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Novel continuous capnodynamic method for cardiac output assessment during mechanical ventilation

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Editor's key points

- The clinical gold standard technique for cardiac output (CO) monitoring involves thermodilution via a pulmonary artery catheter.
- This and other less invasive techniques suffer from several disadvantages.
- The authors have developed a capnodynamic method of non-invasive estimation of CO.
- They now compare the performance of their technique with that of ultrasonic and thermodilution techniques in 10 pigs.

Background. It is important to be able to accurately monitor cardiac output (CO) during high-risk surgery and in critically ill patients. The invasiveness of the pulmonary artery catheter (PAC) limits its use, and therefore, new minimally invasive methods for CO monitoring are needed. A potential method is estimation of CO from endogenous carbon dioxide measurements, using a differentiated Fick's principle to determine effective pulmonary blood flow (EPBF). In this study, we aimed to validate a novel capnodynamic method (CO_{EPBF}) in a wide range of clinically relevant haemodynamic conditions.

Methods. CO_{EPBF} was studied in 10 pigs during changes in preload, afterload, CO increase, and bleeding. An ultrasonic flow probe around the pulmonary artery was used as reference method of CO determination. CO was also measured using a PAC thermodilution technique (CO_{PAC}). CO and other haemodynamic data were recorded before and during each intervention. Accuracy and precision and also the ability to track changes in CO were determined using Bland–Altman, four-quadrant plot and polar plot analysis.

Results. CO_{EPBF} and CO_{PAC} showed equally good agreement, with a tendency to overestimate CO (bias 0.2 and 0.3 litre min^{-1}, respectively). The overall percentage error was 47% for CO_{EPBF} and 49% for CO_{PAC}. The concordance for tracking CO changes was 97 and 95% for CO_{EPBF} and CO_{PAC}, respectively, with an exclusion zone of 15% and radial limits of $\pm 30^{\circ}$.

Conclusions. CO_{EPBF} showed reliable trending abilities, equivalent to CO_{PAC}. CO_{EPBF} and CO_{PAC} also showed low bias but high percentage errors. Further studies in animal models of lung injury and in high-risk surgery patients are warranted.

Keywords: carbon dioxide, measurement; heart, cardiac output; measurement techniques, carbon dioxide; measurement techniques, cardiac output; measurement techniques, thermodilution

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Haemodynamic optimization has been shown to improve perioperative outcomes in high-risk surgical patients.[1 2] In this setting, it is important to accurately monitor cardiac output (CO).[3] The pulmonary artery catheter (PAC)-based thermodilution technique has been the golden standard, but because of its invasiveness and associated complications, its use has declined.[4 5] Less invasive methods, such as the oesophageal Doppler and arterial wave form analysis, have gained increased interest, but are user-dependent or sensitive to changes in vasomotor tone.[6] CO can also be determined from changes in expired carbon dioxide (CO_2) in ventilated patients.[7] A method based on CO_2 rebreathing has been shown to accurately measure and track CO changes; however, this method uses external devices and is only semicontinuous.[8] We have developed a new continuous capnodynamic method by inducing an alternating breathing pattern, causing variations in end-tidal CO_2 (E'_{CO_2}). By using a differentiated Fick's principle, the effective pulmonary blood flow (EPBF, i.e. the blood flow participating in gas exchange) could be derived. EPBF is then used as a surrogate for CO (CO_{EPBF}).[9]

The study aims were to validate CO_{EPBF} in significant and clinically relevant haemodynamic conditions. Reference measurements of CO were made using an ultrasonic flow probe placed around the pulmonary trunk (CO_{TS}).[10] CO was also measured using the clinical gold standard method PAC thermodilution (CO_{PAC}).[5 11] We evaluated both accuracy and precision of absolute values, and also trending ability using four-quadrant and polar plot methodology.[12 13]

Methods

The Animal Research Ethics Committee of Uppsala University approved the study which was performed at the Hedenstierna Laboratory in Uppsala.

Anaesthesia and surgical preparation

Ten pigs, mean weight 28 kg and range 24–29 kg, were sedated with 0.04 mg kg^{-1} atropine (NM Pharma AB, Sweden), 6 mg kg^{-1} tiletamine-zolazepam (Zoletil, Vibrac Laboratories, France), and 2.2 mg kg^{-1} xylazine chloride (Rompun, Bayer AG, Germany) administered intramuscularly. Infusion of 5 μg kg^{-1} fentanyl (Fentanyl B. Braun, Germany), ketamine 30 mg kg^{-1} h^{-1}, midazolam 0.1 mg kg^{-1} h^{-1} and fentanyl 4 μg kg^{-1} h^{-1} was used for maintenance of anaesthesia and rocuronium 2 mg kg^{-1} h^{-1} for muscle relaxation. Ringer's acetate 10 ml kg^{-1} h^{-1} was administered throughout the experiments. After tracheal intubation normoventilation was achieved in a volume-controlled mode (Servo I, Maquet, Solna, Sweden): tidal volume 10 ml kg^{-1}, $F_{I_{O_2}}$ 0.4 and positive end expiratory pressure (PEEP) 5 cm H_2O. A balloon-tipped 7.5 Fr PAC was inserted via the right jugular vein into the pulmonary artery. CO was determined by the mean of three 5 ml bolus injections of ice cold saline (CO_{PAC}). The jugular vein and femoral artery were cannulated for administration of vasoactive drugs and arterial pressure recordings. A 13.5 Fr catheter was placed in an artery for controlled bleeding. An 8 F Fogarty occlusion catheter was inserted into the femoral vein for later vena caval occlusion. A urinary catheter was introduced into the urinary bladder. By a left side thoracotomy a 16-mm ultrasonic flow probe (T 401; Transonic System, Inc., Ithaca, NY, USA) was placed around the pulmonary trunk for continuous measurement of CO (CO_{TS}). The chest was closed and the pigs positioned in a semi-lateral position. The body temperature was maintained at 38–39°C. Pressure readings and signals from the ultrasonic flow probe were sampled into a data acquisition system (version 3.2.7, Acknowledge, BioPac Systems, Santa Barbara, CA, USA).

Measurement of EPBF by CO_{EPBF}

EPBF was calculated in accordance with the new capnodynamic method. The additional software in the ventilator creates recurrent periods of hyperventilation and hypoventilation by varying the inspiratory pause.[14] This breathing pattern (Supplementary Fig. S1) cyclically varies the E'_{CO_2} by ~0.5–1.0 kPa. Expired CO_2 was measured by the ordinary main stream CO_2-transducer and gas flow was analysed by the flow sensor in the ventilator. The CO_2 and flow data were exported to a computer and then analysed using a specially designed software application written in Matlab™ (Mathworks, Natick, MA, USA). The algorithm is based on the assumptions that EPBF, the effective lung volume (ELV), and the carbon dioxide content in venous blood ($CvCO_2$) are constant during the 10 most recent breaths included in the ongoing analysis. By measuring and calculating the dynamic transient changes in E'_{CO_2} and elimination (VCO_2) between each breath, it is possible to use this capnodynamic method without attaining steady-state conditions.[7 9]

The equation below describes a mole balance of CO_2 in the lung and contains three unknown variables: ELV, the lung volume containing CO_2; EPBF, effective pulmonary blood flow participating in gas exchange; and C_vCO_2. The left side reflects the difference in CO_2 content in the lung between two breaths and the first term on the right side describes the circulatory supply of CO_2 in the alveolar compartment between two breaths. The CO_2 content in the lung capillary blood, C_cCO_2, is calculated from the alveolar CO_2 fraction and the dissociation curve described by Capek and Roy[15] in 1988. The second term is the amount of CO_2 eliminated from the lungs by the *n*th tidal volume.

$$ELV \cdot (F_ACO_2^n - F_ACO_2^{n-1}) = EPBF \cdot \Delta t^n \cdot (C_vCO_2 - C_cCO_2^n) - VTCO_2^n$$

ELV, effective lung volume (litre) containing CO_2 at the end of expiration; EPBF, effective pulmonary blood flow (litre min^{-1}); *n*, current breath; $n-1$, previous breath; F_ACO_2, alveolar CO_2 fraction; C_vCO_2, venous carbon dioxide content ($litre_{gas}/litre_{blood}$); $C_cCO_2^n$, lung capillary CO_2 content (calculated from F_ACO_2); $VTCO_2^n$, volume (litre) of CO_2 eliminated by the current, *n*th, breath; Δt^n, current breath cycle time (min).

The test cycle consists of 10 breaths. Each breath creates a new equation. Thus, 10 breaths create 10 equations with 3 unknown variables. By optimizing the fit between the lung model and measured data, the equation system can be solved. Thus, it is possible to determine EPBF, which is the blood flow through the lungs participating in gas exchange.

Experimental protocol

After 30 min of stabilization, baseline measurements were recorded. Then, the haemodynamics were altered by: (i) caval occlusion reducing CO_{TS} by ~50%. (ii) Infusion of phenylephrine (0.11–0.21 μg kg^{-1} min^{-1}) increasing mean arterial pressure (MAP) to ~150% of baseline. (iii) Infusion of nitroprusside (1.4–2.1 μg kg^{-1} min^{-1}) decreasing MAP to 60% of baseline. (iv) Infusion of dobutamine (60–100 μg kg^{-1} min^{-1}) increasing CO_{TS} to ~200% of baseline. (v) A volume challenge of 500 ml colloid (Hesra, Baxter, Chicago, IL, USA). (vi) Reduction of MAP to 35 mm Hg by controlled bleeding. Each haemodynamic intervention was followed by a stabilization period. One baseline reading between every haemodynamic event and three readings during every haemodynamic manipulation were obtained during the experiment. All paired CO data were recorded under haemodynamic steady-state conditions as judged by the ultrasonic flow probe. After the experiment, the animals were killed.

Statistics

The distributions of the differences between CO data obtained from the three methods were tested for normality using the Kolmogorov–Smirnov test. Data are presented as mean (SD). Precision [defined as twice the coefficient of variation, CV (SD/mean)][16] for each monitor device was calculated from the initial three consecutive baseline measurements during haemodynamic steady state. The inherent PAC precision was calculated as twice the coefficient of error (CE) (CV/$\sqrt{3}$), of the three