

Correlation of blood volume values and pulmonary artery catheter measurements

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ABSTRACT

Objective: To correlate the values generated by direct total blood volume measurement with pulmonary artery catheter parameters and commonly used laboratory values in the management of critically ill patients.

Methods: This study was carried out at the Lutheran Medical Center, Brooklyn, New York, United States of America, during the period 1998-1999. We prospectively correlated the total blood volume (TBV) values generated by the blood volume analyzer (BVA)-100 using I131-tagged albumin, with the values obtained from pulmonary artery catheter (PAC) of central venous pressure, pulmonary capillary wedge pressure, cardiac output, and with laboratory values of hematocrit, lactate, arterial blood gas and mixed venous blood, in critically ill patients. Twenty-four intensive care unit (ICU) patients were studied. Inclusion criteria: Admission to the intensive care, pulmonary artery catheter insertion and (APACHE) II Acute Physiology and Chronic Health Evaluation score of 8-30 (mean=17.875). Exclusion criteria: Pediatric patients, hemodynamically normal or stable patients, pregnancy, and critically ill patients that were managed in an ICU setting without PAC catheter. Height and weight were

recorded. After the collection of an initial blood sample (5cc), one cc of I131-tagged albumin (15-25 microcuries) was injected using a patented syringe. Five venous samples were collected after the isotope injection.

Results: The collection times were entered into the BVA-100. Hematocrit measurements were performed in duplicate. Blood samples were centrifuged and one ml from the plasma of each sample was pipetted (in duplicate) into the sample tube then placed into the BVA-100. The results showed that the TBV did not correlate with either pulmonary capillary wedge pressure or central venous pressure, and except for the cardiac output, there is no correlation between pulmonary capillary wedge pressure readings or TBV results and the other parameters considered in this study.

Conclusion: This method can be released from the research fields and can be safely incorporated into the clinical arena. It provides an accurate assessment of the volume status in intensive care unit patients.

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The answers to many questions in the management of critically ill patients require knowledge of a wide variety of parameters. This gives the clinician guidance in the diagnosis and treatment of their diseases. Among these parameters, a lot has been said regarding non-invasive^{1,2} as well as the invasive forms of monitoring of critically ill patients,³ and specifically with regards to the Pulmonary Artery Catheter (PAC). There are many reports in the

literature regarding its efficacy^{4,6} as well as its complications.⁷⁻¹⁰ Higher mortality was found in the patients in whom the PAC was used, as well as increased hospital stay and costs.⁷ Inadequate interpretation of the parameters generated by this catheter by physicians and nurses in charge of these patients^{11,12} has also been reported in the literature. These controversies with the use of the PAC have placed question marks regarding its effectiveness as a

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guidance tool for critically ill patients.¹³ Two other studies provide alternatives for management and obtaining information regarding this group of patients, that are more reliable, safer and less invasive: Transesophageal Echocardiography (TEE) and Blood Volume (BV) measurements. TEE is less invasive and safer than PA Catheterization. It can often be performed more rapidly, and may yield more accurate information,^{13,14} but it has not been widely applied as of the limited number of intensivists who are trained in echocardiography.¹⁵ Blood volume measurements have been available for over 60 years, but are rarely used in acute clinical situations. This is the result of the technical difficulties in rapidly obtaining an accurate BV measurement.¹⁶ Measurement of blood volume in humans first became possible with the development of indicator dye-dilution techniques in 1915, and the development of radioactive isotopes permitted a significant improvement in the measurement of the red cell compartment. ¹¹³I was utilized to measure the plasma compartment by attachment to albumin.¹⁷ The injection of radioactive iodine-labeled albumin is considered the "gold-standard" method for blood volume measurement,¹⁷ and its efficacy has been compared previously with other methods.¹⁸ The knowledge of the blood volume status of a patient is very important, as the main decisions for fluids and cardiovascular system management are usually based on pressure measurements generated by the PAC, which do not accurately indicate volume status.

The purpose of this study is to explore the interrelationships between the main parameters used in critical care, including the values generated by the PAC, and the values obtained using the Blood Volume Analyzer (BVA). Furthermore, we also examined whether blood volume measurements can be used both accurately and safely in the assessment and management of critically ill patients in conjunction with PAC or alone towards the end point of resuscitation.

Methods. The study was performed at Lutheran Medical Center in Brooklyn, New York, United States of America during the period 1998-1999. After approval of the experimental protocol by the Institutional Review Board, written informed consent was obtained from the study patients. Twenty-four ICU patients, 10 men and 14 women aged 42-93 years (median age= 77.5 years) completed the study.

Inclusion/exclusion criteria. Admission to the Medical or Surgical Intensive Care Units, PAC insertion and an APACHE II (Acute Physiology and Chronic Health Evaluation) score of 8-30, mean of 17.875. Exclusion criteria were pediatric patients, hemodynamically normal or stable patients, pregnancy, and critically ill patients that were managed in an ICU setting without the use of a PAC

catheter. The weight (in pounds) and height (in inches) of each of the individuals from the study group was obtained for further calculation of the individual's normal predicted blood volume as a function of the patient's body weight deviation from ideal weight.^{16,17}

Results. Twenty-four patients, 10 men and 14 women, aged 42-93 years (median age=77.5 years) completed the study. The demographic characteristics and clinical diagnoses of the study patients are presented in **Table 1**. The inverse correlation of Pulmonary Capillary Wedge Pressure (PCWP) with Cardiac Output (CO) was statistically significant ($r=-0.43$, $p=0.03$). However, there was no significant correlation between PCWP and each of the hematocrit, plasma lactate, arterial pH, arterial HCO_3 , mixed venous pH, and mixed venous HCO_3 ($r= -0.28, -0.19, -0.30, -0.18, -0.22, -0.11, p= 0.19, 0.38, 0.16, 0.39, 0.29, 0.62$). Central Venous Pressure (CVP) correlated significantly with CO ($r=-0.37$, $p=0.08$), arterial pH ($r=-0.42$, $p=0.04$), and arterial HCO_3 ($r=-0.43$, $p= 0.04$), whereas it did not do so significantly with the hematocrit, plasma lactate, mixed venous pH, or mixed venous HCO_3 ($r=-0.18, -0.13, -0.26, 0.14, p= 0.4, 0.55, 0.22, 0.50$). Results for Blood Volume (BV) measurements were similar to that of PCWP and showed a significant correlation with CO ($r= 0.53$, $p= 0.01$), whereas that with all the other parameters were not significant ($r=-0.05, -0.31, -0.06, -0.04, 0.34, -0.12, p= 0.83, 0.14, 0.78, 0.86, 0.11, 0.59$). Blood volume did not correlate significantly with either PCWP ($r=0.09$, $p=0.67$) or central venous pressure ($r=0.03$, $p=0.87$) readings.

Discussion. Traditionally, the management of critically ill patients has been based on many clinical and laboratory parameters, as well as values generated by the PAC.^{19,20} Many reports in the literature evaluate the lack of reliability of physical signs when used in the assessment of hypovolemia due to acute blood loss and other causes of hypovolemia,²¹ as well as in patients with multiple medical problems.²²⁻²⁴ Among the laboratory parameters, it has been consistently demonstrated that the admission hematocrit correlates poorly with the degree of blood loss and overall mortality.²¹ At the other end of the spectrum, hematocrit changes become almost uninterpretable when the patients have been given large volumes of packed red cells and fluids.³ Since the introduction of the PAC in medical practice by Swan et al²⁵ in 1970, there has been multiple reports in the literature regarding its applications⁴⁻⁶ as well as the morbidity (20-53%) and mortality (0-4%)^{5, 7-10,13, 26} related to its use. Recent reports show a lack of effectiveness of PA catheterization in critically ill medical patients and relatively late-stage surgical patients with organ

Table 1 - Demographic and clinical characteristics of the study patients.

Age	Sex	Height (inches)	Weight (pounds)	Clinical diagnosis/surgical treatment
78	Female	63	154	Septic shock/acute pulmonary edema/acute renal failure
67	Male	69	159	Postoperative CVA/septic shock/radical neck dissection
54	Male	72	222	Sepsis/acute renal failure/CHF
54	Female	60	123	Chronic interstitial fibrosis/bilateral pneumonia/ARDS
78	Female	62	125	COPD/hypothyroidism/diabetes mellitus/CHF/sepsis
83	Female	60	125	Septic shock/CHF/acute renal failure/GI bleeding
86	Female	61	104	MI/CHF/pneumonia
93	Female	67	143	Septic shock
76	Male	67	140	Acute renal failure/cardiogenic shock/GI bleeding
70	Male	71	136	Cardiomyopathy/cystoprostatectomy
71	Male	71	160	Hepaticojejunostomy/vagotomy+pyloroplasty
79	Female	62	99	Intestinal obstruction/release of adhesions
77	Female	60	155	Intestinal obstruction/release of adhesions
79	Female	63	135	AAA repair/left hemicolectomy/embolectomy
70	Female	64	126	Axillary-bifemoral bypass
75	Male	72	187	GI bleeding
73	Male	65	127	Ischemic bowel/small bowel resection
85	Male	69	168	Septic shock
69	Female	62	110	Intestinal obstruction/small bowel resection
42	Male	64	143	CHF/cardiomyopathy
85	Female	60	126	Acute pulmonary edema/respiratory failure
85	Female	60	125.5	Acute renal failure
85	Female	60	165	Rectal bleeding/sigmoid resection
79	Male	72	211	Carcinoma colon/sigmoid resection

CVA - cerebrovascular accident, CHF - congestive heart failure, ARDS - adult respiratory distress syndrome
COPD - chronic obstructive pulmonary disease, GI- gastrointestinal, MI - myocardial infarction, AAA - abdominal aortic aneurysm

failure.² Pulmonary artery catheter complications are grouped into 3 categories.¹⁰ 1. Complications associated with central venous cannulation, including an incidence of pneumothorax that approaches 5%.¹³ 2. Complications related to the flotation and measurement phase that among others include infections and catheter-induced pulmonary artery perforation. The latter complication, although uncommon (0.1-0.2%), carries a 50% mortality²⁷⁻³⁴ especially with patients with pulmonary artery hypertension; 3. Complications that occur during or after the removal of the catheter.^{10, 29}

Important decisions for fluids and cardiovascular system management in critically ill patients are

usually based on PAC results, despite of the fact that pressure measurements obtained from this device do not correlate with volume status. The relationship between pressure and volume depends on a 3rd variable, compliance. If 2 of these 3 variables are unknown, the 3rd can only be estimated crudely.¹³ Additionally, many reports in the literature document the inadequate interpretation of PAC parameters by physicians and nurses in charge of these patients.^{11,12} The study by Connors et al⁷ presents evidence that PAC may not benefit critically ill patients and may even be harmful. Shoemaker et al,³⁵ as well as many other authors, identifies hypovolemia as one of the initiators of shock, as well as hypoxemia, poor tissue

perfusion, and tissue hypoxia. The early identification of these parameters (during the first 8-12 hours) can help in the prevention of shock and improve the outcome of critically ill patients.

In view of these difficulties to manage critically ill patients, other methods with less morbidity and mortality have been published in the literature.^{2,35} These include the use of transesophageal echocardiography^{14,15} and blood volume measurements using different methods as stated previously.

The study of the blood volume measurement started back in 1838, with measurements in animals performed by Valentin utilizing a water dilution method. Herbst in 1888 utilized "bleed-out" experiments with animals. These results later showed to be 50% of true blood volume measurement.¹⁷ Measurement of blood volume in humans first became possible with the development of indicator dye-dilution techniques in 1915. Its use was based on the principle that the concentration of a known quantity of a dye in the blood after mixing, when injected intravenously, is inversely proportional to the volume of blood into which the dye has been injected.¹⁷ Early studies utilized brilliant vital red and a few years later, Evans blue or T-1824 was used. These methods artifactually raised the measured blood volume by 8% due to absorption of the tracer by the reticuloendothelial cells in the early post injection period.¹⁷ Indocyanine green (ICG), a tricarboyanine dye, has been investigated since the 1960's, and has been used in the indicator dilution technique for estimation of cardiac output.³⁶ Recent applications using this dye have been reported for the measurement of blood volume at the bedside.^{17,37} The development of radioactive isotopes permitted a significant improvement in the measurement of the red cell compartment,¹⁷ and the isotopes that initially were used included Cr51, Fe55, Fe59, K42 and P32. I131 was utilized to measure the plasma compartment by attachment to albumin. One advantage of this combination is that the albumin is not treated as a foreign substance, but it transudates out of the circulation at a rate which is a semilogarithmic function of its concentration within the circulation.¹⁷ The injection of radioactive iodine-labeled albumin has been considered the "gold-standard" method for blood volume measurement,¹⁷ and its efficacy has been compared previously with other methods.¹⁷ Albumin tagged with I131 mixes unimpeded in the circulation. It transudates out of the circulation at a rate which is a semilogarithmic function of its concentration within the circulation. Performing a multipoint blood volume analysis can compensate for the problem of loss of tracer from the circulation.¹⁶

In 1977, Feldschuh and Enson¹⁶ demonstrated that blood volume, rather than being a fixed ratio of ml/

kg of body weight, was actually a curvilinear function depending on the degree of leanness or obesity in relation to ideal weight. There is a BV difference of 8% between men and women at any specific height and weight. They reported that normal BV, rather than being in the commonly reported range of 60-85 ml/kg, ranged from an extreme of 42 ml/kg in the extremely obese to 103 ml/kg in very lean individuals. The values selected for BV in relationship to the body's surface are 2566 ml/m² for men and 2245 ml/m² for women.¹⁶ In general, these values are related to body weight, habitus and body surface area. They are neither useful nor reliable when assessing a critically ill patient. The results of this study showed that except for the CO, there is no correlation between PCWP readings or BV results and the other parameters considered in this study (hematocrit, plasma lactate, arterial pH, arterial HCO₃, mixed venous pH, and mixed venous HCO₃). Central venous pressure values deviate from this pattern however, as there is a weak correlation between CVP and arterial pH that is marginally statistically significant. Blood volume measurements did not correlate with either PCWP or CVP, a finding that is compatible with other reports from the literature.^{3,13} According to the old and commonly known belief that that CV, PCWP and CO are parameters of adequacy of resuscitation, we found that these parameters are only indicative of central perfusion rather than global body perfusion which can only be measured by TBV assessments using blood volume method.

Our study is unique in that we chose specific physiologic parameters such as plasma lactate and blood gases that provide a good reflection of the overall physiologic status of the patient. Such parameters are usually ignored by other studies. At the same time, various authors confirmed that blood lactate is a measure of inadequacy of perfusion in critical patients, we found there is no significant correlation of lactate levels and TBV, further result of that project will be published. However, there were many limitations for our study. The small number of patients that were able to complete the study did not permit a robust analysis of results and might have been responsible for the difference between PCWP and CVP regarding their relationship with arterial blood gases. We did not follow up these patients with respect to their short and long term clinical course. Defining clinical end points such as disability or mortality might have been more helpful in better clarifying the usefulness of BV measurements. The procedure itself takes one hour to be completed and is carried out using multiple blood drawings and requires accurate timing. Therefore, it may not be applicable in highly critical patients when time is of prime importance. In addition, the interpretation of computer generated results depends on height, and therefore might be influenced by the

inevitable imprecision of height measurements in such critically ill patients.

In conclusion, this study is unique in that we chose specific physiologic parameters such as plasma lactate and blood gases that provide a good reflection of the overall physiologic status of the patient. Such parameters have not been adequately emphasized by other studies.

Our study looks at the clinical and physiologic validity of direct BV measurement using I131-tagged albumin in critically ill patients. It demonstrates that the application of this method can be released from the experimental and research fields and be safely and effectively incorporated into the clinical arena. Total blood volume results are comparable with the ones obtained from the PAC in critically ill patients. The measurement of the TBV provides the clinician with an accurate tool to assess the volume status of the patient, since decisions based on pressure measurements or indices do not correlate well with volume status. These results open the door to new studies, where the clinical guidance of this method can be used to treat critically ill patients more effectively. However, other factors such as cost, feasibility and technical expertise will ultimately determine the appropriate setting for using the TBV analysis in such patients.

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