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TRANSLATIONAL RESEARCH

Transpulmonary thermodilution cardiac output measurement is not affected by severe pulmonary oedema: a newborn animal study

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Editor's key points

- The effect of pulmonary oedema on reliability of transpulmonary thermodilution cardiac output measurement was investigated.
- Cardiac output was measured in newborn lambs in the presence of increased extravascular lung water.
- Measurement of cardiac output by transpulmonary thermodilution is not affected by severe pulmonary oedema in a newborn lamb model.

Background. The transpulmonary thermodilution (TPTD) technique is widely used in clinical practice for measuring cardiac output (CO). This study was designed to investigate the influence of various levels of pulmonary oedema on the reliability of CO measurements by the TPTD method.

Methods. In 11 newborn lambs pulmonary oedema was induced using a surfactant washout technique. Serial CO measurements using TPTD (CO_{TPTD}) were performed at various amounts of lung water. Simultaneously, CO was measured by an ultrasound flow probe around the main pulmonary artery (CO_{MPA}) and used as the standard reference. CO was divided by the body surface area to calculate cardiac index (CI). Data were analysed using correlational statistics and Bland–Altman analysis.

Results. One lamb died prematurely. A total of 56 measurements in 10 lambs were analysed with a median CI_{MPA} of 2.95 (IQR 1.04) litre min^{-1} m^{-2}. Mean percentage increase in extravascular lung water (EVLW) between the start and the end of the study was 126.4% (SD 40.4). Comparison of the two CO methods showed a mean bias CI of −0.16 litre min^{-1} m^{-2} (limits of agreement ±0.73 litre min^{-1} m^{-2}) and a percentage error of 23.8%. Intraclass correlation coefficients were 0.91 (95% CI 0.81–0.95) for absolute agreement and 0.92 (95% CI 0.87–0.95) for consistency. Acceptable agreement was confirmed by a tolerability-agreement ratio of 0.39. The within-subject correlation between the amount of EVLWI and the bias between the two methods was not significant (−0.02; P=0.91).

Conclusions. CO measurements by the transpulmonary thermodilution technique over a wide range of CI values are not affected by the presence of high EVLWI. The slight underestimation of the CO is independent of the amount of pulmonary oedema.

Keywords: cardiac output; children; haemodynamic; monitoring; pulmonary oedema; thermodilution

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Cardiac output (CO) is measured reliably in newborn animals and children using the transpulmonary thermodilution (TPTD) technique.[1 2] Furthermore, this technology can be used at the bedside to measure cardiac volumes and to quantify the amount of pulmonary oedema, expressed as extravascular lung water (EVLW).[3–5] However, both in adults and in children, the TPTD method slightly overestimates the true CO value.[6–8] Loss of indicator because of the longer distance of the thermal indicator traversing the heart, lungs, and great vessels is suggested as an explanation of the difference in the CO when comparing pulmonary artery with (transpulmonary) femoral artery thermodilution. In addition, there may be other factors that negatively influence the reliability of the TPTD technique. These include indicator loss because of low blood flow or the presence of a left-to-right shunt.[9–11] However, the effect of pulmonary oedema on the reliability of CO measurements is unclear. Theoretically, an increased loss of indicator in the presence of a high amount of pulmonary oedema may occur because a thermal indicator diffuses much more easily through water than through air. Consequently, more heat will be lost into the surrounding tissues. Only a few studies

in adults analysed the dependency of CO measurements on the amount of lung oedema.[9 12 13] However, as infants and young children have a much higher EVLW indexed to body weight (EVLWI) than adults, the impact of these increased amounts of lung oedema may be more pronounced.[14–16] Paediatric studies are, to our knowledge, not available. Therefore, this newborn animal experiment was designed to investigate the influence of various levels of pulmonary oedema on the reliability of CO measurements.

Methods

General

This experiment was performed in accordance with Dutch legislation concerning guidelines for the care and use of laboratory animals and was approved by the local ethics committee on animal research of the Radboud University Nijmegen Medical Centre (RUNMC Licence number RU-DEC 2010-034; CDL-project number 33078). Eleven lambs were studied under general anaesthesia. Premedication consisted of the i.m. administration of midazolam (0.2 mg kg^{-1}), ketamine (10 mg kg^{-1}), and i.v. administration of propofol (2 mg kg^{-1}). General anaesthesia was maintained using inhalation of isoflurane (1–1.5 vol%) and the continuous i.v. administration of sufentanyl (20 μg kg^{-1} h^{-1}), midazolam (0.2 mg kg^{-1} h^{-1}), ketamine (10 mg kg^{-1} h^{-1}), and pancuronium (0.02 mg kg^{-1} h^{-1}) after a loading dose of 0.05 mg kg^{-1}. The depth of anaesthesia was repeatedly assessed by painful stimuli and clinical parameters such as heart rate, spontaneous ventilation, and elevated arterial pressure. The depth of anaesthesia was adjusted when necessary. During the experiment, continuous i.v. dextrose 10% 2 ml kg^{-1} h^{-1} was administered. The lambs were intubated orotracheally using a 4–6 mm (inner diameter) cuffed tracheal tube (Kruse, Marslev, Denmark). The lungs were mechanically ventilated in a pressure-controlled mode using tidal volumes of ~10 ml kg^{-1} (Datex-Ohmeda anaesthesia machine) and an inspiratory-to-expiratory ratio of 1:2. Normocapnia, guided by capnography with the CO_2SMO Plus Respiratory Profile Monitor (Model 8100, Respironics, Pittsburgh, USA), was achieved by adjusting the minute volume ventilation to maintain an end-tidal CO_2 tension between 4.0 and 5.5 kPa. Impaired oxygenation was treated by adjusting the positive end expiratory pressure (PEEP) and the fraction of inspired oxygen (F_{IO_2}) to maintain the oxygen saturation >95%. A servo-controlled heating mattress and an external heating lamp were used to maintain core temperature between 38 and 40°C. At the end of the experiment, the animals were killed with an overdose of pentobarbital (150 mg kg^{-1} i.v.).

Instrumentation

Immediately after induction of anaesthesia, a thermal-dye-dilution probe (PV2023, Pulsion, Germany) equipped with a thermistor for the detection of changes in blood temperature and a fibreoptic probe to detect plasma levels of green dye was inserted in the femoral artery. In the contralateral femoral vein, a central venous catheter (5Fr, 2 lumen, 13 cm, Arrow, Germany) was inserted for the administration of fluid and drugs. At the same site a femoral artery catheter (20 Ga, single lumen, 12 cm, Arrow, Germany) was introduced for arterial pressure monitoring and blood sampling. All intravascular catheters were inserted by a surgical cut-down technique. A left-sided thoracotomy was performed and the remains of a native ductus arteriosus were ligated. An ultrasound transit time perivascular flow probe (10 or 12 mm) (PAX series, Transonic Systems, Ithaca, NY) was placed around the main pulmonary artery to measure reference CO (CO_{MPA}). The flow probe signal was checked for zero flow values directly postmortem. Ultrasound transit time flow probes use a two-way ultrasound technique. By calculating the difference between transit times upstream and downstream, the blood flow (Q_{MPA}) is measured. Care was taken to avoid air within the flow probe by applying sufficient quantities of acoustic gel. After the placement of the flow probe, the thorax was closed. The animals were positioned either supine or lying on the right side throughout the experiment.

Pulmonary oedema was induced using a surfactant washout lavage model.[17] In short, lambs underwent repetitive saline lavages (10–35 ml kg^{-1} $lavage^{-1}$ 37°C NaCl 0.9%) of the lung in order to induce surfactant depletion and provoke acute lung injury (ALI). Before the lavages the lambs were pre-oxygenated using an F_{IO_2} of 1.0. After the lavages, the animals were stabilized for 30 min before measurements of ventilatory and haemodynamic parameters and blood gases were obtained. Between lavages the PEEP and minute volume ventilation were increased to maintain oxygen saturation and end-tidal CO_2 within the normal range.

Transpulmonary thermodilution

Transpulmonary thermodilution CO (CO_{TPTD}) was measured by rapid injection of 5 ml ice-cold saline (NaCl 0.9%) into the femoral venous catheter. Changes in temperature were detected by the thermistor connected to a COLD monitor (Pulsion, Munich, Germany). The theoretical background of measuring CO by analysis of the dilution curves and calculation using the Steward Hamilton equation is described elsewhere.[18] Besides CO, blood volumes and extravascular lung water can be calculated from the measurement of the mean transit time (Mts) and downslope time (Dst) of the dilution curves.[5 19] Before a series of thermodilution measurements, the central venous catheter was flushed with 1–2 ml of ice-cold saline. Each thermodilution curve was visually inspected for artifacts or signs of an inadequate measurement. We used the mean value of three bolus injections of 5 ml of ice-cold (<10°C) saline.

Other measurements

We measured invasive arterial pressure and central venous pressure, continuous electrocardiogram, heart rate, arterial oxygen saturation, end-tidal CO_2, respiratory frequency, tidal volume, airway pressures, and body core temperature. During the thermodilution measurements, all other

haemodynamic variables, including CO_{MPA}, were recorded simultaneously with a 200-Hz sampling rate using a computer system with special biomedical registration software (Poly, Inspektor Research Systems, Amsterdam, The Netherlands). The exact time span of the dilution measurement was marked in the registration system. The reference CO was calculated using the mean value of CO_{MPA} measurements over the same three periods as the mean value of three consecutive TPTD measurements.

Protocol

After instrumentation, baseline measurements of CO (TPTD and CO_{MPA}) respiratory and haemodynamic parameters and blood gases were obtained. Repetitive saline lavage procedures were performed in either one or two subsequent sessions of 10–30 ml kg^{-1}, depending on the recovery of the lambs during the procedure. After each lavage procedure, a pause of 30 min was instituted for cardiorespiratory stabilization, followed by repeated measurements of the above-mentioned parameters. A blood transfusion was administered if the haemoglobin (Hb) was <3.5 mmol $litre^{-1}$. Dobutamine or epinephrine was administered when indicated.

Statistical analysis

The CO values were indexed (CI) to body surface area (BSA). The BSA of the lambs was calculated using the following formula: $BSA = weight^{2/3} \times 0.121$.[20] The statistical variability in the CO during the measurement periods is expressed as the coefficient of variance (CV). This is calculated by dividing the standard deviation (SD) of the mean by the mean of the CO_{MPA} results during each separate measurement period. The results are expressed as percentages ($=100\% \times$ SD/mean). We defined a CV of $\leq 5\%$ as acceptable for reliable CO_{TPTD} measurements. Intraclass correlation coefficients, using the two-way mixed model, were calculated for consistency and absolute agreement between the CO measurement methods. In addition, data were analysed using the method described by Bland and Altman.[21] The difference between the two methods (bias) was calculated by subtracting the value of CI_{MPA} from CI_{TPTD}. The bias was plotted against the mean CI [$(CI_{TPTD}+CI_{MPA})/2$]. The limits of agreement (LOA) were calculated by multiplying the SD of the bias by 1.96. The percentage error was calculated using the following formula: [(1.96 $\times$ SD of the bias)/mean CI_{MPA}] $\times$ 100%, using mean CI_{MPA} as the reference.[22] As the number of measurements per animal varied, we corrected for the repeated measurements.[23] The strength of agreement was also calculated by the agreement-tolerability-interval ratio, with acceptable agreement defined as a ratio <1.[24] The tolerability interval is estimated from the 95% range of the observed CI data. The agreement interval is calculated from the range of the LOA. Differences between the bias of low/high CI ($</\geq 3.0$ litre min^{-1} m^{-2}), lowest/highest quartile of EVLWI groups and low/high ($</\geq 8$ cm H_2O) PEEP were analysed by the Mann–Whitney test. Differences between the LOA were analysed by comparison of standard deviations test (*F*-test). Differences between the start and final results of EVLWI, $Pa_{O_2}/F_{I_{O_2}}$ ratio, and PEEP were analysed by the Wilcoxon signed-rank test. The percentage bias of the CO_{TPTD} compared with the reference CO is calculated by (bias/mean CO_{MPA}) $\times$ 100%. Within-subject correlation statistics were used in the comparison of PEEP, EWLWI, and $Pa_{O_2}/F_{I_{O_2}}$ ratio with the bias by analysis of covariance for repeated-measurements.[25] Calculations and data management were performed using Excel for Windows. Statistical calculations were performed with MedCalc (Med-Calc Software, Mariakerke, Belgium).

Results

One lamb died soon after the first lavage, before reliable CO measurements could be performed. Ten lambs with an age between 1 and 3 weeks and with a median weight of 8.8 kg [interquartile range (IQR) 2.8] were studied. The characteristics of the lambs are shown in Table 1. The pulmonary lavages and high ventilator pressures induced cardiorespiratory instability in all animals. We excluded four CO measurements, each from a different lamb, because of CV $>5\%$.

A total of 56 measurements were analysed with a median CO_{MPA} of 1.63 (IQR 0.71) litre min^{-1} and CI_{MPA} of 2.95 (IQR 1.04) litre min^{-1} m^{-2}. Intraclass correlation coefficients were 0.91 (95% CI 0.81–0.95) for absolute agreement and 0.92 (95% CI 0.87–0.95) for consistency. Differences between the two CO methods are shown in the Bland–Altman plot (Fig. 1). The mean bias of the CI was -0.16 litre min^{-1} m^{-2} (LOA ± 0.73 litre min^{-1} m^{-2}). The percentage error was 23.8%. Correction for unequal repeated measurements per lamb revealed LOA in the same range (± 0.75 litre min^{-1} m^{-2}) and a percentage error of 24.4%. The tolerability interval was 1.7–5.4 litre min^{-1} m^{-2} and the agreement-tolerability-interval ratio was 0.39.

Separate analysis of the lower and higher CI measurements showed comparable percentage errors 22% [$CI<3.0$ litre min^{-1} m^{-2}; $n=28$; mean bias -0.06 (LOA 0.51) litre min^{-1} m^{-2}] and 23% [$CI\geq 3.0$ litre min^{-1} m^{-2}; $n=28$; mean bias -0.27 (LOA 0.85) litre min^{-1} m^{-2}]. We subsequently determined the bias and level of agreement of the CI measurements for different amounts of EVLWI and showed a mean bias of -0.28 (LOA 0.57) litre min^{-1} m^{-2} and percentage error of 16.1% in the lowest quartile of EVLWI vs -0.27 (LOA 0.33) litre min^{-1} m^{-2} and percentage error of 21.8% in the highest quartile of EVLWI. Differences in the bias and LOA were significant in the low/high CI ($P=0.014$ and $P=0.008$) groups, but not in the low/high EVLWI ($P=0.75$ and $P=0.84$) groups.

The initial median EVLWI was 16.0 ml kg^{-1} (IQR 3.8), which increased after multiple lung lavage procedures to a final median EVLWI of 34.3 ml kg^{-1} (IQR 9.1). The mean percentage increase of EVLWI between the start and the end of the study was 126.4% (SD 40.4). The increment of EVLWI worsened oxygenation. The median $Pa_{O_2}/F_{I_{O_2}}$ ratio decreased from 403 (IQR 173) to 73 (IQR 54). The median PEEP had to be increased during the experiment from 5 cm H_2O (IQR

Table 1 Characteristics of the lambs

Lamb	Weight (kg)	Age (days)	Total lavages (ml kg^{-1})	CO measurements (*n*)	Mean CO_{MPA} (± SD) (litre min^{-1})	Mean CI_{MPA} (± SD) (litre min^{-1} m^{-2})
1	8.1	21	125	7	1.89 (0.13)	3.86 (0.27)
2	7.4	21	303	5	1.06 (0.29)	2.31 (0.63)
3	4.1	7	293	6	1.00 (0.09)	3.24 (0.29)
4	7.4	14	68	2	2.48 (0.81)	5.39 (1.77)
5	10.2	17	294	6	2.06 (0.49)	3.62 (0.86)
6	9.4	18	191	4	2.05 (0.14)	3.81 (0.26)
7	Died				Excluded	Excluded
8	8	15	420	8	1.01 (0.26)	2.08 (0.54)
9	9.9	16	242	3	1.61 (0.25)	2.89 (0.45)
10	11.5	19	184	7	1.82 (0.25)	2.95 (0.40)
11	12.3	22	98	8	1.61 (0.23)	2.50 (0.36)

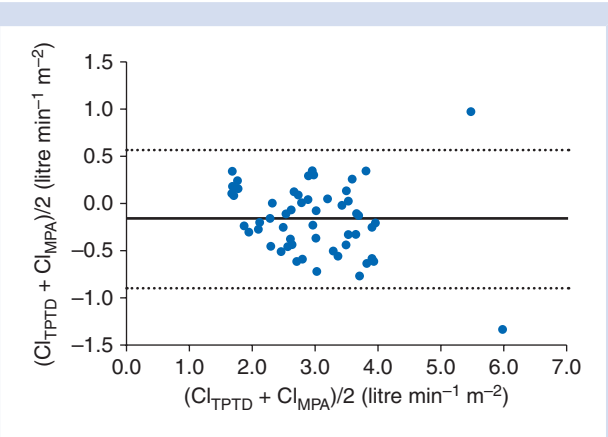

Fig 1 Bland–Altman plot comparing the cardiac index values by the TPTD method (CI_{TPTD}) and the peri-vascular flow probe around the main pulmonary artery (CI_{MPA}).

0) up to 16 cm H_2O (IQR 10). The differences in these parameters between the start and final measurements were analysed by the Wilcoxon signed-rank test (all P=0.02) and are shown in Figure 2. The overall CO_{TPTD} measurements underestimated slightly the CO with 6%, increasing up to 7% bias in the highest (>30 ml kg^{-1}) EVLWI values.

When we compared the bias and LOA between the two CO measurements during low PEEP (n=22) and high PEEP (n=32), these differences were not statistically significant (P=0.98 and P=0.11). The within-subject correlations between the amount of EVLWI, Pa_{O_2}/FI_{O_2} ratio, or the PEEP and the bias between the two CO measurement methods were r=−0.02 (P=0.91), r=0.09 (P=0.56) and r=0.10 (P=0.5), respectively, and are illustrated in Figure 3.

Discussion

In this newborn animal model, the TPTD method accurately measured CO in the presence of severe pulmonary oedema (increase more than 125%). The bias and LOA were small and the percentage error around 24% is within the range of acceptance.[22] The high intraclass correlation coefficient and the low (<0.5) agreement-tolerability-interval ratio, taking the reference range of the observed data of the study as tolerability interval into account, support the acceptable strength of agreement and imply the EVLWI to be irrelevant in this study.[24] The initial EVLWI values in our paediatric animal model were higher than normal indexed EVLW values known from adult studies, but in agreement with the high EVLWI found in young children.[14–16 26] Our results show no important dependency of the bias between the two CO methods and the amount of EVLW, but rather a scatter of differences that need to be considered.

It has been estimated that with the TPTD method, up to 9% of the thermal indicator may be lost during passage through the pulmonary circulation.[27] In critically ill paediatric patients without pulmonary oedema, TPTD overestimates the CO up to 4.4% compared with pulmonary artery thermodilution.[6] This is in agreement with adult studies.[6–10 28] Our results did not show overestimation of the CO_{TPTD}. An explanation for this discrepancy could be that, in contrast to others, we used an ultrasound flow probe as reference method, which is not influenced by other factors. Most human studies use pulmonary artery thermodilution as the reference method, which is influenced by the traversing distance of the indicator and the transient effect of ice water on the heart rate.[29 30]

Only a few adult studies focus on the influence of pulmonary oedema on the reliability of CO measurements using the TPTD technique. A retrospective study in adult surgical intensive care patients showed no dependency of the bias between TPTD and pulmonary artery thermodilution CO measurements on the amount of pulmonary oedema.[12] In this study, however, the amount of EVLWI was relatively low (mean 9.1 ml kg^{-1}) compared with the much higher EVLWI values in children. Another adult study in ARDS patients with a high mean EVLWI of 20.2 ml kg^{-1} showed similar results.[13] This may be explained by re-entry of the lost cold thermal indicator into the flowing blood. An older

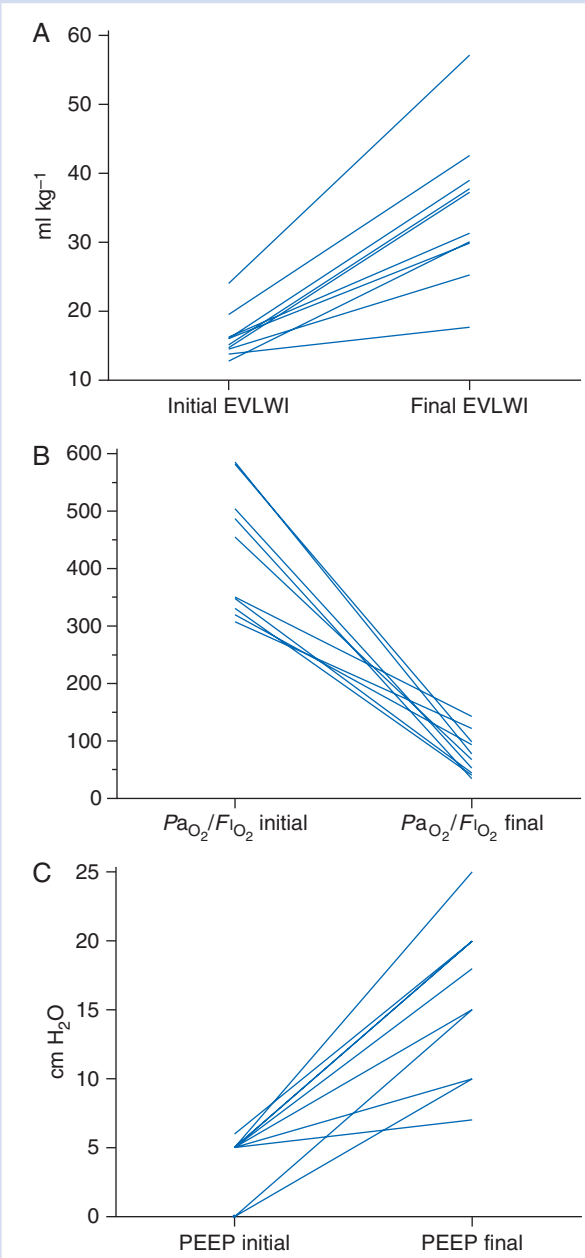

Fig 2 Wilcoxon signed-rank test plot comparing the change in indexed extravascular lung water (EVLWI; ml kg^{-1}) (A), $Pa_{O_2}/F_{I_{O_2}}$ ratio (B) and PEEP (cm H_2O) (C) from the start to the end of the experiment for each lamb separately.

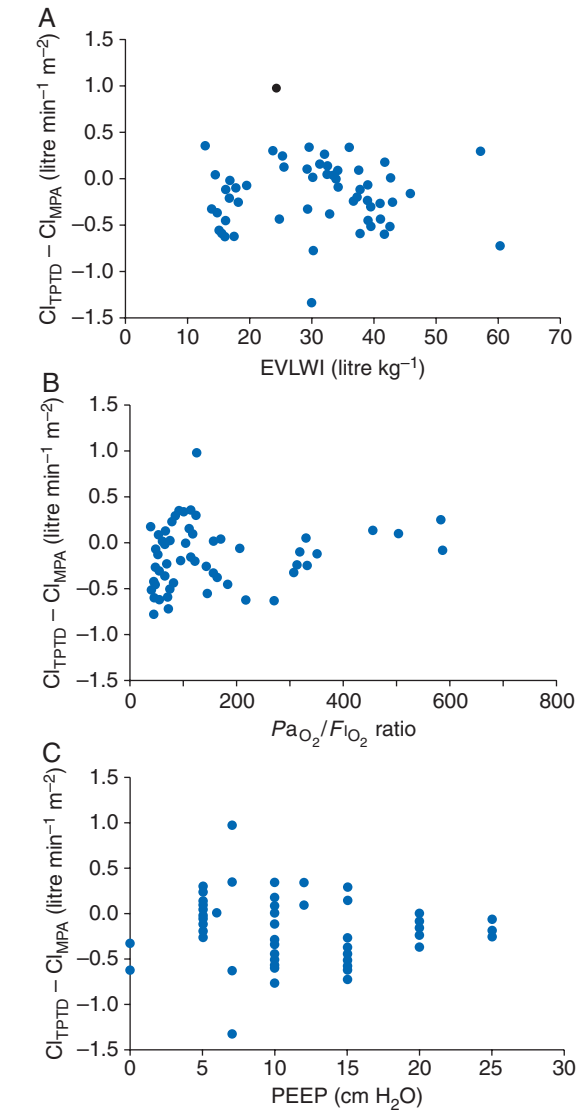

Fig 3 Scatter plots of the bias of CI measurements by the TPTD method (CI_{TPTD}) and the peri-vascular flow probe around the main pulmonary artery (CI_{MPA}) on the *y*-axis and EVLWI (A) (within-subject $r=-0.02$), $Pa_{O_2}/F_{I_{O_2}}$ ratio (B) (within-subject $r=0.09$) and PEEP (C) (within-subject $r=0.10$) on the *x*-axis.

study found a decrease in thermal loss as EVLW accumulates with a negative correlation between the bias and the EVLW.[9] The measured values of EVLWI in this adult study ranged from 1.9 up to 27.5 ml kg^{-1}. In our study, the EVLWI values ranged from 12.8 up to 60.2 ml kg^{-1}. In agreement with the latter study, our results also show a slight (6%) underestimation of the mean CO_{TPTD}.

These findings suggest that in the presence of severe pulmonary oedema, other factors compensate for the possible loss of the thermal indicator. Factors governing the temperature exchange between blood and interstitial fluid are the velocity of diffusion of the cold indicator, the surface area for exchange, the volume of the interstitial fluid into which cold diffuses, and the flow of blood, which determines the time during which temperature exchange must occur.[31] So, as a result of perfusion alterations induced by pulmonary oedema, PEEP or both, the surface area for exchange is reduced compensating thermal indicator loss in oedematous lung tissue. However, our study could not demonstrate an effect of PEEP on the bias between CO measurements. Blood flow alteration is another factor influencing the loss of thermal indicator. High CO states may not allow sufficient time for equilibration

with the extra vascular fluids and therefore less thermal indicator may be lost.[9] On the other hand, low CO values result in more indicator loss at lower flow rates.[32 33] This influence of blood flow on bias is confirmed in our study comparing low with high CO values. However, the error margin of the measurements remains fractionally the same. The higher the CO, the wider the LOA and vice versa, resulting in comparable percentage errors at high and low CO values.

Limitations

Despite variable haemodynamic circumstances, we included only measurements during stable blood flow. We corrected for the unequal and repeated CO measurements per lamb. The animals were either lying supine or on their right side, which could influence the distribution of pulmonary oedema, atelectases, and ventilation–perfusion mismatch and may have influenced our measurements in the comparison between the animals. We had no clinical indication to assume intracardiac shunting. We used a common model to induce EVLW increment with well-described pathophysiological and morphological characteristics.[17 34 35] However, this surfactant depletion model does not share all features of ALI/ARDS in humans. Finally, the difference in normal values of EVLWI between children and adults may not be real but the result of a difference in age-related changes in the ratio of lung weight to body weight ratio.[36]

Conclusions

Haemodynamic monitoring plays a crucial role in the treatment of critically ill patients. In particular, patients with capillary leakage and ALI require tight fluid management avoiding the risk of overzealous fluid administration while maintaining sufficient intravascular volume status. The transpulmonary thermodilution technique provides reliable CO monitoring over a wide range of clinical conditions. Our study shows that CO measurements are not affected by severe pulmonary oedema in a newborn lamb model.

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Declaration of interest

None declared.

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References

1 Lemson J, de Boode WP, Hopman JC, Singh SK, van der Hoeven JG. Validation of transpulmonary thermodilution cardiac output measurement in a pediatric animal model. *Pediatr Crit Care Med* 2008; **9**: 313–9

2 Tibby S. Transpulmonary thermodilution: finally, a gold standard for pediatric cardiac output measurement. *Pediatr Crit Care Med* 2008; **9**: 341–2

3 Michard F, Schachtrupp A, Toens C. Factors influencing the estimation of extravascular lung water by transpulmonary thermodilution in critically ill patients. *Crit Care Med* 2005; **33**: 1243–7

4 Katzenelson R, Perel A, Berkenstadt H, *et al.* Accuracy of transpulmonary thermodilution versus gravimetric measurement of extravascular lung water. *Crit Care Med* 2004; **32**: 1550–4

5 Sakka SG, Ruhl CC, Pfeiffer UJ, *et al.* Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution. *Intensive Care Med* 2000; **26**: 180–7

6 McLuckie A, Murdoch IA, Marsh MJ, Anderson D. A comparison of pulmonary and femoral artery thermodilution cardiac indices in paediatric intensive care patients. *Acta Paediatr* 1996; **85**: 336–8

7 Holm C, Melcer B, Horbrand F, Henckel von Donnersmarck G, Muhlbauer W. Arterial thermodilution: an alternative to pulmonary artery catheter for cardiac output assessment in burn patients. *Burns* 2001; **27**: 161–6

8 Sakka SG, Reinhart K, Meier-Hellmann A. Comparison of pulmonary artery and arterial thermodilution cardiac output in critically ill patients. *Intensive Care Med* 1999; **25**: 843–6

9 Bock JC, Barker BC, Mackersie RC, Tranbaugh RF, Lewis FR. Cardiac-output measurement using femoral-artery thermodilution in patients. *J Crit Care* 1989; **4**: 106–11

10 Friesecke S, Heinrich A, Abel P, Felix SB. Comparison of pulmonary artery and aortic transpulmonary thermodilution for monitoring of cardiac output in patients with severe heart failure: validation of a novel method. *Crit Care Med* 2009; **37**: 119–23

11 Nusmeier A, de Boode WP, Hopman JC, Schoof PH, van der Hoeven JG, Lemson J. Cardiac output can be measured with the transpulmonary thermodilution method in a paediatric animal model with a left-to-right shunt. *Br J Anaesth* 2011; **107**: 336–43

12 Pohl T, Kozieras J, Sakka SG. Influence of extravascular lung water on transpulmonary thermodilution-derived cardiac output measurement. *Intensive Care Med* 2008; **34**: 533–7

13 Zollner C, Briegel J, Kilger E, Haller M. Retrospective analysis of transpulmonary and pulmonary arterial measurement of cardiac output in ARDS patients. *Anaesthesist* 1998; **47**: 912–7

14 Schiffmann H, Erdlenbruch B, Singer D, *et al.* Assessment of cardiac output, intravascular volume status, and extravascular lung water by transpulmonary indicator dilution in critically ill neonates and infants. *J Cardiothorac Vasc Anesth* 2002; **16**: 592–7

15 Lubrano R, Cecchetti C, Elli M, *et al.* Prognostic value of extravascular lung water index in critically ill children with acute respiratory failure. *Intensive Care Med* 2011; **37**: 124–31

16 Lemson J, Backx AP, van Oort AM, Bouw TP, van der Hoeven JG. Extravascular lung water measurement using transpulmonary thermodilution in children. *Pediatr Crit Care Med* 2009; **10**: 227–33

17 Wang HM, Bodenstein M, Markstaller K. Overview of the pathology of three widely used animal models of acute lung injury. *Eur Surg Res* 2008; **40**: 305–16

18 Reuter DA, Huang C, Edrich T, Shernan SK, Eltzschig HK. Cardiac output monitoring using indicator-dilution techniques: basics, limits, and perspectives. *Anesth Analg* 2010; **110**: 799–811

19 Proulx F, Lemson J, Choker G, Tibby SM. Hemodynamic monitoring by transpulmonary thermodilution and pulse contour analysis in critically ill children. *Pediatr Crit Care Med* 2011; **12**: 459–66

20 Stowe CM, Good AL. Estimation of cardiac output in calves and sheep by the dye and Fick oxygen techniques. *Am J Physiol* 1960; **198**: 987–90

21 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307–10

22 Critchley LA, Critchley JA. A meta-analysis of studies using bias and precision statistics to compare cardiac output measurement techniques. *J Clin Monit Comput* 1999; **15**: 85–91

23 Bland JM, Altman DG. Agreement between methods of measurement with multiple observations per individual. *J Biopharm Stat* 2007; **17**: 571–82

24 Columb M. Clinical measurement and assessing agreement. *Curr Anaesth Crit Care* 2008; **19**: 328–9

25 Bland JM, Altman DG. Calculating correlation coefficients with repeated observations: Part 1—correlation within subjects. *BMJ* 1995; **310**: 446

26 Lopez-Herce J, Bustinza A, Sancho L, *et al.* Cardiac output and blood volume parameters using femoral arterial thermodilution. *Pediatr Int* 2009; **51**: 59–65

27 Lewis FR, Elings VB, Hill SL, Christensen JM. The measurement of extravascular lung water by thermal-green dye indicator dilution. *Ann N Y Acad Sci* 1982; **384**: 394–410

28 Goedje O, Hoeke K, Lichtwarck-Aschoff M, Faltchauser A, Lamm P, Reichart B. Continuous cardiac output by femoral arterial thermodilution calibrated pulse contour analysis: comparison with pulmonary arterial thermodilution. *Crit Care Med* 1999; **27**: 2407–12

29 Harris AP, Miller CF, Beattie C, Rosenfeld GI, Rogers MC. The slowing of sinus rhythm during thermodilution cardiac output determination and the effect of altering injectate temperature. *Anesthesiology* 1985; **63**: 540–1

30 Faybik P, Hetz H, Baker A, Yankovskaya E, Krenn CG, Steltzer H. Iced versus room temperature injectate for assessment of cardiac output, intrathoracic blood volume, and extravascular lung water by single transpulmonary thermodilution. *J Crit Care* 2004; **19**: 103–7

31 Oppenheimer L, Elings VB, Lewis FR. Thermal-dye lung water measurements: effects of oedema and embolization. *J Surg Res* 1979; **26**: 504–12

32 van Grondelle A, Ditchey RV, Groves BM, Wagner WW Jr, Reeves JT. Thermodilution method overestimates low cardiac output in humans. *Am J Physiol* 1983; **245**: H690–2

33 Renner LE, Morton MJ, Sakuma GY. Indicator amount, temperature, and intrinsic cardiac output affect thermodilution cardiac output accuracy and reproducibility. *Crit Care Med* 1993; **21**: 586–97

34 Fuchs JR, Kaviani A, Watson K, Thompson J, Wilson JM, Fauza DO. Intratracheal pulmonary ventilation improves gas exchange during laparoscopy in a pediatric lung injury model. *J Pediatr Surg* 2005; **40**: 22–5

35 Manaligod JM, del-Stenzel EM, Meyers PA, Bing DR, Connett JE, Mammel MC. Variations in end-expiratory pressure during partial liquid ventilation: impact on gas exchange, lung compliance, and end-expiratory lung volume. *Chest* 2000; **117**: 184–90

36 Lemson J, Merkus P, van der Hoeven JG. Extravascular lung water index and global end-diastolic volume index should be corrected in children. *J Crit Care* 2011; **26**: 432.e7–12

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