Comparison of Minimally and More Invasive Methods of Determining Mixed Venous Oxygen Saturation

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Objective: **To investigate the accuracy of a minimally invasive, 2-step, lookup method for determining mixed venous oxygen saturation compared with conventional techniques.**

Design: **Single-center, prospective, nonrandomized, pilot study.**

Setting: **Tertiary care hospital, university setting.**

Participants: **Thirteen elective cardiac and vascular surgery patients.**

Interventions: **All participants received intra-arterial and pulmonary artery catheters. Minimally invasive oxygen consumption and cardiac output were measured using a metabolic module and lithium-calibrated arterial waveform analysis (LiDCO; LiDCO, London), respectively. For the minimally invasive method, Step 1 involved these minimally invasive measurements, and arterial oxygen content was entered into the Fick equation to calculate mixed venous oxygen content. Step 2 used an oxyhemoglobin curve spreadsheet to look up mixed venous oxygen saturation from the calculated mixed venous oxygen content. The conventional "invasive" technique used pulmonary artery intermittent thermodilution cardiac output, direct sampling of mixed venous and arterial blood, and the "reverse-Fick" method of calculating oxygen consumption.**

Measurements and Main Results: **LiDCO overestimated thermodilution cardiac output by 26%. Pulmonary artery catheter-derived oxygen consumption underestimated metabolic module measurements by 27%. Mixed venous oxygen saturation differed between techniques; the calculated values underestimated the direct measurements by between 12% to 26.3%, this difference being statistically significant.**

Conclusion: **The magnitude of the differences between the minimally invasive and invasive techniques was too great for the former to act as a surrogate of the latter and could adversely affect clinical decision making.**

KEY WORDS: mixed venous oxygenation, oxygen consumption, cardiac output, pulmonary artery catheter, minimally invasive

MIXED VENOUS OXYGEN saturation monitoring is a valuable diagnostic and prognostic tool.[1–12] A decrease in mixed venous oxygen saturation and/or partial pressure from typical values of 75% and 5.3 kPa, respectively,[13] which is accompanied by an adequate oxygen consumption are early indicators of a mismatch between oxygen consumption and oxygen delivery.[1,11] Mixed venous saturation and partial pressure, therefore, are useful resuscitation endpoints in the critically ill patient.[1–12] Mixed venous oxygenation also may be important in determining arterial oxygenation in the presence of a shunt.[14]

Determination of mixed venous oxygen saturation currently necessitates pulmonary artery catheter placement with intermittent mixed venous blood sampling and/or continuous reflectance oximetry.[15] Despite pulmonary arterial catheterization being associated with very low complication rates in experienced hands,[16] it is an invasive technique with significant risks. A minimally invasive method of determining mixed venous oxygen saturation could expand the use of less invasive measurement techniques, with benefits for patient care. The authors proposed and prospectively tested the accuracy of a 2-step method of calculating mixed venous oxygen saturation without using a pulmonary artery catheter.

The hypothesis tested was that estimation of venous oxygenation from data obtained indirectly using minimally invasive measurement techniques could be used as a surrogate of values obtained from invasive mixed venous blood sampling. The primary outcome was mixed venous oxygen saturation determined using the 2 techniques.

METHODS

The authors designed and conducted a single-center, prospective, nonrandomized, pilot study that was approved by the University of Stellenbosch Human Research Ethics Committee (Project N10/03/076). Patients scheduled for elective cardiac (on- or off-pump coronary artery bypass grafting, valve replacement, or repair) and vascular surgery were eligible to be included, provided that the attending anesthesiologist was of the opinion that the patients' management would benefit from pulmonary artery catheter monitoring. Eligible patients gave prior written, informed consent.

Exclusion criteria included patients with contraindications for lithium administration (eg, first trimester of pregnancy, preexisting lithium therapy, weight less than 40 kg, and renal and/or liver failure) and the presence of physiologic states in which the LiDCO device (LiDCO, London, England) would not measure cardiac output accurately (eg, aortic valve regurgitation,[17] intra-aortic balloon counterpulsation, arrhythmias, and an obviously damped arterial pressure tracing). Additional exclusion criteria that would prompt intraoperative withdrawal of the patient from the study included issues that would thwart

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accurate metabolic module monitoring,[18] such as peak airway pressures exceeding 35 cmH_2O, an inspired oxygen fraction exceeding 0.7, or the use of nitrous oxide. Conditions potentially making thermodilution cardiac output determination unreliable (eg, severe tricuspid or pulmonary regurgitation, intracardiac shunts) also excluded patients from the study. Attending anesthesiologists inserted a right internal jugular, 4-lumen, thermodilution pulmonary artery catheter (Edwards Lifesciences, Irvine, CA) and a brachial 20-gauge, 32-mm long arterial catheter into all patients. The anesthetic technique was left to the attending anesthesiologist's discretion.

Details of Conventional, Invasive Data Collection

"Invasive" cardiac output was defined as the average of 3 pulmonary artery catheter thermodilution cardiac output (CO_{TD}) measurements, randomly spaced with respect to the respiratory cycle. The same cardiac output computer and same type of pulmonary artery catheter were used in every patient. Before obtaining CO_{TD} measurements, the authors confirmed the presence of a typical pulmonary artery pressure waveform and that intravenous fluid or blood or blood products were not being administered faster than 100 mL/hr. A manufacturer-applied constant for the specific pulmonary artery catheter, estimated injectate temperature, and injectate volume was entered into the cardiac output computer. Room-temperature 10 mL of "normal" saline was drawn into a 10-mL syringe and the syringe was placed into a closed 3-way stopcock on the "blue" central venous line of the 4-lumen pulmonary artery catheter.[19] Injectate temperature was measured using an inline sensor. A cardiac output module attached to a GE Datex Ohmeda S5 monitor (SOMA Technology, Inc., Bloomfield, CT) was used to compute cardiac output. After the "inject now" instruction was displayed, the 3-way stopcock was turned and manual administration of the indicator commenced. Attention was paid to injecting within 4 seconds using a steady, continuous motion.[19] The thermodilution curve was inspected and cardiac output calculations associated with irregular waveforms were rejected.

Mixed venous and arterial blood samples were analyzed without delay using a blood gas analyzer (GEM Premier 3500; Ilex, Milano, Italy) that was calibrated according to the manufacturer's instructions. To confirm that sampling was performed slowly enough and that pulmonary capillary blood had not been withdrawn, the authors accepted a particular sample pair only if the venous-arterial carbon dioxide partial pressure difference exceeded 0.5 kPa. For determination of oxygen content, 1 g of fully saturated hemoglobin was assumed to be able to transport 1.39 mL of oxygen (Table 1, Equation 3).

Oxygen consumption was calculated from the product of arteriovenous oxygen content difference and the mean CO_{TD} for that measurement cycle (see Table 1, Equations 2 and 4), the so-called "reverse-Fick" method.[20] The arterio-venous oxygen content difference was calculated from analysis of mixed venous and arterial blood samples.

Details of Less Invasive Data Collection

Minimally invasive cardiac output was determined using lithium-calibrated arterial waveform analysis (LiDCO). Calibration was performed with 0.3 mmol (2 mL) of lithium chloride solution, injected into the central venous line, and was repeated a maximum of 3 times until "good calibration" was registered by the LiDCO device.[21] This implied an arterial plasma lithium dilution curve with a peak between 0.2 and 0.8 mM. If more than 3 calibration attempts were required, the patient was withdrawn from the study. In no individual was the cumulative dose of lithium chloride solution allowed to exceed

Table 1. Selected Formulas Used in This Study

Formula	Used to Calculate
Equation 1 $CvO_2 = CaO_2 - [VO_2 / CO]$	Mixed venous oxygen content from minimally invasive cardiac output, calorimetric determination of oxygen consumption, and arterial blood sample
Equation 2 $VO_2 = CO \times [CaO_2 - CvO_2]$	Oxygen consumption using data obtainable via a pulmonary artery catheter and arterial sample
Equation 3 $CvO_2 = [1.39 \times Hb \times SvO_2 / 100] + [0.003 \times PaO_2]$	CvO_2 mixed enous oxygen content calculated using mixed venous blood sample
Equation 4 $CaO_2 = [1.39 \times Hb \times SaO_2 / 100] + [0.0031 \times PaO_2]$	PaO_2 partial pressure of oxygen content calculated using arterial blood sample
Equation 5 Oxygen saturation % $= PO_2{}^3 + [2.667 \times PO_2]$	Simplified oxyhemoglobin dissociation curve formula used in Excel spreadsheet to calculate saturation values from 0 to 100[65]
Equation 6 PvO_2 corrected $= [PvO_2$ actual$] * 1\hat{0}[0.024[37 - T] + 0.40$ $[pHv - 7.40] + 0.06[\log10[40] - \log10[PvCO_2]]$	Formula used to correct PvO_2 for temperature, pH, and $PvCO_2$[23]

Abbreviations: CaO_2 and CvO_2, arterial and mixed venous oxygen content in milliliters of oxygen per deciliter, respectively; VO_2, whole body consumption in mL/kg/min; CO, whole body cardiac output in L/min; Hb, hemoglobin concentration in g/dL; SvO_2, mixed venous oxygen saturation expressed as percentage; PaO_2, partial pressure of oxygen in arterial blood in kPa; SaO_2, arterial oxygen saturation expressed as a percentage; T, body temperature in Celsius; pHv, mixed venous pH; $PvCO_2$, mixed venous partial pressure of carbon dioxide in kPa.