British Journal of Anaesthesia **111** (2): 286–92 (2013)
Advance Access publication 18 February 2013 · doi:10.1093/bja/aet021

BJA

TRANSLATIONAL RESEARCH

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

A. Nusmeier[1]*, S. Vrancken[2], W. P. de Boode[2], J. G. van der Hoeven[1] and J. Lemson[1]

[1] Department of Intensive Care Medicine and [2] Department of Pediatrics, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

* Corresponding author. E-mail: a.nusmeier@ic.umcn.nl

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

Accepted for publication: 15 January 2013

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 ($F_{I_{O_2}}$) 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 $F_{I_{O_2}}$ 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