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Blood volume measured by ultrasound and radioisotope dilution in critically ill subjects

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ARTICLE INFO

Article history:
Received 2 May 2016
Received in revised form
26 July 2016
Accepted 24 August 2016
Available online 31 August 2016

Keywords:
Blood volume
Ultrasound dilution
Radioisotope dilution
Critically ill

ABSTRACT

Background: Accurate bedside assessment of circulating blood volume (BV) continues to challenge clinicians in their attempt to implement goal-directed therapy in the critically ill subject. The aim of this investigation was to comparatively evaluate BV measurements obtained by ultrasound and radioisotope dilution methodologies in adult subjects admitted to a surgical intensive care unit.

Materials and methods: Fifty subjects with concurrent central venous catheters and peripheral arterial lines underwent measurement of BV using both ultrasound and radioisotope dilution (BV-RD) methods. The ultrasound dilution method was performed using a 30-mL injectate (BV-UD30) and a 60-mL injectate (BV-UD60) of isotonic saline.

Results: There were 24 paired data points for the BV-UD30 and 40 paired data points for the BV-UD60 measurements. Spearman's rank-order correlation demonstrated a positive relationship comparing both the BV-UD30 ($r = 0.46$, $P = 0.0249$) and the BV-UD60 ($r = 0.80$, $P < 0.0001$) to values obtained by radioisotope measurements. Bland–Altman analysis showed a mean bias of 1329 mL with limits of agreement (LOA) ± 2559 mL comparing BV-RD and BV-UD30, and a mean bias of 62 mL with LOA ±1353 mL for BV-RD and BV-UD60.

Conclusions: This preliminary investigation shows that the BV-UD60 had better agreement with BV-RD, compared with the BV-UD30, but its utility appears limited by a large LOA. As this technology continues to evolve, the ultrasound dilution approach may potentially become a feasible means to calculate BV in critically ill surgical subjects.

Introduction

The bedside assessment of circulating blood volume (BV) has been, and remains, one of the most problematic challenges that clinicians encounter in the management of critically ill subjects. Although it is indisputable that the maintenance of a euvolemic state is a meritorious goal for the critically ill, particularly in the era of goal-directed therapy, there exists no uniform consensus as to what constitutes the ideal surrogate parameter(s) that accurately, and quantitatively, predicts BV with a robust degree of certainty.[1-10] Against this backdrop, traditional means of invasive hemodynamic monitoring that were often used to assist in the separation of the complex interactions between surrogate estimates of BV, preload, and cardiac function, such as the pulmonary artery catheter (PAC), have been gradually losing favor with the implementation of

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http://dx.doi.org/10.1016/j.jss.2016.08.077

evidence-based guidelines and the rising veneration for patient safety.[11] Not at all surprisingly, to fill this chasm, there has been a technological resurgence of a number of innovative, minimally invasive modalities, all entrusted with the promise of providing direct measurements of BV to provide timely alternatives to assist in hemodynamic management.[8-10,12-14]

Within this framework, conventional methodology used to estimate an unknown volume has been historically anchored conceptually in the indicator dilution technique. First reported nearly a century ago, the use of different indicators, such as Evans Blue dye, indocyanine green and radioisotopic tracers, have been used to effectively determine BV.[14,15] The current reference method for BV analysis, as published by the International Committee for Standardization in Haematology (ICSH) in 1980, requires the simultaneous measurement of chromium-51 tagged red blood cells and radiolabeled serum albumin.[16] Of significance clinically, this well-accepted double-isotope technique is both a laborious and time-consuming process, rendering this approach unfeasible and impractical for routine use in the intensive care unit setting. Advancements in bioengineering have culminated in the development of a commercially available, US Food and Drug Administration-approved, semiautomated, single-isotope method that calculates BV (BVA-100 Analyzer, Daxor Corporation, New York, NY).[7-9,17] As described elsewhere, this apparatus has measurably diminished the toils associated with the double-isotope technique, and it is emerging as a viable means for point-of-care testing to determine BV in the critical care setting.[7-9,14] Notably, when the methodology was being developed, a mathematical model was constructed, and it was found that subjects tested validated this model, with measured BV correlating well with this model. There was no significant systematic divergence based on weight, height, or deviation from ideal weight and systematic errors related to fixed ratios of BV to body weight are corrected for by this approach through a proprietary algorithm.[17-20] It should be highlighted that this single-isotope technique for measurement of BV has been tested in a variety of settings, both in the ambulatory and in-patient environment, and a number of reports in the peer-reviewed literature support its feasibility and practicality, generalizability, and validity.[7-9,17-20] This approach has been found to be equivalent to concurrent radioisotopic measurement of plasma volume (PV) and red blood cell volume (RBCV), using chromium-51 tagged red cells, and iodine-125 tagged albumin.[17,21]

Notwithstanding, we, too, have been evaluating the efficacy and practicality of integrating BV analysis, using this device, in guiding fluid and red blood cell management in the surgical intensive care unit since 2004.[7-9,22] A prospective randomized trial conducted in our institution demonstrated improved survival when critically ill surgical subjects with septic shock, severe sepsis, severe respiratory failure, and cardiovascular collapse were managed by BV-guided fluid and red blood cell therapy applying results obtained by use of this particular methodology.[22] Despite our findings, and those of other investigators, there are constraints that impede more widespread use of this methodology. Some of these include the time duration required for BV measurement in the critically ill subject, where intravascular volume may be rapidly fluctuating in a dynamic equilibrium, the fundamental requirement to maintain fluid, colloid, and vasoactive pharmacologic agent administration constant during the period of measurement, patient safety considerations inherent in the infusion of a radioisotope, and the pragmatic requirement for radioisotope and nuclear medicine technologists being readily available. In an effort to continually build on prior work to refine our approach to the determination of circulating BV, we have pursued other contemporary methods for BV measurement that may be more amenable to generalized use in critical care units.

The COstatus System (Transonic Systems, Ithaca, NY) for determining BV, based on the ultrasound dilution method, has been introduced as an alternative means to calculate this fundamental hemodynamic parameter at the bedside.[23-26] This promising device has been prior validated for cardiac output measurements compared against pulmonary artery thermodilution and transpulmonary thermodilution methods in animal models, pediatric patients, and in adult subjects, but there is a paucity of studies that address the comparability of this modality for BV measurements.[23-26] Some advantages of this device, compared with use of radioisotope dilution methods, include the use of readily available and less cost isotonic saline as the indicator substance, reusable sensors, a relatively short duration of measurement time (approximately 10 min), its general availability for obtaining BV measurements at any time, and the ability to perform repetitive measurements within a short interval of time, given that it is not hampered by the need to allow for time to elapse between measurements for radioactive decay and clearance to occur. Moreover, the isotonic saline indicator has thus far had no reported adverse side effects in a variety of subject cohorts studied, which broadly comprise critically ill neonatal and pediatric subjects, adult hemodialysis subjects, and others.[23-26] Despite the fact that there have also been no adverse side effects associated with use of the radioisotope dilution technique, this technique is not approved for use in children or pregnant subjects, which limits its utility across a broad range of subject cohorts.[8,9] The procedural setup for this consists of a simple assembly of tubing with ultrasound sensors that bridge *in situ* arterial and central venous catheters present in many critically ill subjects (Fig. 1). The physiologic principles that constitute the basis of this methodology have already been described in more detail elsewhere.[23-26] In brief, after isotonic saline administration through a central venous catheter is performed, the sensors record the change in velocity of the blood. The injection of saline, at body temperature, decreases the blood ultrasound velocity, resulting in the genesis of dilution curves. This temporal decrease in blood velocity during the relatively short period of measurement has had no reported adverse consequences.[24-26] Calculation of cardiac output can be obtained in this manner, and it is based on the Stuart–Hamilton principle.[23-26] The Active Circulation Blood Volume Index (ACVI), defined as the volume of blood that immediately supports cardiac output through quick, multiple recirculation through the heart, lungs, and other low resistance organs, such as the brain, liver, and kidneys, indexed to body weight, is also calculated.[23-26]

The aim of this study was to determine if circulating BV measured by ultrasound dilution technology (BV-UD) is