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Accuracy of impedance cardiography for evaluating trends in cardiac output: a comparison with oesophageal Doppler

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Editor's key points

- Impedance cardiography (ICG) was compared with oesophageal Doppler monitoring (ODM) in determining cardiac output (CO) in general surgery patients.
- In a modified polar plot analysis, CO variations correlated significantly between the two methods.
- ICG is a reliable non-invasive method comparable with ODM in investigating CO trends in general surgical patients.

Background. Impedance cardiography (ICG) enables continuous, beat-by-beat, non-invasive, operator-independent, and inexpensive cardiac output (CO) monitoring. We compared CO values and variations obtained by ICG (Niccomo™, Medis) and oesophageal Doppler monitoring (ODM) (CardioQ™, Deltex Medical) in surgical patients.

Methods. This prospective, observational, single-centre study included 32 subjects undergoing surgery with general anaesthesia. CO was measured simultaneously with ICG and ODM before and after events likely to modify CO (vasopressor administration and volume expansion). One hundred and twenty pairs of CO measurements and 94 pairs of CO variation measurements were recorded.

Results. The CO variations measured by ICG correlated with those measured by ODM [$r=0.88$ $(0.82-0.94)$, $P<0.001$]. Trending ability was good for a four-quadrant plot analysis with exclusion of the central zone ($<10\%$) [95% confidence interval (CI) for concordance (0.86; 1.00)]. Moderate to good trending ability was observed with a polar plot analysis (angular bias: $-7.2°$; 95% CI $-12.3°$; $-2.5°$; with radial limits of agreement $-38°$; $24°$). After excluding subjects with chronic obstructive pulmonary disease, a Bland–Altman plot showed a mean bias of 0.47 litre min^{-1}, limits of agreements between -1.24 and 2.11 litre min^{-1}, and a percentage error of 35%.

Conclusion. ICG appears to be a reliable method for the non-invasive monitoring of CO in patients undergoing general surgery.

Keywords: monitoring; cardiopulmonary, monitoring; ultrasound

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Recent studies have shown that cardiac output (CO) monitoring in the operating theatre reduces morbidity and shortens length of hospital stay after surgery.[1–6] In these studies, the goal was to maintain oxygen delivery and avoid oxygen debt. Anaesthesiologists need less invasive ways of continuously monitoring CO. There is now sufficient evidence to support the use of oesophageal Doppler monitoring (ODM) for routine cardiac monitoring.[7] Thoracic impedance cardiography (ICG) is a non-invasive, continuous, operator-independent, and cost-effective tool for CO monitoring.[8] While some studies have found good agreement between impedance and a reference technique, others have found high limits of agreements reflecting a lack of interchangeability between the ICG and reference techniques.[9] Poor reliability could be because of a poor signal-to-noise ratio, strict requirements for lead placement that make ICG incompatible with certain types of surgery,[10 11] and lack of accuracy in determining left ventricular ejection time (LVET).[12] Bioreactance has been used to overcome these

difficulties. Bioreactance measures the frequency modulation and signal phase shift of an electrical current crossing the thorax, the variations of which are related to changes in the volume of the thoracic aorta.[13] This technology significantly enhances the signal-to-noise ratio.[13] Nevertheless, conflicting results have been found with bioreactance in the clinical context.[14–17]

Recently, the manufacturer of the Niccomo™ ICG monitor (Medis Medizinische Messtechnik GmbH, Ilmenau, Germany) developed a new algorithm and new signal measurement hardware, so that aortic opening and closure could be detected more accurately. By definition, thoracic impedance ($Z=R+jX$) measures the added vector between resistance (R) and phase shifted reactance (jX) that is the result of capacitance and inductance.[18] Therefore, thoracic impedance variations measure the impedance variations induced by stroke volume (SV)[8] to the resistance and the reactance of the thorax. According to the manufacturer, the new design provides greater

sensitivity and a higher signal-to-noise ratio, so that even very small impedance signals (and thus, blood volume variations) can be reliably detected. On this basis, it is possible to reduce the overall low pass filtering of the signal, which yields a much more information-rich ICG waveform and provides a clearer depiction of the fiducial points required for the calculation of the SV. Furthermore, the system's algorithms for artifact elimination and detection of the fiducial points have been optimized. The new algorithm should allow better acquisition of the X point corresponding to aortic valve closure.[19] Recognition of each heart beat on the electrocardiogram (ECG) and determination of the exact times of aortic opening and closure might also improve the accuracy of the Niccomo™ monitor. In the present study, we compared the ability of ICG and that of ODM to evaluate absolute CO values and CO trends.

Methods

Ethical aspects

The study's objectives and procedures were approved by the local institutional review board (*Comité de protection des personnes Nord-Ouest II*, Amiens, France). Written informed consent was waived because the board considered that the study procedures were part of routine practice.

Subjects

A prospective, observational study was conducted over a 2-month period (February and March 2012) in the Department of Anesthesiology at Amiens University Medical Center (Amiens, France). The inclusion criterion was age ≥ 18 yr, with use of ODM during surgery. Patients with preoperative arrhythmia, history of right or left ventricular failure, valvular aortic disease, frequent ectopic beats or spontaneous breathing or contraindications to ODM probe insertion were excluded.

Anaesthesia

Monitoring consisted of three-lead ECG, pulse oximetry, and non-invasive arterial pressure monitoring. Balanced general anaesthesia was used in all the subjects. Induction was performed with propofol or etomidate and either remifentanil or sufentanil, according to the anaesthesiologist's preference. All the patients received neuromuscular block with i.v. cisatracurium (0.15 mg kg^{-1}) or rocuronium (0.6 mg kg^{-1}). Tracheal intubation with a single lumen tracheal tube was performed to obtain airway control with mechanical ventilation in the volume-controlled mode. Tidal volume (VT) was 8–9 ml kg^{-1} of ideal body weight (IBW), with ventilatory frequency adjusted to maintain end-tidal CO_2 concentrations of 4.0–4.66 kPa and a positive end-expiratory pressure (PEEP) of 3–5 cm H_2O. Anaesthesia was maintained with either propofol or inhaled desflurane or sevoflurane.

Measurements

Clinical data [age, gender, weight, height, body mass index (BMI), type of surgery, ASA physical status, Lee score, history of heart failure, hypertension, peripheral arterial disease,

coronary syndrome, stroke, chronic kidney disease, diabetes chronic obstructive pulmonary disease (COPD), and smoking status] and ventilatory data (tidal volume, plateau pressure, and end-expiratory pressure) were recorded at baseline.

The CO derived from ODM (CO_{ODM}) or ICG (CO_{ICG}) and haemodynamic data were recorded before and after treatments likely to modify CO (vasopressor administration or volume expansion). The indications for these interventions were left to the anaesthetist's discretion. Subjects were studied after 5 min with stable haemodynamic variables, constant ventilator settings, and stable drug administration. A first set of measurements [heart rate (HR), systolic arterial pressure (SAP), mean arterial pressure (MAP), diastolic arterial pressure (DAP), SV_{ODM}, CO_{ODM}, flow time corrected (FTc), peak velocity (PV), SV_{ICG}, and CO_{ICG}] was recorded at baseline. Possible treatments were volume expansion (infusion of 500 ml crystalloid solution over 10 min), bolus of phenylephrine (50–100 µg), or norepinephrine infusion (0.03–0.15 µg kg^{-1} min^{-1}). A second set of measurements (HR, SAP, MAP, DAP, SV_{ODM}, CO_{ODM}, FTc, PV, SV_{ICG}, and CO_{ICG}) was recorded at the end of the treatment (after 5 min of haemodynamic stability).

Oesophageal Doppler monitoring

The position of the ODM probe (CardioQ™, Deltex Medical, Gamida, Eaubonne, France) was adjusted to obtain the best signal for descending aortic blood velocity.[20] Given that aortic wall motion is possible, we sought to avoid the occurrence of non-laminar flow by narrowing the frequency range (blunt velocity profile). The narrow frequency range has a characteristic shape, with bright borders and dark inner part. The probe was systematically repositioned before each measurement, as recommended.[20] On the basis of continuous aortic blood flow measurements, the acquisition software automatically calculated the SV average over 30 s. The inter-observer variability of the method is good and ranges between 3 and 10%.[21] The reproducibility of SV measurement was tested before the study; SV was measured twice in 10 patients by the same observer and by a second observer in two studies of our group:[22 23] intra-observer reproducibility was 0.3 and 0.5% (0.1–4.0%) and inter-observer reproducibility was between 1.1 and 2% (3–5%). CO, SV, FTc, and PV were recorded continuously (beat by beat) from aortic blood velocity, and their mean values were calculated over 30 s using the Excel® file generated by the CardioQ™.

ICG monitoring

Four Niccomo™ dual-electrode patches (i.e. eight electrodes in all) were placed as recommended by the manufacturer. Current intensity and frequency were 1.5 mA and 85 kHz. The ICG signal is the first derivative of the thoracic impedance (dZ/dt). By taking gender, height, body weight, basal impedance (Z_0), dZ/dt, and ejection time into account, the software calculates the SV using Bernstein's equation[8] excluding distortions or artifacts in the ICG signal. The SV was calculated beat by beat and averaged over 30-s periods.

Statistical analysis

Sample size was calculated in order to demonstrate equivalence between ΔCO_{ODM} and ΔCO_{ICG}. With a two-sided alpha risk of 0.05, a beta risk of 0.2, a Pearson correlation between ΔCO_{ODM} and ΔCO_{ICG} of 0.8, and an expected SD of 0.9 for ΔCO, 31 pairs of ΔCO measurements were needed to demonstrate equivalence with a margin of 0.3 (in a paired test). Given that the ΔCO measurements were repeated an average of three times per subject, the variance inflation factor[24] was estimated to be 1.6 for an intra-class correlation coefficient of 0.3. The adjusted minimum sample size (i.e. the number of pairs of ΔCO measurements) was therefore 50.

The normality of quantitative data was verified using the Kolmogorov–Smirnov test, and data are expressed as mean (SD).

The relationship between CO_{ODM} and CO_{ICG} was analysed using a linear, mixed-effects model. Agreement between CO_{ODM} and CO_{ICG} was analysed with scatter plots and Bland–Altman plots. Percentage error was calculated as 1.96 SD of the bias divided by mean CO; this value was considered clinically acceptable if <30%. The influence of the population's characteristics on the bias was systematically screened with a Wilcoxon test.

Given that the radial limits of agreement (RLA) approach assumes that each data pair is independent,[25] it is not valid for repeated measures. Accordingly, we developed a polar plot method for repeated measures. Trending ability was studied with two different methods: a four-quadrant plot and a polar plot. We calculated the concordance rate (in the four-quadrant plot only), the angular bias and its SD, and the RLA (in the polar plot only).[25] A detailed description of the polar plot method for repeated measures is provided as an appendix. Data at the centre of the polar plot correspond to small changes in CO; the associated, large, random error (statistical noise) component makes it difficult to assess trending.[26] Hence, receiver operating characteristic curves were drawn to make judgements about the discriminative power of different ΔCO values. An optimal ΔCO exclusion value of 10% (mean CO: 4.91 litre min^{-1}, hence 10%=0.5 litre min^{-1}) was found. Our exclusion zone limits reflect those commonly used in concordance analysis.[26]

Results

In the 2-month study period, 36 subjects were enrolled. Four of these were subsequently excluded because of frequent ectopic beats (n=2) or poor ODM signal acquisition (n=2). In the final study population of 32 subjects, 128 pairs of measurements were obtained, and subject characteristics were mean (range) age 71 (49–86) yr, and, mean (SD) weight 73 (13) kg, height 167 (11) cm, and BMI 26 (6) kg m^{-2}. Twelve subjects were ASA II and 20 were ASA III. Indications for ODM monitoring were orthopaedic surgery (n=19, 59%), vascular surgery (n=9, 28%), and visceral surgery (n=4, 12%). Indications for intra-operative intervention were hypotension and CO optimization. Subjects were treated with vasopressors [phenylephrine bolus (50–100 μg), n=4, or norepinephrine infusion

(0.03–0.15 μg kg^{-1} min^{-1}), n=2] or volume expansion (n=22). Four subjects received both treatments.

At baseline, SAP was 102 (20) mm Hg [mean (SD)], DAP was 59 (13) mm Hg, MAP was 73 (14) mm Hg, and HR was 65 (13) bpm. Respiratory parameters—tidal volume/IBW: 7.9 (0.6) ml kg^{-1}; respiratory rate 11 (2) min^{-1}; plateau pressure 16 (4) cm H$_2$O; PEEP 3 (2) cm H$_2$O.

As shown in Figure 1A, CO_{ICG} correlated with CO_{ODM} (r=0.84; P<0.001). Mean CO was 4.80 (1.87) litre min^{-1} for ICG and 4.91 (1.74) litre min^{-1} for ODM. A Bland–Altman plot (Fig. 1B) showed that the mean bias was 0.10 litre min^{-1} and the limits of agreements were −1.90 litre min^{-1} and 2.11 litre min^{-1}. Percentage error was 41% according to Critchley and Critchley's method.[27] There was no statistically significant bias related to the following parameters: ASA score, Lee score, history of heart failure, hypertension, peripheral arterial disease, coronary syndrome, stroke, chronic kidney disease, diabetes mellitus, and smoking status. However, mean bias differed significantly when comparing COPD patients and non-COPD patients [−0.99 (−3.43; 0.26) and 0.09 (−1.03; 2.31), respectively [values are median (min;max)]; P<0.05]. After excluding COPD patients, the Bland–Altman plot showed a mean bias of 0.47 litre min^{-1}, limits of agreements of −1.24
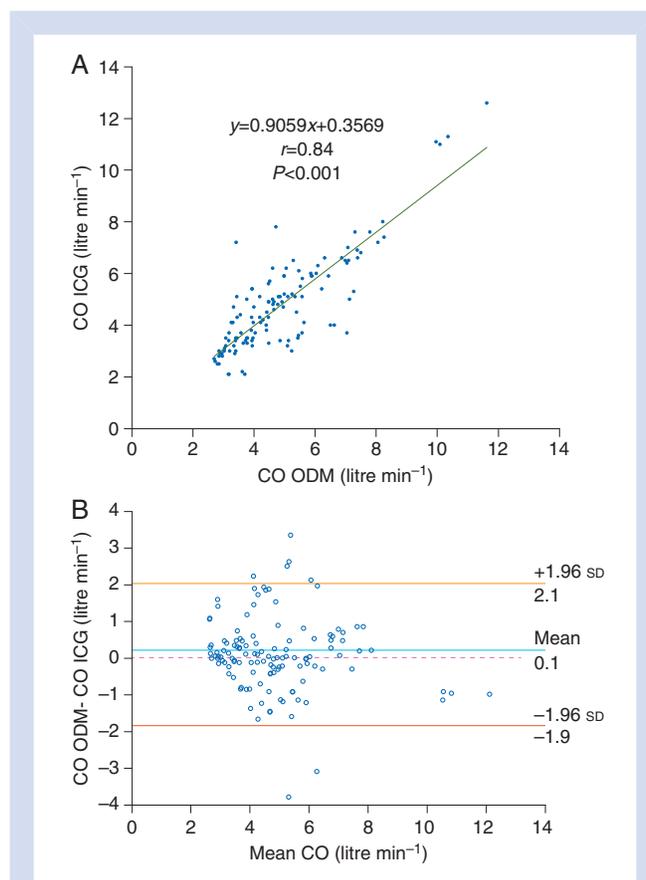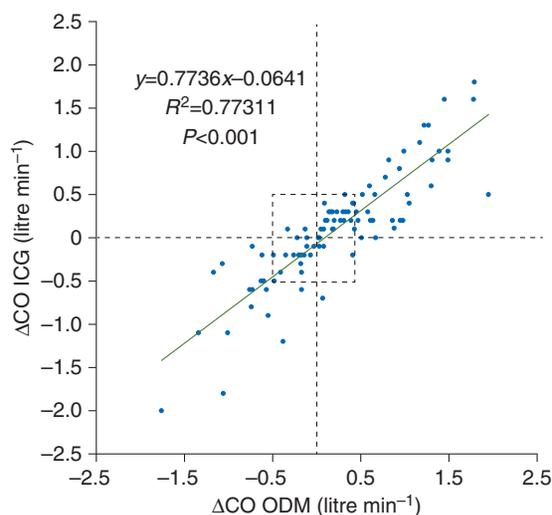

Fig 1 (A) Pearson coefficient for the correlation between CO_{ODM} and CO_{ICG} (n=130, r=0.84, P<0.001). (B) A Bland–Altman plot (mean bias: 0.10 litre min^{-1}; limits of agreements: −1.90 and 2.11 litre min^{-1}). The percentage error was 41%.[27]

and 2.11 litre min^{-1}, and a percentage error of 35%. The ICG-derived LVET correlated with ODM-derived LVET ($r=0.69$, $P<0.0001$).

As shown in Figure 2, variations in CO_{ICG} were correlated with variations in CO_{ODM} [$n=93$, $r=0.88$ $(0.82-0.94)$, $P<0.0001$]. For four-quadrant analysis with exclusion of the central zone data (variations $<10\%$), the trending ability was good [$n=93$, 95% confidence interval (CI) for concordance 0.86; 1.00]. After exclusion of CO variations $<10\%$, moderate to good trending ability was observed in a polar plot analysis (angular bias: $-7.2°$; 95% CI $-12.3°$; $-2.5°$), with RLAs of ($-38°$; $24°$) (Fig. 3).[25] For trending induced by vasopressors and fluids, the angular biases were $-0.48°$ (95% CI -8.72; 9.67; RLA $-23.85°$; $24.80°$) and $-9.44°$ (95% CI $-14.94°$; $-3.93°$; RLA $-38.58°$; $19.70°$), respectively. As shown in Figure 4, 95% inclusion rate was obtained for a radial sector size of 32°, which indicates moderate to good trending ability.[25]

Discussion

Four-quadrant analysis and polar plot showed that ICG trending ability was clinically acceptable relative to ODM when fluids or vasopressors were administered. After exclusion of data at the centre of the plot, the ICG–ODM concordance rate was above the value recommended by Critchley and colleagues.[26] The polar plot method revealed moderate to good trending and low angular bias. The advantage of the polar plot methodology over the four-quadrant plot is that the former takes account of the magnitude of the ΔCO (rather than calculating concordance based on the direction of change only, which can create bias).[26] Although the changes were in the same direction, their magnitudes can differ significantly.
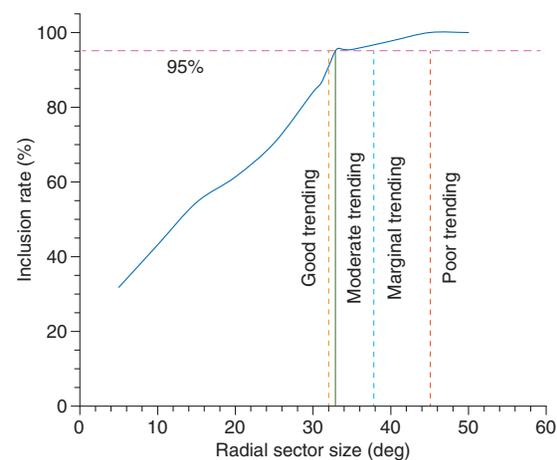
Although a modified, repeated-measures version of the Bland–Altman method has been published,[28] interpretation of the limits of agreement can be complicated when repeated ΔCO measurements from the same patient are obtained under different clinical conditions.[26] The RLA approach[25] is not valid for repeated measures, since it assumes that each data pair is independent. This would be unacceptable, as CO in a given subject will be correlated with subsequent measurements in the same individual.

Our new polar plot methodology for repeated measures has the advantage of taking into account low-magnitude ΔCO
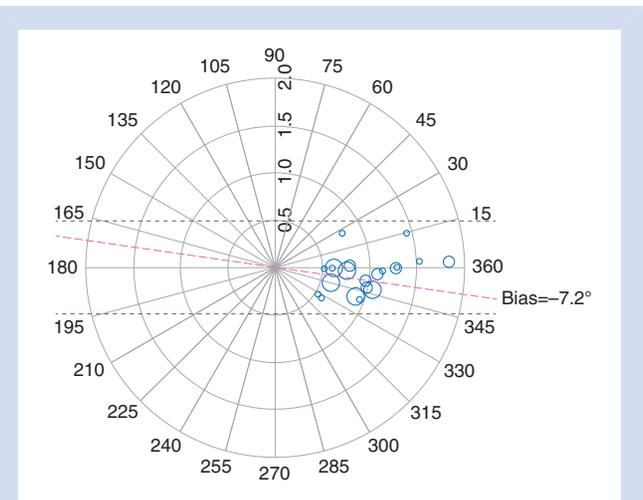
Fig 3 Polar plot for ΔCO values as a function of the number of ΔCO measurements per subject (1, 2 or 3). After exclusion of CO variations <0.5 litre min^{-1}, the angular bias was $-7.2°$ ($-12.3°$; $-2.5°$) and the RLA were $-38°$ and 24°. Measurements were recorded for $n=22$ subjects (ΔCO >0.5 litre min^{-1}).

Fig 2 Pearson coefficient for the correlation between ΔCO_{ODM} and ΔCO_{ICG} [$n=93$, $r=0.88$ $(0.82-0.94)$, $P<0.0001$] and a four-quadrant analysis with exclusion of central zone data (<0.5 litre min^{-1}). Good trending ability was observed in the four-quadrant plot analysis ($n=93$, 95% CI 0.86; 1.00).

Fig 4 Inclusion rate as a function of the radial sector size. The 95% inclusion rate was obtained for a radial sector of 32°, which corresponds to moderate to good trending.[25]

measurements that produce large polar angles. In the standard polar plot, most of the ΔCO measurements greater than $\pm 30°$ RLA were associated with ΔCO values between 0.59 and 0.78 litre min^{-1} with large within-subject variability. After averaging ΔCO values, the final angle is a more accurate reflection of the concordance of ΔCO measurements. Unlike angular bias, RLAs were broader for the new method ($-38°$; 24°) than for the conventional method ($-35°$; 22°), taking account of within-subject variability. This observation emphasizes that despite the conventional application of a 10% exclusion zone (0.5 litre^{-1} min), points slightly above this cut-off point can be associated with a large angle and thus make it more difficult to assess the level of concordance. Our new method can overcome this difficulty.

We did not use a pulmonary artery catheter (PAC) as a reference for CO measurement. Monitoring with a PAC is associated with complications,[29] a single bolus cannot be used easily to assess trends, and new thermistor wire CO PACs are less precise[30] and have a long time response.[31] The ability of minimally invasive ODM to detect changes in CO has been demonstrated.[32–34] Even though the ODM device used here (CardioQ^{TM}, Deltex Medical) measures neither instantaneous aortic diameter nor percentage split between the upper body and lower body, ODM is a minimally invasive method for CO measurement, and there is now sufficient evidence to support its use for routine cardiac monitoring.[7] Given that aortic diameter varies with aortic pressure, accurate measurement of SV and PV could be influenced by this variable.[35] Some clinical situations (shock, sepsis, laparoscopy, and epidural analgesia) modify the percentage split of flow between the upper and lower body.[36–38] None of our subjects experienced these events. Moreover, the clinical relevance of ODM has mainly been validated by assessing relative changes in SV in high-risk surgical patients.[1–6] ODM has been used to guide CO optimization with goal-directed fluid administration protocols. In these studies, researchers observed SV trends (rather than absolute values), which enhances the outcomes in high-risk surgical patients.[1–6 39] Hence, studying trends rather than absolute values is clinically relevant and avoids the need to estimate (i) aortic diameter and flow distribution and (ii) the geometric electrical size of the thorax.

Studies of ICG have reported conflicting results and are difficult to compare with each other because they were conducted with devices of different generations, different physical models, and different equations. The reference (comparator) method also differed from one study to another, although PAC thermodilution was most common. Subject characteristics also varied widely and ranged from healthy volunteers to patients with heart failure receiving pharmacological or surgical treatment. Two relatively dated meta-analyses[40 41] yielded overall correlation coefficients of 0.81 and 0.82, respectively. In a more recent meta-analysis, Peyton and Chong found that the overall correlation coefficient was 0.79 for ICG and thermodilution.[9] This value was similar to those for ODM (0.69), the Fick method applied to CO_2 (0.57), and contour analysis of the pulse wave (0.75).[9] In the present study, the correlation coefficient for CO_{ICG} and

CO_{ODM} was 0.84, which is similar to Peyton and Chong's value for thermodilution. In our Bland and Altman analysis, the Niccomo's^{TM} percentage error for CO_{ICG} (41%) was out of the clinically acceptable range (± 30%). However, after excluding COPD patients ($n=9$), we determined this value to be 35%. In fact, Peyton and Chong have suggested that the percentage limits of agreement for comparing two CO monitoring techniques should be raised from ± 30 to ± 45%.[9] In contrast to our present results, Fellahi and colleagues showed that the percentage error between transthoracic echocardiography and Niccomo's^{TM} CO_{ICG} measurement was 53%.[12] Furthermore, there are reports of a lack of agreement between CO measured by ICG and a reference technique (usually thermodilution) in various subgroups of subjects.[42–45] We observed a stronger correlation between ICG-derived LVET and Doppler-derived LVET ($r=0.69$, $P<0.000$) than Fellahi and colleagues ($r=0.27$, $P<0.03$).[12] This suggests that the new hardware and algorithm indeed improved the device's performance. However, disparities between our results and the literature data might also be related to the use of different reference methods.

Several factors are known to influence ICG readings in particular clinical situations. Surgery in the area of the diaphragm or affecting the chest can decrease the accuracy of ICG, as the technique shows a poor correlation after cardiac surgery or major abdominal surgery.[46] Critchley and colleagues have demonstrated that abdominal opening and closure can change bias over time.[47] They also demonstrated (in dogs and humans) that vasodilatation/vasoconstriction status, lung fluid balance, and acute lung injury can decrease the accuracy of ICG compared with thermodilution.[11 48 49] The application of positive airway pressure to modify CO can also be a cofounding factor that changes the thoracic volume and influences impedance measurements.[12 50] Indeed, we found that ICG was less accurate in patients with COPD, possibly because of differences in thoracic volume.

Our study had some other limitations. The sample size was not very large, even though the study had sufficient statistical power. We investigated a small variety of surgical procedures. The vasodilation and fluid loading treatments were not standardized but nevertheless reflected 'real life' in the operating theatre. Cost-effectiveness and outcome studies are now needed to establish whether or not the device provides clear benefits.

Authors' contributions

E.L. and Y.M. designed the research; E.L., J.S., C.B., P.-G.G., S.P., A.K., and B.D. collected the data; E.L., Y.M., M.D., and H.D. analysed the data; M.D. performed the statistical analysis; E.L., Y.M., M.D., and H.D. wrote the paper.

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Declaration of interest

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Appendix: the polar plot method for repeated measures

The modified Bland–Altman method for repeated measures can be used to calculate the mean of repeated measures for each method and for each individual. The mean angles for each subject can then be used to compare the two methods (based on an RLA of $\pm 30°$). The bias between the two methods is not affected by averaging the repeated measures. However, the variation in the differences between original measurements is underestimated by this practice because the measurement error is, to a certain extent, eliminated. Advanced statistical calculation is therefore necessary to take these measurement errors into account.

A random effects model was used to estimate within-subject variation after accounting for other observed variations,[51] in which each subject presented a different bias, magnitude, and angle over the observation period. An appropriate polar plot for repeated measures was created on the basis of within-subject variance estimated from the random effects model. According to the Bland–Altman method,[52] the SD of the angles of the repeated measures can be calculated from within-subject SD estimates. The random effect is the sequence or the measurement time over the observation period.

We also developed a new presentation of the polar plot by using the average ΔCO measurements for each subject. Each subject is represented once (by a circle) in the plot. The diameter of the circle is proportional to the number of measurements recorded for that subject. To assess RLA with this method, components of the variance for the polar angle were estimated in a mixed-model analysis of variance. To evaluate uncertainty in the estimated parameter (concordance rate and angular bias), 1000 bootstrap replications[53] were carried out and 95% percentile-based confidence intervals were established. Using a conservative approach, the lower confidence limit for the RLA was defined as the 2.5% percentile of 1000-bootstrap lower limits of agreement and the upper confidence limit was defined as the 97.5% percentile of 1000-bootstrap lower limits of agreement.

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