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Pulmonary blood volume measured by contrast enhanced ultrasound: a comparison with transpulmonary thermodilution

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Editor's key points

- This study investigates the agreement between measuring intrathoracic blood volume ($ITBV^{UCA}$) by Ultrasound contrast agent (UCA)-dilution using contrast enhanced ultrasound (CEUS) or transpulmonary thermodilution (TPTD) *in vitro* and *in vivo*.
- *In vitro*, $ITBV^{UCA}$ showed an excellent agreement over the whole range of true volumes and flows.
- In patients, a good correlation was found between the $ITBV^{UCA}$ and PBV by TPTD.
- A considerable bias was noted in the thermodilution derived volumes compared with literature.

Background. Blood volume quantification is essential for haemodynamic evaluation guiding fluid management in anaesthesia and intensive care practice. Ultrasound contrast agent (UCA)-dilution measured by contrast enhanced ultrasound (CEUS) can provide the UCA mean transit time (MTT) between the right and left heart, enabling the assessment of the intrathoracic blood volume ($ITBV^{UCA}$). The purpose of the present study was to investigate the agreement between UCA-dilution using CEUS and transpulmonary thermodilution (TPTD) *in vitro* and *in vivo*.

Methods. In an *in vitro* setup, with variable flows and volumes, we injected a double indicator, ice-cold saline with SonoVue®, and performed volume measurements using transesophageal echo and thermodilution by PiCCO®. In a pilot study, we assigned 17 patients undergoing elective cardiac surgery for pulmonary blood volume (PBV) measurement using TPTD by PiCCO® and ITBV by UCA-dilution. Correlation coefficients and Bland-Altman analysis were performed for all volume measurements.

Results. *In vitro*, 73 experimental MTT's were obtained using PiCCO® and UCA-dilution. The volumes by PiCCO® and UCA-dilution correlated with true volumes; r_s=0.96 (95% CI, 0.93–0.97; $P<0.0001$) and r_s=0.97 (95% CI, 0.95–0.98; $P<0.0001$), respectively. The bias of PBV by PiCCO® and $ITBV^{UCA}$ were −380 ml and −42 ml, respectively. In 16 patients, 86 measurements were performed. The correlation between PBV by PiCCO® and $ITBV^{UCA}$ was r_s=0.69 (95% CI 0.55–0.79; $P<0.0001$). Bland-Altman analysis revealed a bias of −323 ml.

Conclusions. ITBV assessment with CEUS seems a promising technique for blood volume measurement, which is minimally-invasive and bedside applicable.

Clinical trial registration. ISRCTN90330260

Keywords: blood volume determination; contrast echocardiography; indicator dilution techniques; thermodilution

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Blood volume quantification is an essential part of haemodynamic evaluation to guide fluid management in anaesthesia and intensive care practice. While cardiac filling pressures, such as central venous pressure and pulmonary artery occlusion pressure, are frequently used to estimate preload, volumetric preload parameters obtained with transpulmonary thermodilution (TPTD) proved to be superior to this end.[1–3] With TPTD, arterial thermodilution curves are obtained after injection of a bolus of cold saline in a central vein, providing intrathoracic blood volume (ITBV) and global end-diastolic volume (GEDV).[4] Both parameters significantly relate to changes in stroke volume and cardiac index in various clinical settings.[1–3 5–7] However, TPTD requires insertion of catheters and installation of a device, which is time consuming and not always feasible during anaesthesia.

Recently, contrast-enhanced ultrasound (CEUS) has been proposed as a minimally-invasive, alternative method for blood volume measurement. With CEUS, transpulmonary indicator dilution curves are obtained with a small amount of ultrasound contrast agent (UCA) injected in a peripheral vein. In a previous experimental study, we demonstrated that volume estimation with CEUS in *in vitro* conditions was accurate and showed excellent agreement with volume estimation by thermodilution.[8–11] Moreover, we demonstrated the clinical feasibility of pulmonary blood volume (PBV) measurements with CEUS in patients.[8 9] However, comparison of CEUS with TPTD is currently lacking. In this study, we therefore aimed to investigate the agreement between volumes obtained by UCA-dilution and TPTD in an *in vitro* setup as well as in a pilot study in patients.

Methods

In vitro setup

The agreement of volumes derived from TPTD and UCA-dilution was tested in an *in vitro* setup as previously described.[10] The setup consisted of a network of tubes - mimicking the pulmonary vessels - connected to a roller pump (Cobe Stoeckert multiflow bloodpump, Stoeckert Instruments, Munich, Germany) (Fig. 1). Degassed water was used as transport medium and the in- and out-flow tubes were submerged in a water-filled basin at 37°C. A transesophageal (TEE) probe X7-2t (Philips Healthcare, Andover, MA, USA) was also submerged in the water-filled basin to optimize the acoustic impedance while insonifying the tubes. In the outflow tube a 5 F thermistor-tipped catheter, PV2015 (Pulsion Medical Systems, Munich, Germany) was positioned at the point where the ultrasound beam intercepted the inflow and outflow tubes. With each measurement, a syringe with 20 ml of 4°C saline and 0.2 ml SonoVue® (Bracco SpA, Milan, Italy) was injected into the inflow tube through an injection point consisting of a single lumen central venous line (Blue flextip catheter, Arrow®, Reading, PA, USA) and an injectate temperature sensor PV4046 (Pulsion Medical Systems, Munich, Germany). This SonoVue® dose ensures a linear relationship between concentration and measured acoustic intensity, which is essential for application of the indicator dilution theory.[10]

The injectate temperature sensor and the PiCCO® catheter were connected via an interface cable to the PiCCO® plus monitor (Pulsion Medical Systems, Munich, Germany), which was connected to a computer. Data were accessible with PiCCO®-Win software (Pulsion Medical Systems, Munich, Germany). After a thermodilution measurement, the software provided time, cardiac output (CO), GEDV, $ITBV^{TH}$, extravascular lung water (EVLW), mean transit time (MTT), and down-slope time (DSt).

The volume of the network between the ultrasound interception points was varied to create different system-volumes, namely 890, 718, 530, and 356 ml. All tubes were isolated with polyethylene covers (Climaflex®, NMC, Eynatten, Belgium) preventing heat loss and the hydrodynamic circuit was open to avoid indicator recirculation. The flow generated by the roller pump was varied between 1 and 4 litres min^{-1} in increments of 0.5 litre min^{-1} and controlled by a flow sensor (Flow controller ARS 260, Biotech, Vilshofen, Germany) positioned at the end of the circuit.

The TEE probe made cross-sectional B-mode images of the inflow and outflow tubes (Fig. 2). The ultrasound scanner (iE33, Philips Healthcare, Andover, MA, USA) used harmonic imaging,

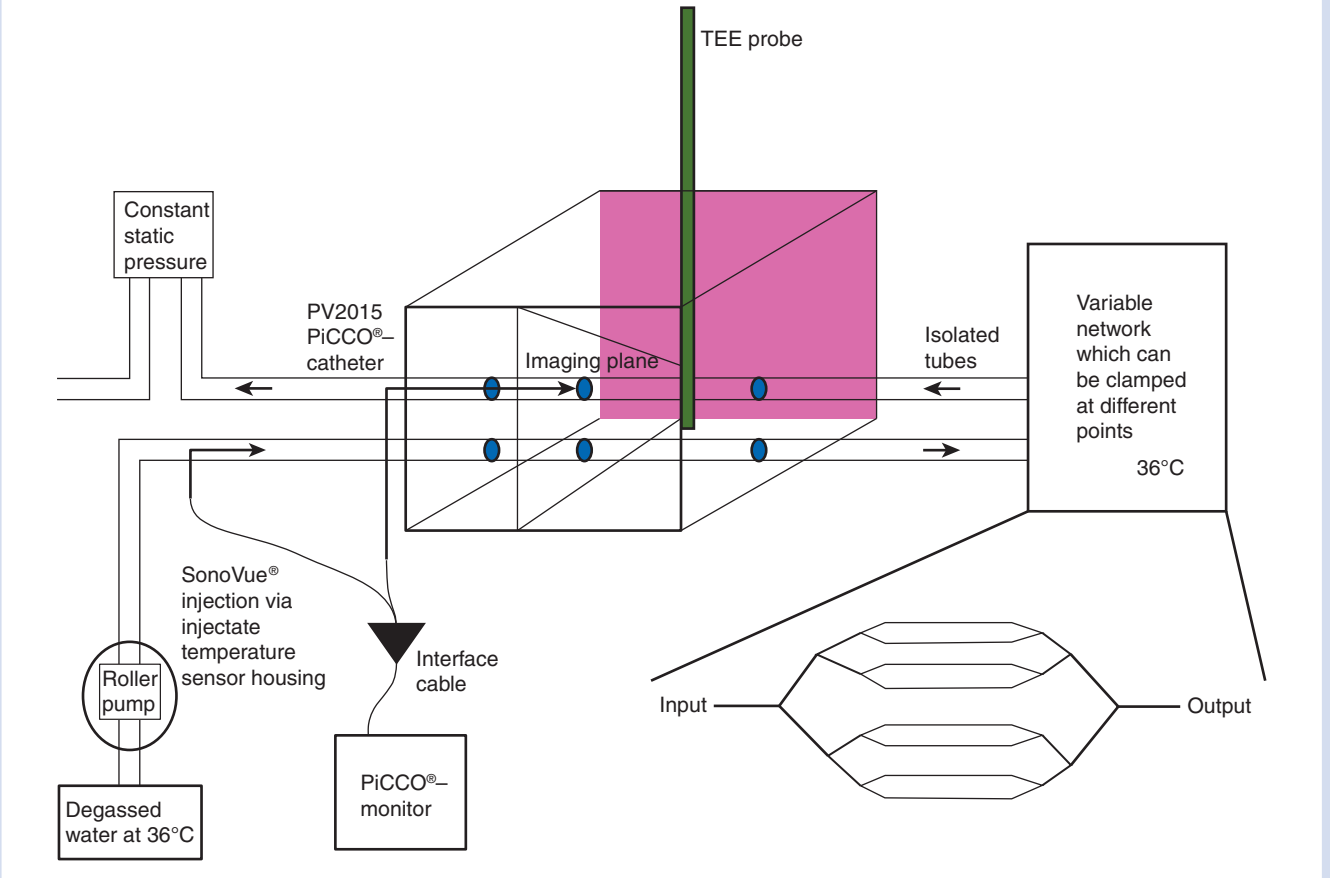

Fig 1 Schematic overview of the *in vitro* setup.