

Five algorithms that calculate cardiac output from the arterial waveform: a comparison with Doppler ultrasound

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Abstract

Background: Different mathematical approaches are used to calculate arterial pulse pressure wave analysis (PPWA) cardiac output. The CardioQ-Combi is a research oesophageal Doppler (CO_{ODM}) monitor that includes these five fundamental PPWA algorithms. We compared these PPWA cardiac output readings to CO_{ODM} and suprasternal USCOM Doppler (CO_{US}) over a range of cardiac output values induced by dopamine infusion in patients undergoing major surgery. USCOM acted as a control.

Methods: Serial sets of cardiac output data were recorded at regular intervals as cardiac output increased. Formulae included: cardiac output calculated from systemic vascular resistance (CO_{MAP}), pulse pressure (CO_{PP}), Liljestrand-Zander formula (CO_{LZ}), alternating current power (CO_{AC}) and systolic area with Kouchoukos correction (CO_{SA}). The reference method for comparisons was CO_{ODM}. Statistical methods included: Scatter plots (correlation), Bland-Altman (agreement) and concordance (trending) and polar (trending).

Results: From 20 patients 255 sets of cardiac output comparative data were collected. Mean cardiac output for each method ranged between 5.0 and 5.5 litre min⁻¹. For comparisons between CO_{US} and the five PPWA algorithms with CO_{ODM}: Correlation was best with CO_{US} (R²=0.81) followed by CO_{LZ} (R²=0.72). Bias ranged between 0.1 and 0.5 litre min⁻¹. Percentage error was lowest with CO_{US} (26.4%) followed by CO_{LZ} (35.2%), others (40.7 to 56.3%). Concordance was best with CO_{US} (92%), followed by CO_{LZ} (71%), others (64 to 66%). Polar analysis (mean(standard deviation)) were best with CO_{US} (-2.7 (21.1)), followed by CO_{LZ} (+4.7 (26.6)).

Conclusions: The Liljestrand-Zander PPWA formula was most reliable compared with oesophageal Doppler in major surgical patients under general anaesthesia, but not better than USCOM.

Key words: cardiac output; doppler; pulse wave analysis

Reliable cardiac output monitoring is needed in anaesthesia and intensive care.¹ Currently available cardiac output monitors lack precision and many fail to trend cardiac output reliably.² One of the most popular modalities being promoted is arterial pulse

contour analysis. However, several different methods of analyzing and calculating cardiac output from the arterial pulse pressure wave exist,³ with several different devices available on the market. The algorithms differ in performance and especially

Accepted: April 22, 2015

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Editor's Key Points

- Arterial pulse pressure wave analysis (PPWA) is a relatively new technique for assessing cardiac output.
- A new version of an oesophageal Doppler monitor also incorporates one of several algorithms used for PPWA.
- The authors compared the performance of five of these algorithms with suprasternal and oesophageal Doppler measurements.

the ability to track changes in cardiac output under more extreme circulatory conditions, such as high cardiac output states in liver cirrhosis⁴ and pharmacologically induced vasoconstriction.⁵

Deltex Medical have recently released a new cardiac output monitor, the CardioQ-ODM+ (Deltex Medical Ltd., Chichester, England), that combines both oesophageal Doppler monitoring with pulse pressure wave analysis (PPWA) and uses the Liljestrand-Zander formulae.⁶ The choice of this particular algorithm was based on studies using a research model of the CardioQ-ODM™ called the Combi that was able to capture the patient's arterial pulse wave and calculate cardiac output using nine different formulae, as described by Sun and colleagues.³

Our group at The Chinese University of Hong Kong has worked with Doppler cardiac output monitoring in recent years and developed a system of measuring accurate cardiac output trend lines during major surgery using an in tandem two Doppler cardiac output methodology, or dual Doppler.⁷ When using Doppler methods to measure cardiac output it is possible to pick up the wrong flow signal (i.e. erroneous readings) and dual Doppler reduces the chance of this happening because readings and flow signals are counter checked. Although the system does not provide highly accurate cardiac output readings, it does provide a reliable assessment of changes in cardiac output during surgery, against which other non-Doppler modalities can be compared and evaluated. In particular it detects any deviations from the trend line of cardiac output changes, by the test device as circulatory conditions change, a problem common to existing pulse contour technology.⁵

The purpose of this prospective observational study was to compare five fundamentally different algorithmic approaches of calculating cardiac output, from the arterial pulse wave against the two Doppler methods, in patients undergoing major surgery. Oesophageal Doppler was designated as the reference cardiac output method because of its inclusion in the CardioQ-ODM+ monitor, whilst suprasternal Doppler was used as the control method against which the performances of the five PPWA algorithms were compared. The PPWA methods evaluated were cardiac output calculated from systemic vascular resistance (CO_{MAP}), pulse pressure (CO_{PP}), Liljestrand-Zander formula (CO_{LZ}), alternating current (AC) power (CO_{AC}) and systolic area with Kouchoukos correction (CO_{SA}).³

Methods**Study subjects**

The present study was approved by The Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee. Adult patients of ASA I, II or stable III undergoing major surgery at Prince of Wales Hospital (Hong Kong) from March 2014 to June 2014 were recruited. Patients diagnosed with arrhythmias, aortic aneurysm, valvular disease, oesophageal disease, or having implanted pacemaker/cardioverter were

excluded from the study. The study procedure was explained to all patients and written informed consent was obtained on the day before surgery. The study was conducted in conformity with the principles of Helsinki declaration.

Anaesthetic technique

All patients were unpremedicated and induced with i.v. propofol (2–3 mg kg⁻¹) and fentanyl (1 µg kg⁻¹). Neuromuscular block was achieved and maintained with atracurium. General anaesthesia was maintained with inhaled sevoflurane (1–3 Vol%) in oxygen enriched air and analgesia with opioids including remifentanyl continuous infusion. The lungs were mechanically ventilated to maintain end-tidal carbon dioxide between 35 and 40 mm Hg via a tracheal tube. Ventilator pressures were kept constant throughout. Patients were routinely monitored with noninvasive blood pressure, electrocardiography and pulse oximetry.

A 20G cannula was inserted into the radial artery after induction of anaesthesia and it was connected to the CardioQ-Combi monitor. To secure the arterial line and ensure continuous signal quality throughout the study, the cannula was carefully taped and the wrist strapped in extension.

Cardiac output monitoring equipment**CardioQ-Combi monitor**

The oesophageal Doppler monitor used in the study was a research model with additional software, that used nine different PPWA algorithms to calculate cardiac output. The CardioQ Doppler probe was inserted into the patient's oesophagus via the nose and advanced to the lower oesophagus where it insonated blood flow in the descending thoracic aorta. Cardiac output was calculated as the product of the velocity time integral (n.b. also called stroke distance) and a derived constant based on the cross-sectional area of the descending aorta, insonation angle (i.e. 45°) and split ratio (i.e. proportion of blood flow to the lower body).⁸ The cross-sectional area of descending aorta is derived from a nomogram that uses body surface area and age.

Arterial pressure system

The arterial pressure wave which was a transduced analog electrical signal, from the patient's radial arterial cannula, was fed into the back of the CardioQ-Combi monitor from a free standing Datex-Ohmeda S5 (GE Healthcare, Helsinki, Finland) patient monitor. After zeroing the arterial line, a flush test was performed to ensure that the arterial pressure measurement system was critically damped. The level of damping was also checked frequently during the study. PPWA cardiac output data were accepted when the level of damping after the square wave was 2–3 oscillations. The CardioQ-Combi monitor displayed the PPWA cardiac outputs in a separate pressure based data window as a column of values.

PPWA algorithms

A fuller description of the five selected algorithms is as follows (Table 1): (1) CO_{MAP} where cardiac output is calculated from mean arterial pressure which is affected by systemic vascular resistance;⁹ (2) CO_{PP} where pulse pressure is used as a surrogate of stroke volume and is based on a Windkessel model;¹⁰ (3) CO_{LZ} where the Liljestrand-Zander formula compensates for the dependence on arterial pressure of arterial compliance;⁶ (4) CO_{AC} where the algorithm makes use of the power of arterial pressure signal which is derived from root-mean-square pressure;¹¹ (5) CO_{SA} where cardiac output is calculated from the area under

Table 1 Pulse Pressure wave analysis (PPWA) algorithms used in the study. CO, cardiac output; SV, stroke volume; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; ABP, arterial blood pressure; T, duration of cardiac cycle ($T = \sqrt{HR/60}$); T_{sys} , duration of systole (estimated as 30% of T); T_{dia} , duration of diastole ($T_{dia} = T - T_{sys}$). *Commercial PPWA monitor that utilizes the same underlying principle as the formula

Algorithm	Formula (CO = SV × HR)	Commercial use*
Mean arterial pressure (CO_{MAP}) ⁹	$SV = k \times MAP$	N/A
Pulse pressure (CO_{PP}) ¹⁰	$SV = k \times PP$	FloTrac-Vigileo
Liljestrand-Zander (CO_{LZ}) ⁶	$SV = k \times (PP / (SBP + DBP))$	CardioQ-ODM+
Alternating current power (CO_{AC}) ¹¹	$SV = k \times \sqrt{\int_T (ABP(t) - MAP)^2 dt}$	LiDCO
Systolic area with correction (CO_{SA}) ^{12 13}	$SV = k \times (1 + (T_{sys}/T_{dia})) \times \int_{systole} ABP(t) dt$	PiCCO

the systolic part of arterial waveform, with a simple correction related to the ratio of systolic-to-diastolic duration.^{12 13}

External Doppler CO monitor

The USCOM (USCOM Ltd., Sydney, Australia) is a noninvasive external Doppler device that is used to measure cardiac output intermittently. A handheld probe placed in sternal notch is used to insonate the blood flow across the aortic valve.¹⁴ The probe can also be placed on the left anterior chest wall to insonate pulmonary valve blood flow via the 3rd–4th left intercostal space. Stroke volume is calculated as the product of the velocity time integral and aortic/pulmonary valve area, which is derived from the Nidorf algorithm and is based on patient height.¹⁵

Study protocol

Data collection was performed during the operation when no major interventional changes occurred and thus stable levels of surgical stimulation were maintained. For example, during a laparoscopic procedure the study would start after insufflation of peritoneum and end before deflation. During the study, dopamine was infused through a dedicated i.v. line and the rate was increased in $1 \mu\text{g kg}^{-1} \text{min}^{-1}$ incremental steps every 15–20 min to increase cardiac output. The goal was to increase the rate to $8 \mu\text{g kg}^{-1} \text{min}^{-1}$ but only if the patient tolerated the accompanying increases in blood pressure and heart rate, which was left to clinical judgment. The CardioQ-Combi and USCOM were used to obtain a series of increasing cardiac output readings from each patient.

The oesophageal CardioQ probe was inserted shortly after induction of anaesthesia. The probe depth and rotation was adjusted to obtain a signal that had well outlined triangular profile, with clear beginning and ending and of maximum peak velocity. The probe insertion depth was kept constant throughout the study. Initial internal calibration of the PPWA CO formulae was performed using the oesophageal Doppler CO (CO_{ODM}) reading, after stable heart rate and arterial pressure readings (i.e. 3-min period) were attained. The Combi pressure based reading software had a calibration function. The USCOM was used at intervals via the suprasternal route, to measure external Doppler CO (CO_{US}). The USCOM scan data was considered acceptable when its Cattermole score was above 5 out of 12.^{14 16} Simultaneous measurements of CO_{ODM} , CO_{US} and the five PPWA algorithms were performed at 15–20 min intervals and after the dopamine rate had been increased. It was impractical to take Doppler readings at exactly the same time. Therefore, the CardioQ probe was first refocused and CO_{ODM} plus PPWA cardiac output readings were recorded. Then USCOM probe was placed and focused to obtain the CO_{US} reading. The Doppler scans

were performed by one of the three experienced operators (L.C., J.Z. and L.H.) and usually were completed within 60 s. To ensure that the two Doppler monitors were measuring the same haemodynamics, heart rate was used as a guide. Any set of the readings that differed by more than 2 beat min^{-1} was rejected. All study cardiac output data were saved as screenshots by the two monitors and were later downloaded to a USB memory stick.

Statistics and data analysis

Sample size

A sample size (n) of 17 achieves 90% power to detect a cardiac output difference of 0.5 litre min^{-1} between the null hypothesis variance of 0.25 litre min^{-1} and the alternative hypothesis variance of 0.75 litre min^{-1} using a two-sided, χ^2 test with significance level (alpha) of 0.05. We extended to include 20 patients in the study.

Data analysis

Data collected during the study was compiled using Excel spreadsheets (Microsoft, Redmond, WA, US). To eliminate bias as a result of calibration errors, the CO_{US} data were retrospectively recalibrated for each patient, by multiplying their CO_{US} readings by a constant derived from the ratio of the first set of CO_{ODM} and CO_{US} readings (CO_{ODM}/CO_{US}). This resetting of data was equivalent to the internal calibration performed by the Combi software on all the PPWA cardiac outputs that were initially calibrated against the CO_{ODM} readings. Normality of data was tested with Kolmogorov-Smirnov one-sample test.

A scatter plot containing data from all patients was drawn and correlation analyses performed for all cardiac output comparisons. A R^2 value more than 0.6 and 0.8 indicate reasonable and good correlation between measurements, respectively. Bland-Altman analysis¹⁷ was performed to assess the agreement between CO_{ODM} and the five PPWA algorithms. Analysis between CO_{ODM} and calibrated CO_{US} was also performed for comparison. Percentage error (PE) was calculated as $PE = 1.96 \text{ SD mean}^{-1}$ cardiac output (%) and a PE less than 30% was deemed as acceptable precision.¹⁸

The trending abilities of the five PPWA cardiac output algorithms and CO_{US} were analysed using concordance analysis on a four quadrant plot.¹⁹ Changes in serial cardiac output readings (ΔCO) were calculated by subtracting consecutive cardiac output readings. Concordance rate was defined as the percentage of data points in which the change direction of pairs of measurements agree.¹⁹ To exclude random measurement error a central exclusion zone of 15% of mean cardiac output, or 0.8 litre min^{-1} , was applied.²⁰ A concordance rate above 92% is deemed as good trending ability.¹⁹

Half-moon polar plots were also drawn using the ΔCO trend data.²¹ Tramlines arising from the exclusion zone and 30° radical limits of agreements (RLOA) were added to the plots, to help show data point dispersion around the zero axis. However, there is no consensus on these boundary lines. The polar analysis also shows the presence of any systematic bias between sets of readings as cardiac output increased. In particular, if the two compared cardiac outputs do not increase in parallel, the mean angle of the plot (θ) will diverge from the zero axis. The polar statistics of most interest in the study are the mean polar angle, which should be $<\pm 5^\circ$ and its standard deviation (SD) from which the RLOA are derived.

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp, Armonk, NY, USA). A *p* value of less than 0.05 was considered significant. Graphs were drawn using GraphPad Prism, Version 6c (GraphPad software Inc., La Jolla, CA, USA). Polar plots were drawn using Sigma-Plot version 7.1 (Systat Software Inc, San Jose, CA, USA).

Results

Twenty-three patients were recruited. One 63-year old female patient developed tachycardia during operation and her data was

Table 2 Patient characteristic data of studied patients. (*n*=20). Values are expressed as mean (SD), mean (range) or absolute numbers, as appropriate

Age (yr)	65 (49–80)
Gender (M/F)	13/7
Height (cm)	166 (9)
Weight (kg)	67 (14)
BMI ($\text{kg}\cdot\text{m}^{-2}$)	24.3 (3)
ASA physical status (I/II/III)	3/16/1
Study duration (min)	133 (61–193)
Datasets	13 (8–18)
Dopamine infusion rate ($\mu\text{g}\cdot\text{kg}\cdot\text{min}^{-1}$)	4 (1–6)
Surgery	
Robotic prostatectomy	4
Robotic cystectomy	1
Laparoscopic/robotic bowel resection	8
Open bowel resection	2
Laparoscopic nephrectomy	2
Open nephrectomy	2
Intra-abdominal sarcoma resection	1

later excluded. Acceptable USCOM scans could not be achieved in one 78-year old male patient. In a third patient undergoing emergency operation, dopamine was never given because of intraoperative hypertension.

A total of 255 sets of cardiac output data were collected from 20 patients, 13 male and 7 female, using the two Doppler monitors and five PPWA algorithms. The mean (SD) age was 65 (range 49–80) yr, height 166 (9) cm and weight 67 (14) kg. Dopamine was used in all 20 patients with infusion rates that ranged from 1 to 7 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (Table 2).

Cardiac output data

The mean (range) patient cardiac output values of CO_{ODM} , CO_{US} and the five PPWA algorithms are shown in Table 3. There were no significant differences in these readings between the different methods and algorithms ($P>0.05$).

Scatter plots and correlation

Scatter plots with regression lines for all six cardiac output comparisons with CO_{ODM} are shown in Fig. 1. The calibrated CO_{US} had the best alignment with least dispersion of data points from the regression line with R^2 of 0.81 (Fig. 1, upper left), where the correlation coefficient R^2 provides an objective measure of data point alignment along the regression line. The other five PPWA algorithms exhibited greater dispersion and lower R^2 values that ranged from 0.52 to 0.72. Amongst the five PPWA algorithms, CO_{LZ} has the best correlation with CO_{ODM} , with a R^2 of 0.72.

Bland-Altman analysis

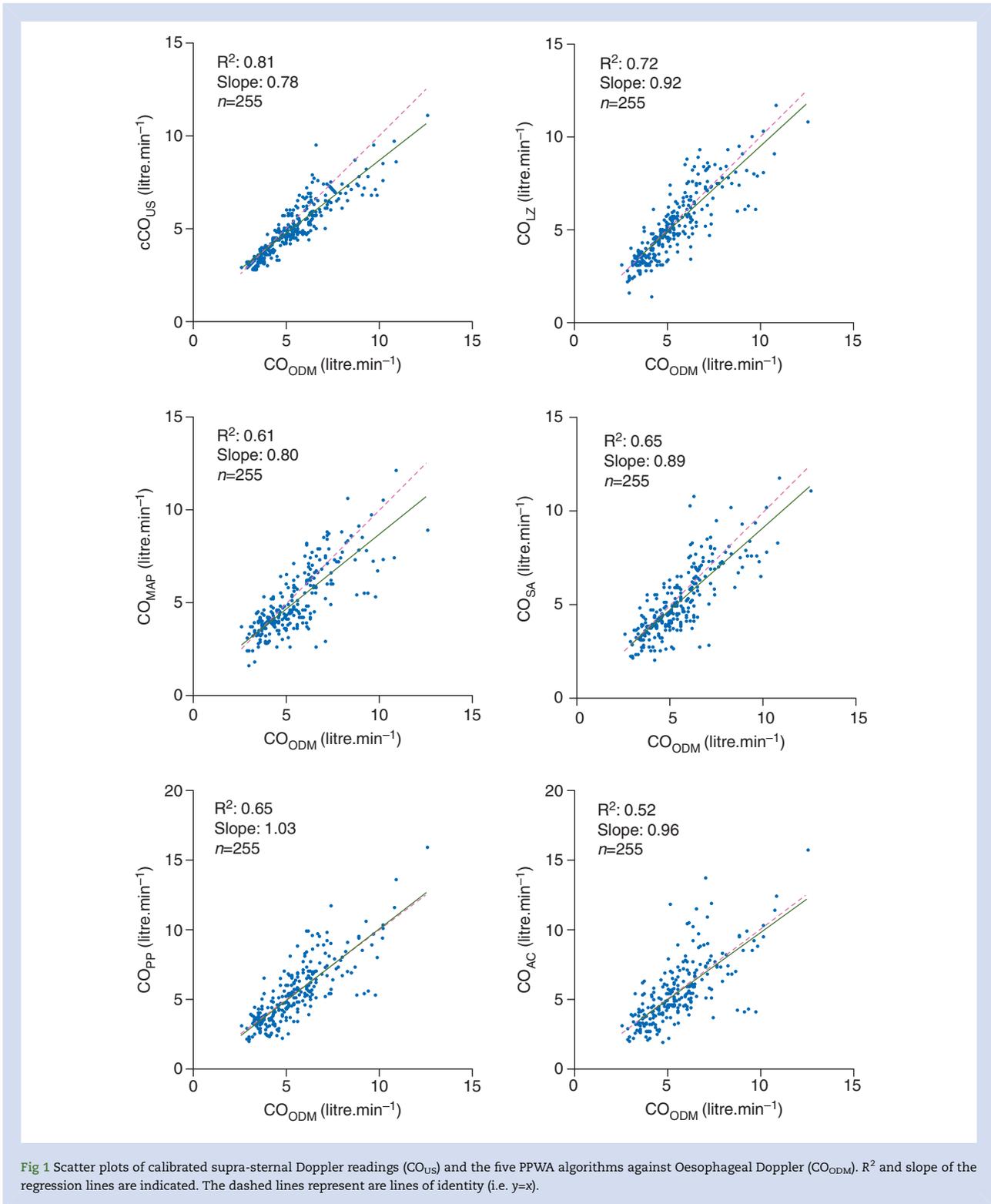
The bias between the five PPWA algorithms and CO_{ODM} ranged from 0.1 to 0.5 litre min^{-1} . The bias between calibrated CO_{US} and CO_{ODM} was 0.4 litre min^{-1} . Of the five PPWA algorithms, the Bland-Altman analyses showed that CO_{LZ} had the best agreement with CO_{ODM} , the PE being 35.2%, which was less than the calibrated CO_{US} with a PE of 26.4% (Table 4). Analysis of variance showed significant unequal homogeneity of the variance of the six methods ($P<0.0001$), which is seen as different spread patterns of scatters on the Bland-Altman plots (Fig. 2).

Concordance and polar analysis

After subtraction to create ΔCO , 235 sets of data that compared CO_{US} and the five PPWA algorithms with CO_{ODM} were available

Table 3 Cardiac output (CO) measured by oesophageal Doppler, supra-sternal Doppler (USCOM) and the five PPWA algorithms. Results of 255 series of measurements from 20 patients

Method	Mean cardiac output (litre min^{-1})	Range of cardiac output	
		Minimum (litre min^{-1})	Maximum (litre min^{-1})
Doppler Technique			
Oesophageal (CO_{ODM})	5.5	2.6	12.6
Calibrated Supra-sternal (CO_{US})	5.2	2.8	11.1
Pressure based algorithms			
Mean arterial Pressure (CO_{MAP})	5.1	1.6	12.1
Pulse Pressure (CO_{PP})	5.4	2.0	15.9
Liljestrand-Zander (CO_{LZ})	5.3	1.4	11.7
Alternating current power (CO_{AC})	5.4	1.9	15.7
Systolic area with correction (CO_{SA})	5.2	2.1	11.9



for trend analysis. The four-quadrant plots are shown in Fig. 3 and concordance rates after exclusion of central zone data are presented in Table 4. The central exclusion zones were set at 0.8 litre min⁻¹ and which was 15% of the mean cardiac output for the study data. The concordance rate for CO_{US} was 92%, whilst

the rates for the five PPWA algorithms ranged from 64 to 71%, with CO_{LZ} being the highest.

According to polar analysis, the CO_{US} with CO_{ODM} data had the least dispersion (i.e. SD of $\theta=21.1^\circ$) and least axial rotation of data (i.e. $\theta=-2.7^\circ$). Of the PPWA algorithms, the CO_{LZ} and CO_{MAP}

Table 4 Bland-Altman and concordance analysis of USCOM and the five PPWA algorithms against oesophageal Doppler. Calibrated CO_{US} was used for comparisons statistics. Bias, mean difference between studied six cardiac output data and oesophageal Doppler; LOA, Limit of agreement; PE, percentage error, calculated as PE (%)=1.96*standard deviation of bias/mean cardiac output. Polar angle is presented as mean [standard deviation (SD)]

Method	Bland-Altman plot (n=255)				Four quadrant plot (n=235)	Polar plot (n=235)
	Bias (litre min ⁻¹)	Lower LOA (litre min ⁻¹)	Upper LOA (litre min ⁻¹)	PE (%)	Concordance rate (%)	Angle (SD) (°)
CO _{US}	0.4	-1.1	1.8	26.4	92	-2.7 (21.1)
CO _{MAP}	0.5	-1.8	2.7	41.5	66	+3.8 (28.8)
CO _{PP}	0.1	-2.5	2.6	45.5	66	+17.6 (25.0)
CO _{LZ}	0.2	-1.7	2.2	35.2	71	+4.7 (26.6)
CO _{AC}	0.1	-3.0	3.2	56.3	65	+19.6 (25.4)
CO _{SA}	0.3	-1.9	2.5	40.7	64	+8.1 (29.0)

showed the best agreement, with the reference methods having lowest polar angles (θ) (i.e. +4.7 and +3.8, respectively), but data dispersion based on SD calculations were similar to the other methods (i.e. sds for all algorithms ranged from 25.0° to 29.0°) (Table 4 and Fig. 4).

Discussion

The present study compared (i) scatter plots with correlation, (ii) Bland-Altman agreement and (iii) trending abilities (i.e. four quadrant plot concordance and polar analysis) of five different fundamental PPWA algorithms with cardiac output readings from oesophageal Doppler in patients undergoing major surgery. The use of supra-sternal Doppler (USCOM) in the protocol, and confirming that the oesophageal Doppler readings were not erroneous (i.e. Dual Doppler methodology), also provided a control standard against which the PPWA comparisons could be compared. The results from the study demonstrated that the two Doppler techniques trended each other reliably during major surgery (i.e. concordance rate 92% and mean (SD) polar angle of -2.7 (21.1°)), and they were also in good agreement (i.e. Bland-Altman analysis) over the duration of data collection but only after the USCOM readings were recalibrated to eliminate differences in external calibration (PE 26.4%). Of the five evaluated PPWA algorithms, the Liljestrand-Zander formula was the best because it had the best agreement (PE 35.2%) and ability to trend cardiac output changes induced by dopamine (infusion rate up to 6–7 $\mu\text{g kg}^{-1} \text{min}^{-1}$) against oesophageal Doppler (i.e. concordance rate 71%). However, both these statistical estimates fell below the current acceptance criteria of <30 and >92% for PE and concordance, respectively.

Cardiac output monitoring is useful not only for haemodynamic assessment but also for guiding fluid therapy and the administration of vasoactive agents or inotropes.²² Confirming validity of the PPWA algorithms is desirable before accepting them as standards in guiding clinical treatments. Trending is particularly important because of the use of dynamic variables. The five algorithms selected for evaluation by this study calculate cardiac output using different components of the arterial pressure wave, and thus represent different mathematical approaches. These underlying principles of the algorithms are utilized in a range of currently available commercial cardiac output monitors, such as FloTrac-Vigileo, LiDCO, PiCCO^{23 24} and CardioQ-ODM+, as shown in Table 1. The MAP based formula was chosen because it was the original mathematical concept used for estimating cardiac output from blood pressure, from Ohm's law⁹ but it was not used by any of the current commercial devices.

To our knowledge, the present study is unique for being conducted during major surgery under general anaesthesia, which is a common clinical scenario for using cardiac output monitoring. Dopamine infusion was administered to change circulatory conditions but it has different circulatory effects when different infusion rates are administered: it acts on dopaminergic receptors to cause selective vasodilation at low dose (1–3 $\mu\text{g kg}^{-1} \text{min}^{-1}$) and binds to β_1 -adrenergic receptors to increase contractility and cardiac output (i.e. desired effect) at intermediate dose (3–10 $\mu\text{g kg}^{-1} \text{min}^{-1}$).²⁵ The impacts of these effects are important as they frequently occur during anaesthesia for major surgery and can potentially confound the accuracy of PPWA derived cardiac output readings. However, the vasodilator effects of dopamine and system vascular resistance were not studied.

The oesophageal Doppler was used as the primary reference method, as all the PPWA data were generated by the CardioQ-Combi system and initially all the PPWA cardiac output algorithms were calibrated to the oesophageal Doppler reading. In addition supra-sternal Doppler was used to eliminate erroneous readings and as control standard for CO_{ODM} comparisons. As the two Doppler monitors are measuring blood flow at different sites and are calibrated by different internal nomograms, USCOM readings were recalibrated for each patient data series, to eliminate any systematic error that arose from differences in initial setting up calibration between the two devices. This data transformation is justified because the same data alignment technique was used for the PPWA data by virtue of the Combi's initial calibration. The comparison between the two Doppler methods provided a set of good statistical data against which we could standard set the performance of the five PPWA algorithms. The validity of USCOM against CardioQ CO readings had been shown by our group in a recent previous study.⁷

The correlation analyses confirmed what was apparent from visual inspection of the scatter plots (Fig. 1), that the alignment between USCOM and CardioQ data was good as $R^2=0.81$, but data from the PPWA algorithms was less well aligned as R^2 ranged from 0.52 to 0.72, with the Liljestrand-Zander formula being the best aligned. This type of data comparison was criticized in the 1980s and resulted in the introduction of Bland-Altman analysis.¹⁷ The Bland-Altman analyses in the present study showed that the accuracy of the different formulae varied significantly, with the Liljestrand-Zander formula having the smallest variations (i.e. lowest PE) amongst the five algorithms. Only the PE of the USCOM comparisons met the universally accepted criteria of <30% for Bland-Altman analysis, whereas those from the five PPWA algorithms exceeded the criteria¹⁸ (Table 4). The wide dispersion of data points seen on the scatter and Bland-Altman

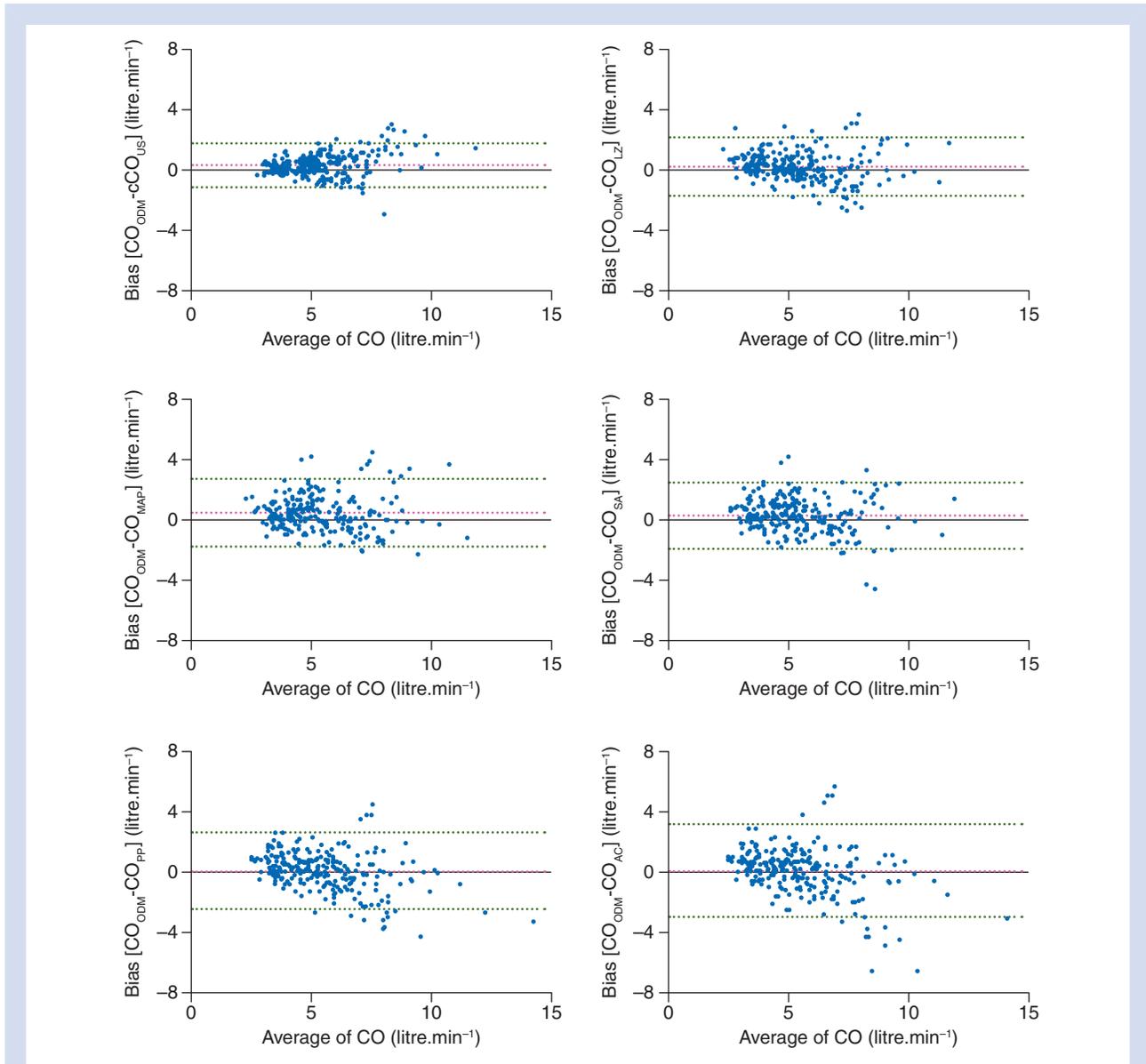


Fig 2 Bland-Altman plots of calibrated supra-sternal Doppler reading (cCO_{US}) and the five PPWA algorithms compared with Oesophageal Doppler (CO_{ODM}). Bias and limits of agreement are shown by dotted lines.

plots indicates a lack of consistency in measurements over the range of cardiac outputs. Although the five PPWA algorithms displayed similar mean cardiac output values as the two Doppler methods, they often had a large spread of cardiac output values and showed differences in agreement levels with oesophageal Doppler over this spread (Fig. 2).

The concordance analyses provided an against USCOM rate of 92%, which just met the 92% threshold set for good trending. None of the PPWA algorithms showed good trending ability although the Liljestrand-Zander formula had the highest rate of 71% (Table 4). The main advantage of using the polar transformation and drawing plots is that it shows not only data dispersion (i.e. lack of accuracy and concordance), but also lack of parallel increases in cardiac output between monitors by virtue of the polar angle. Whereas calibrated USCOM against oesophageal Doppler

increased in parallel and had an angle of -2.7° , the PPWA algorithms for pulse pressure and AC power in particular showed a distinct lack of parallel increase with angles of 18° and 20° , respectively. Despite having lower dispersion statistics (i.e. lower sds) the lack of parallel increases in cardiac output would add to the lack of agreement in Bland-Altman analysis. The Liljestrand-Zander formula performed better because its cardiac output increases were more aligned and parallel to the oesophageal Doppler readings.

In the present study, none of the PPWA algorithms showed good precision and trending ability but Liljestrand-Zander formula performed the best. A French study²⁶ which had included all nine algorithms used in the CardioQ-Combi monitor showed a similar result, albeit in neurosurgical patients receiving volume expansion and phenylephrine. No external reference method

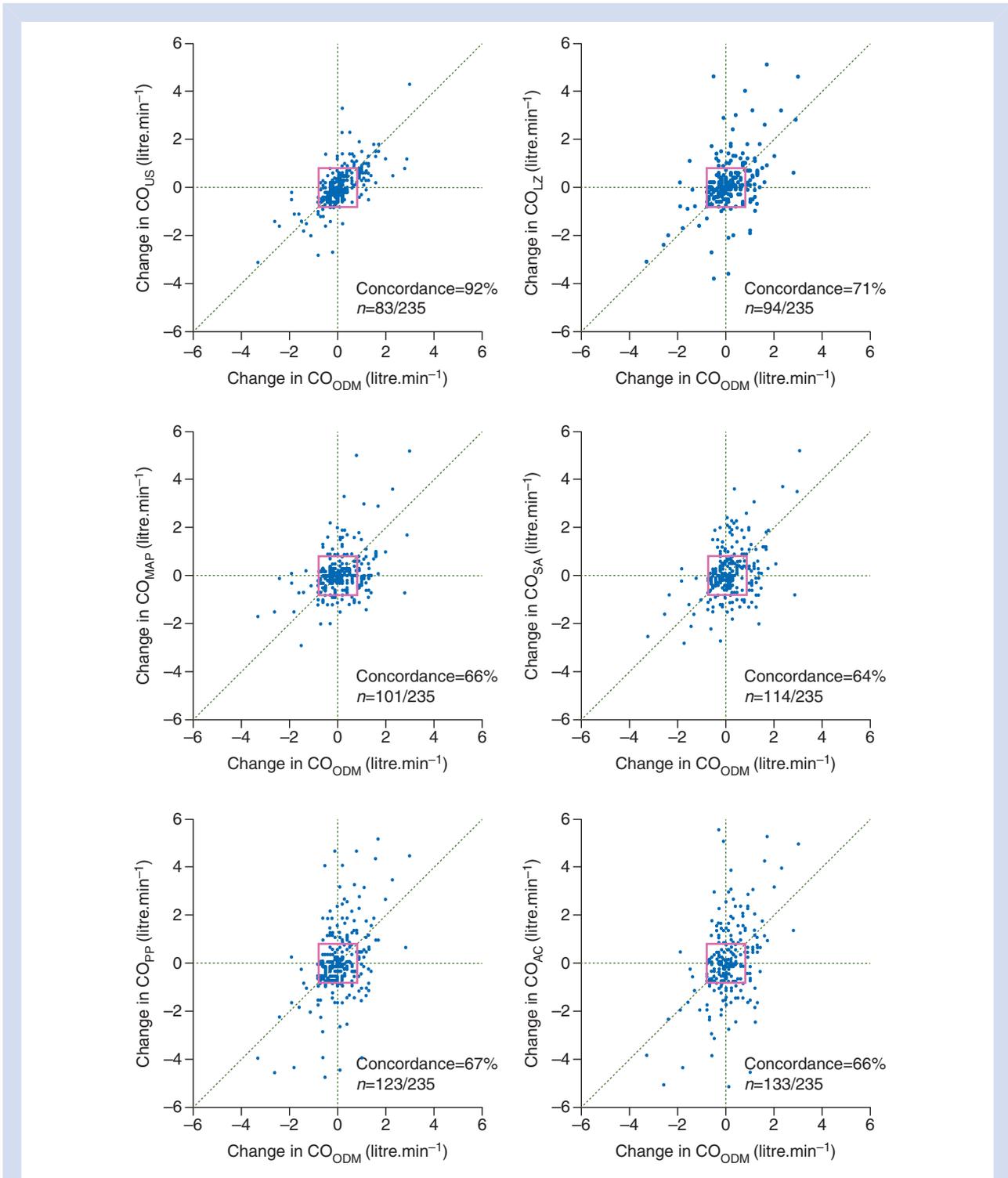
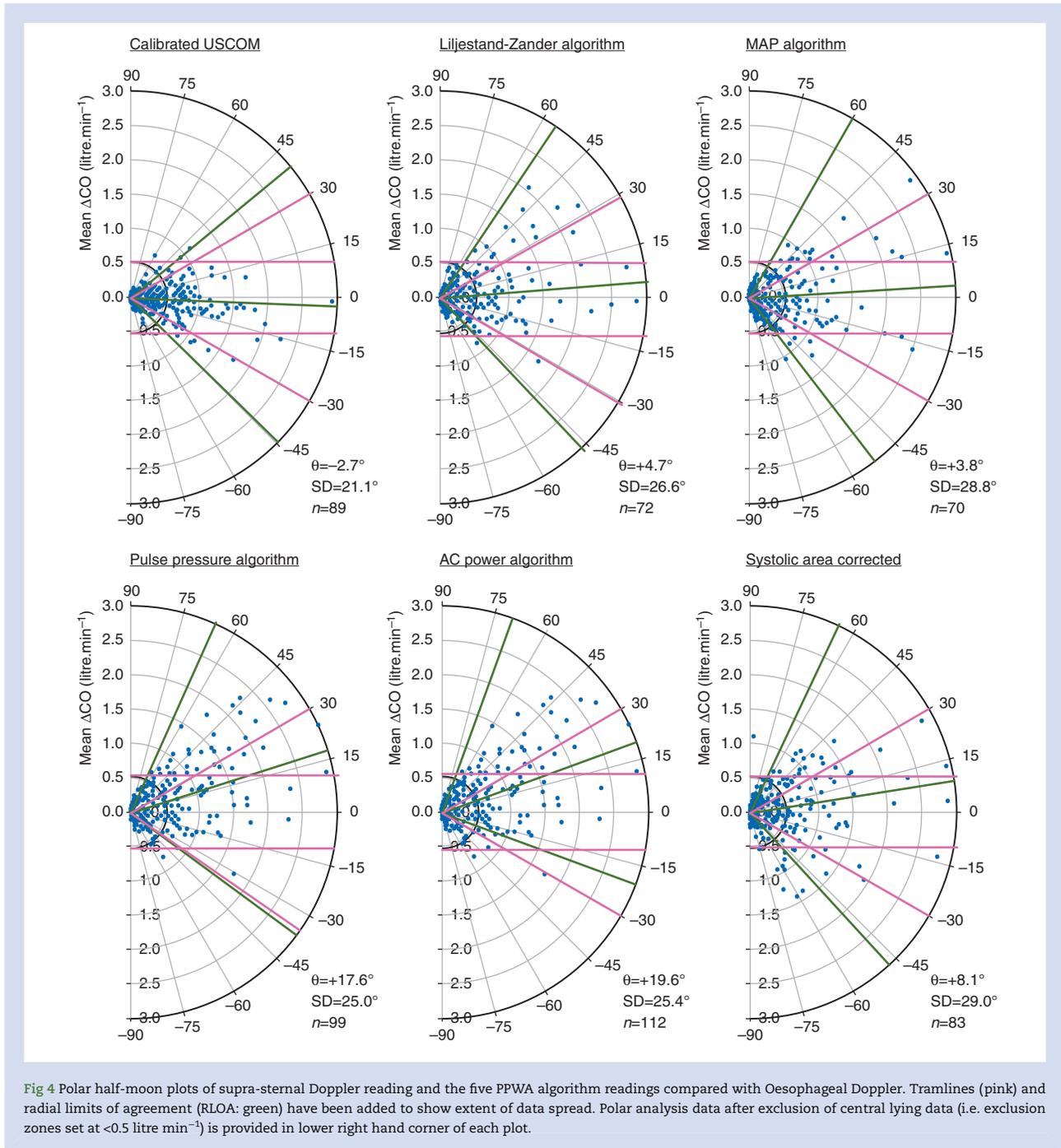


Fig 3 Four-quadrant concordance plots of supra-sternal Doppler reading (CO_{US}) and the five PPWA algorithms compared with oesophageal Doppler (CO_{ODM}). The central exclusion zone is 15% of mean cardiac output (0.8 litre min⁻¹).

such as supra-sternal Doppler was used. Hadian and colleagues²⁷ studied the algorithms of three commercially available monitors using pulmonary artery catheter thermodilution, or continuous cardiac output, as their reference in standard post-cardiac surgery patients. These authors found that the FloTrac, LiDCO and

PiCCO did not show good cardiac output trending results against pulmonary artery catheter, which is in agreement with the present findings. In another study by de Wilde and colleagues,²⁸ five arterial contour techniques were compared with thermodilution, also in cardiac surgery patients. LiDCO and PiCCO



algorithms were included and the results also did not show good agreement and trending ability. When reviewing the plots of these studies, it appears that the present studies' data points are more dispersed with smaller R^2 values and this may reflect the use of dopamine in the present study to change the circulatory conditions, which was not used in the de Wilde and colleagues²⁸ study protocol. The impact of changing arterial load on PPWA cardiac output algorithms has previously been demonstrated in a study evaluating 8 formulae using the CardioQ-Combi system in intensive care patients.²⁹ The change of circulatory condition may also explain the relatively low concordance rate found between USCOM and oesophageal Doppler readings

when compared with 96.6% for our previous study.⁷ The variation in peripheral resistance caused by the dopamine infusion may have resulted in a change in distribution of blood flow between the upper and lower body, and altered the split ratio of descending thoracic aorta blood flow. As the calibration factor for oesophageal Doppler includes a fixed constant that accounts for this split in blood flows, changes in the split ratio will cause offsets in oesophageal Doppler reading relative to USCOM.³⁰ The reduced slope of the regression line on the scatter plot between CO_{US} and CO_{ODM} (Fig. 1, uppermost left) of 0.78, compared with 0.88 from our previous study data is another clue that suggests an altered split ratio, and this could be an area of further study.

The Liljestrand-Zander formula performed better in terms of precision and trending ability than the other four PPWA algorithms, although it still did not meet our acceptance criteria. This formula is derived from the Windkessel model, but also takes into account variations in arterial capacitance, which are as a result of changes in arterial pressure.⁹ Therefore, changes in circulatory conditions are partly compensated for by using graded pulse pressure in the cardiac output calculation, and hence explains the better performance of this algorithm in the present study. Therefore, our findings support the use of the Liljestrand-Zander formula for PPWA cardiac output monitoring in the recently released CardioQ-ODM+ monitor.

The study did have some limitations. Firstly, a 'gold standard' reference method such as thermodilution was not included in the protocol. However, the detrimental complications related to pulmonary artery catheter insertion and use, mean that it is seldom used routinely today in many countries for anaesthesia practice.³¹ Therefore, using it in the present study would have been difficult to justify ethically in Hong Kong. Furthermore, our group has recently shown that Doppler methods can be used as an alternative reference standard.⁷ Secondly, we only studied the performance of the algorithms in a small cohort of patients in a restricted clinical settings, general anaesthesia using a dopamine infusion, thus our findings may not be applicable for other settings such as vasopressor use in the intensive care. Thirdly, our results do not fully reflect the performances of currently available PPWA devices, such as FloTrac-Vigileo, LiDCO and PiCCO, as we were evaluating the underlying mathematical approaches and not using these devices.

Conclusions

None of the evaluated PPWA algorithms demonstrated good agreement or trending ability. Amongst the five fundamental PPWA algorithms, the Liljestrand-Zander formula showed the best precision and trending ability, albeit against the oesophageal Doppler method in major surgical patients under general anaesthesia. Therefore, it was the most suitable PPWA algorithm for use intraoperatively to monitor cardiac output and our study supports its inclusion in the new CardioQ-ODM+.

Authors' contributions

Study design/planning: L.C.
Study conduct: J.Z., L.C., L.H.
Data analysis: J.Z., L.C.
Writing paper: J.Z., L.C.
Revising paper: All authors

Declaration of interest

L.C. is a member of Combi group, an international group of researchers investigating the use of oesophageal Doppler with pressure based monitoring, and has received non-monetary sponsorship from Deltex Medical Inc. (Chichester, England) in the form of equipment and disposable probes. J.Z. and L.H. none declared.

Funding

The oesophageal Doppler device (Combi monitor) and probes used in the study were provided by Deltex Medical Inc. (Chichester, England).

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Handling editor: A. R. Absalom