe pre-eclampsia in the immediate post-partum period.

Methods

After approval from the University of Cape Town Ethics Committee, informed written consent was obtained for the use of the LiDCO*plus* monitor in 18 patients in whom a PAC (Edwards Life Sciences, Irvine, CA, USA) had been introduced via the right internal jugular vein, to assist in the medical management of complicated severe pre-eclampsia. Arterial cannulation had been performed in all cases to assist arterial pressure control and for arterial blood gas determinations, before recruitment into the study. The aim of the study was to establish the bias and limits of agreement of CO

measurements between the two monitors, after both central and peripheral venous calibrations with lithium chloride. In eight patients, the comparison was continued for up to 4 h after peripheral calibration, in order to establish whether there was a time-based effect necessitating re-calibration.

The protocol for the comparison between the CO measurements was as follows. During stable haemodynamic conditions (<15% change in heart rate and mean arterial pressure over 3 min), two calibrations, 5 min apart, were performed with 0.3 mmol lithium chloride administered via the proximal lumen of the PAC. If the calibration factors differed by more than 15%, a third determination was performed, and the average calibration factor of the two closest readings was used for subsequent beat-by-beat estimation of the CO from the LiDCO*plus* monitor. Four consecutive thermodilution (TD) determinations, 1 min apart, were then performed via the central venous port of the PAC, using cold saline. The three closest values were averaged and recorded. This step was repeated twice at 15 min intervals. At each epoch, the CO obtained from the TD measurements was compared with the mean of the LiDCO*plus* values averaged during the 30 s subsequent to the TD measurements. The LiDCO*plus* monitor was then re-calibrated by an identical method using a lithium chloride injection via a forearm vein, and the comparison with the TD method repeated as described above. In addition, further comparisons were performed in eight patients at 120 and 240 min after peripheral venous calibration.

Statistical analysis

A linear mixed-effects regression model was used to examine the CO method (LiDCO*plus* and TD), calibration method (central and peripheral venous), and measurement time epochs, and the possible interactions of these factors. This model took into account the repeated measurements done in each patient and utilized the Kenward–Roger method[4] for the calculation of the degrees of freedom for the model inference. The patient was specified as the random effect. The difference between methods at each time point or for pooled data was estimated by least squares means based on the model specified. Since there was an interaction between CO method and calibration method, separate analyses were done for each route of calibration. The comparison between CO methods at 120 and 240 min after peripheral calibration also used a linear mixed-effects regression model and this analysis included all the measurement time epochs in all patients to improve precision and power.

The mean values for LiDCO*plus* and TD were compared during each measurement time epoch (0, 15, and 30 min). Using the method described by Bland and Altman[5] for assessing the agreement between measurement techniques, differences between LiDCO*plus* and TD CO determinations were plotted against the mean values for these pairs at each measuring point. The bias [mean difference and 95% confidence interval (CI)] and limits of agreement [bias (2 SD) of the difference] were determined and used to summarize the level of agreement between the methods. The confidence interval and limits of agreement utilized the standard error estimate of the least square mean difference between the methods from the relevant linear mixed-effects model. For the limits of agreement, this standard error was multiplied by the square root of the degrees of freedom to obtain an estimate of the SD of the pooled mean difference.

Results

Eighteen patients were recruited during the period April 2006–March 2009. These patients were admitted to the Special Care Unit at the Maternity Centre at Groote Schuur Hospital, Cape Town, with complications of severe pre-eclampsia. The indication for pulmonary artery catheterization was a clinical diagnosis of pulmonary oedema in 13 cases. Two of these patients had abruptio placentae. The remaining five patients had oliguric renal failure; of these, one was associated with severe haemolysis, elevated liver enzymes and low platelets (HELLP) syndrome, three with abruptio placentae, and one with a ruptured uterus. No patients were mechanically ventilated during the study. The median (range) time post-delivery at recruitment was 48 (24–96) h.

Five patients required three central venous calibrations and six required three peripheral venous calibrations. For the central and peripheral lithium calibration, the data from 17 of 18 and 16 of 18 recruited subjects, respectively, were analysed. In one exclusion, peripheral oedema precluded adequate flow for a peripheral calibration curve, and in the other, the arterial cannula was dislodged by a restless patient.

A description of mean values for the two CO methods at the specified measurement time epochs is shown in Table 1.

There was no time-based effect associated with the comparison between LiDCO*plus* and TD for the time epochs 0, 15, and 30 min after calibration. There was a significant difference between the comparisons between monitors, related to whether calibration was central or peripheral. For the comparison between TD and LiDCO*plus* using central venous calibration, TD exhibited a significant positive bias of 0.58 litre min^{-1} (95% CI: 0.77 to 0.39). After peripheral venous calibration, there was no significant bias [0.16 litre min^{-1} (95% CI: −0.37 to 0.06)]. Since the bias, or lack thereof, was consistent with time, data were pooled for the epochs 0, 15, and 30 min. The Bland–Altman plots of individual CO measurements by LiDCO*plus* *vs* TD are shown in Figures 1 and 2. The estimated limits of agreement for the central venous and peripheral venous calibration were −2.12 to 0.96 and −1.50 to 1.20 litre min^{-1}, respectively.

Of the eight patients in whom the measurements were continued to 120 and 240 min after peripheral calibration, the data from seven were analysed. (In one patient, peripheral calibration was performed before central venous calibration, in error.) Using a linear mixed-effects regression model, differences in mean CO at the specified measurement

times were derived (Table 2). When comparing LiDCO*plus* and TD, there was no time-based effect at 120 or 240 min post-calibration. There was a significant time effect overall with the 0, 15, and 30 min mean values being significantly lower than the CO mean at 240 min.

Discussion

This study is the first in the peripartum period to compare CO measurements obtained from TD with the central and peripheral lithium chloride calibration of the LiDCO*plus* device. In addition, the effect of time on the agreement between TD and LiDCO*plus* measurements after peripheral calibration was examined. Of the patients admitted to Groote Schuur Hospital Maternity Unit with severe pre-eclampsia, only ~0.5% require a PAC. This was reflected by the lengthy recruitment period of 3 yr.

Three studies in the non-obstetric population have examined the validity of the peripheral *vs* central venous route for calibration.[6–8] All showed good correlation between CO measurements obtained after central and peripheral venous calibrations. One investigation showed that there was a better agreement between CO readings if the peripheral injection was made proximal to the wrist.[6] In our study, the peripheral calibration injection was done via a forearm vein. In only one patient was flow inadequate for calibration, due to severe peripheral oedema. At least two calibrations were performed via each route. This has recently been shown to improve the coefficient of variation to 6% and allows for the detection of a change of 17% between the two measurements.[9]

The present investigation suggests that in the immediate post-partum period in pre-eclamptic patients, peripheral venous calibration is associated with an insignificant bias when compared with TD and that bias is less than when calibration is via the central route. Results from a previous study differed, in that CO measurements after both central and peripheral lithium calibrations were lower than simultaneously obtained TD measurements, by 0.53 and 0.54 litre min^{-1}, respectively.[6]

The absence of a time-based effect when comparing the monitors for the first 4 h after calibration is in agreement with the two publications from the non-obstetric literature.[10 11] A recent investigation in a small number of critically ill patients suggested that re-calibration is required after 4 h.[12]

Current opinion is that a new CO technique should be accepted if the limits of agreement are up to 30% when compared with current reference methods.[13] This study shows the limits of agreement of -1.5 to 1.2 litre min^{-1} for peripheral calibration, which are very similar to those quoted in a recent study on post-cardiac surgical patients, comparing LiDCO*plus* with continuous cardiac index monitoring via a PAC ($\pm$1.3 litre min^{-1}).[14] For the average CO in the region of 7 litre min^{-1} in the present study population group, this is well within the 30% range. Although the CIs are relatively wide, the very low bias when compared with the PAC suggests that this form of pulse waveform analysis could be used in place of the more invasive monitor in the perioperative management of complicated severe pre-eclampsia. This is particularly relevant in view of the recent literature, suggesting that the measurement of central venous and/or pulmonary capillary wedge pressure is a poor guide to fluid volume responsiveness in critical care.[15]

A recent comparison between bioimpedance measurements and LiDCO*plus* in the setting of short-term significant changes in vascular tone,[16] together with the data presented in this investigation, suggests that this form of pulse waveform analysis may be of great value both in obstetric anaesthesia research and in the management of critically ill obstetric patients. In situations when vascular tone is rapidly changing, trend measurements are of greater value

Table 1 Mean CO values for each CO method and calibration method at the specified measurement time epoch

CO method	Calibration method	Time (min)	*n*	Mean CO (litre min^{-1})	SD	Minimum	Maximum
LiDCO	Peripheral	0	16	7.27	1.63	3.9	10.4
		15	16	7.36	1.65	4.0	10.5
		30	16	7.41	1.72	4.1	10.4
		120	7	7.38	1.74	5.2	9.7
		240	7	7.66	1.65	4.9	9.4
	Central	0	17	7.16	1.48	3.6	9.4
		15	16	6.87	1.38	3.6	8.9
		30	17	7.00	1.49	3.7	9.1
TD	Peripheral	0	16	7.49	1.43	4.3	9.6
		15	16	7.44	1.44	4.3	10.1
		30	16	7.57	1.58	4.4	11.0
		120	7	7.57	1.52	5.4	9.2
		240	7	8.14	1.93	5.2	11.1
	Central	0	17	7.75	1.52	4.2	9.2
		15	16	7.55	1.58	4.1	10.8
		30	17	7.47	1.44	4.3	9.8

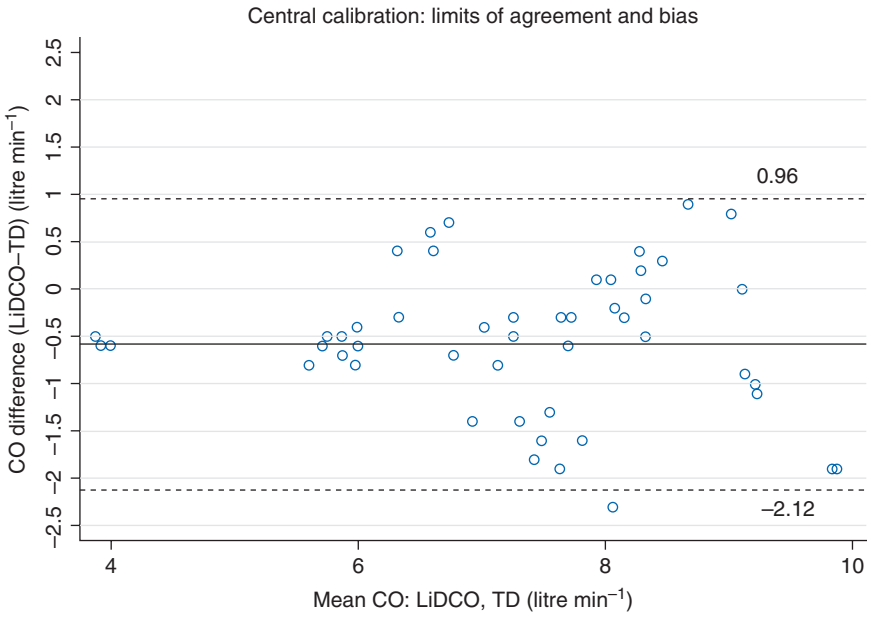

Fig 1 Bland and Altman comparison between TD and LiDCO*plus* after central venous calibration. Bias: −0.58 litre min^{-1}, 95% confidence interval: −0.77 to −0.39 litre min^{-1}. Dotted lines show limits of agreement.

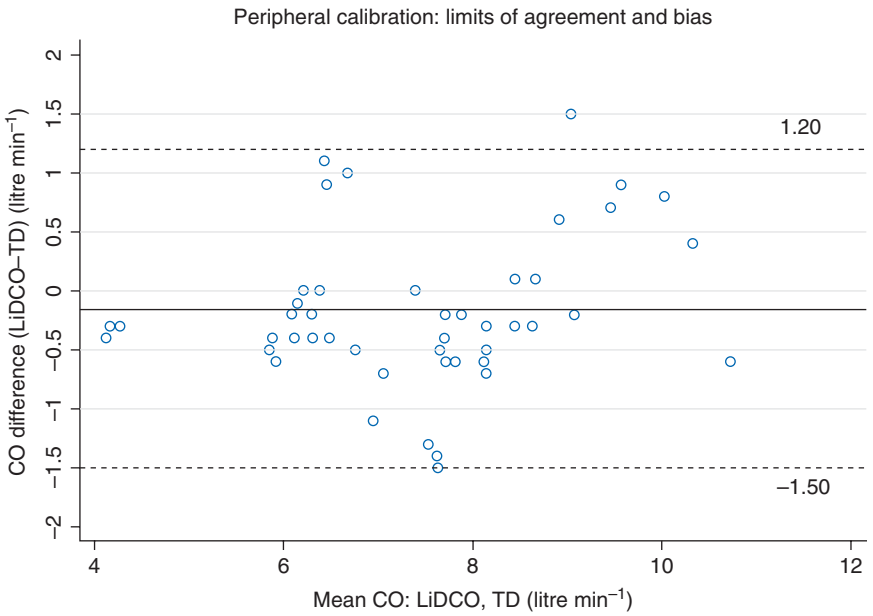

Fig 2 Bland and Altman comparison between TD and LiDCO*plus* after peripheral venous calibration. Bias: −0.16 litre min^{-1}, 95% confidence interval: −0.37 to 0.06 litre min^{-1}. Dotted lines show limits of agreement.

Table 2 Differences in CO at the specified measurement time epochs (least-squares means). CI, confidence intervals. *Mean value over five measurement times

Time	Difference in CO (LiDCO−TD)	*P*-value	95% CI	
			Lower	Upper
0	−0.23	0.30	−0.65	0.20
15	−0.08	0.71	−0.51	0.35
30	−0.16	0.45	−0.59	0.27
120	−0.19	0.57	−0.84	0.46
240	−0.49	0.14	−1.14	0.16
	−0.23*	0.06	−0.46	0.01

than absolute values. During stable monitoring conditions, the results presented in this study suggest adequate accuracy for the measurement of absolute values.

Conflict of interest

None declared.

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