



Direct Blood Volume Measurement Correlated with Improved Survival in Critical Care Patients

Mihae Yu, MD, and Danny Takanishi Jr., MD, of The University of Hawaii, The Queen's Medical Center are Principal Investigators on several studies that have examined the impact of blood volume measurement in critical care patients. Findings from their studies were reported as five poster presentations at the recent Society for Critical Care Medicine in Miami, FL. One of their key findings was that direct blood volume measurement correlated with improved survival. 100 critically ill surgical patients were randomized into either of two treatment arms: resuscitation decisions in the blood volume group were based on both the blood volume as well as pulmonary artery catheter (PAC) measurements. In contrast, resuscitation decisions in the control group were based on PAC measurements alone. The findings showed that use of blood volume measurement in addition to PAC monitoring allowed more precise quantitation of patients' needs for fluids and red cells. This ultimately resulted in a significant improvement in mortality in patients for whom therapy was guided by both blood volume analysis and PAC (8% mortality) vs. PAC alone (24% mortality; P= 0.02).

Another study, entitled "A Comparison of Pulse Pressure and Blood Volume Measurement" examined whether there was a correlation between pulse pressure – a surrogate marker of cardiac fluid responsiveness to fluid infusion – and intravascular blood volume. Simultaneous

Recent Publications

Mitchell T. Saltzberg, MD, FACC, Medical Director of Heart Failure at the ChristianaCare Health System authored the following review article, which is currently in press:

"Blood Volume Analysis Coupled with Ultrafiltration in the Management of Congestive Heart Failure – Guided Therapy to Achieve Euvolemia" US Cardiology, 2010; 7(1):72-75.

measurement of pulse pressure and blood volume in 100 critically ill surgical patients

showed that there is no relationship between these two variables.

A third study, entitled “The Relationship Between Inferior Vena Cava (IVC) Collapsibility Ratio and Measured Whole Blood Volume in Surgical Critical Care Patients” examined the correlation between IVC and blood volume. Collapsibility of the IVC is calculated as the difference between the maximum and minimum diameters of the IVC throughout the

Multicenter Study of Blood Volume Analysis in ICU Now Recruiting Investigators

Daxor is now recruiting Investigators to participate in a multi-center trial of BV analysis in the ICU. This study will be led by Principal Investigator Dr. Mihae Yu of The University of Hawaii, The Queen’s Medical Center. If your site may be interested in participating in this study, or if you have further questions about it, please contact Stephen Feldschuh at: (917) 553-8604; stephen@daxor.com or Frank Garcia at: (808) 499-5090; fgarcia@daxor.com

respiratory cycle. IVC is sometimes used as an estimate of central venous pressure – which is an imperfect correlate for blood volume – in critically ill patients. However, retrospective examination of data collected from 43 surgical critical care patients showed no relationship between IVC and blood volume.

These studies are extremely important as they demonstrate that three commonly used markers for critical care patient resuscitation

status (Pulse pressure, IVC and PAC) do not provide accurate estimates of patients’ blood volumes. Blood volume data is an extremely important factor in optimizing resuscitation of critically ill patients, and this information can be accurately obtained only by direct measurement of intravascular blood volume. Physicians who continue to rely on imprecise surrogate measures of volume status may under- or overtransfuse their patients with fluids and red blood cells, thereby doing harm to the patients they are trying to help. A fundamental goal of Daxor Corporation is to make direct blood volume measurement the standard of care in the treatment of critically ill patients in the intensive care unit.

In addition, Drs. Yu and Takanishi performed two studies which examined the rate of transudation of albumin across the capillaries, which is another measurement provided by the Blood Volume Analyzer-100 (BVA-100). Albumin is an essential carrier protein, which helps to maintain blood pressure. These studies focused on the rate of loss of albumin from the intravascular system, which is very slow in normal individuals. In patients with sepsis, however, loss of vascular integrity results in loss of fluids and proteins and a corresponding decrease in blood volume. The medical term for this is “leaky capillary syndrome”, and it may result in collapse of blood pressure and sudden death. With repair of the vascular injury, these intravascular fluid losses are minimized and patients can recover. One of the studies, entitled “Activated Protein C (APC) and Corticosteroids Decrease the Rate of Albumin Transudation in Septic Shock” examined whether APC and corticosteroids may affect capillary permeability in 75 patients with severe sepsis/septic shock. The results show that

either corticosteroids alone or APC and corticosteroids together significantly decreased elevated transudation rates. A lower mortality rate was observed in the group receiving corticosteroids alone relative to the APC and corticosteroid combination group. Although it has long been assumed that the corticosteroid hydrocortisone stabilizes capillary transudation in septic shock, this study is the first involving direct blood volume measurement and albumin capillary loss to actually demonstrate this.

Another study, entitled “Elevated Transcapillary Albumin Escape: A Marker of Increased Mortality” directly examined the relationship between albumin leak rate and mortality in 100 patients requiring radial or pulmonary artery catheter for acute resuscitation of severe sepsis, septic shock, cardiogenic shock and/or Acute Respiratory Distress Syndrome. Patients with a normal albumin leak rate 5-7 days after resuscitation showed markedly lower mortality (7.8%) than patients with elevated albumin leak rate (27.9%). This study confirms that transcapillary albumin escape is, in fact, a marker for increased mortality. This opens up the possibility of using this measurement to evaluate the efficacy of different therapies in reducing capillary albumin leak.

The following investigators were involved in these studies: Mihae Yu, MD, Danny Takanishi,

Jr., MD, David Inouye, MD, Michael Hayashi, MD, Kevin Pei, MD, Kurt Edwards, MD, Sharon Takiguchi, MD, Shirley Domingo, MD, Marc Osborne, MD, Susan Steinemann, MD, Fedor Lurie, MD, Maimona Ghows, MD, and Sharon Moran, MD. Abstracts which describe their findings were published in the December 2009

TEAM-UF Study

15 of 50 patients have been enrolled into the TEAM-UF Study, which is led by Principal Investigator Mitchell T. Saltzberg, MD, FACC at the ChristianaCare Health System. The objective of this study is to determine whether using blood volume measurement to help guide fluid removal with ultrafiltration in patients hospitalized with decompensated heart failure leads to improved outcomes.

Supplement (Volume 37, Number 12) of the *Critical Care Medicine* journal. Further details can be found in the poster presentations, which are available on Daxor’s website at www.daxor.com/sccm2010.asp.

Blood Volume Analysis Can Distinguish True Anemia from Hemodilution in Critically Ill Trauma Patients

Martin A. Schreiber, MD, FACS, Chief of the Division of Trauma, Critical Care and Acute Care Surgery at the Oregon Health and Science University is Principal Investigator for a study

which examines whether blood volume measurement can be used to monitor volume status and to decrease the number of tests and interventions in trauma patients. Philbert Van,

MD, of his research team gave an oral presentation of their findings at the recent Western Trauma Association Annual Meeting in Telluride, CO. They performed serial blood volume measurements on 27 critically ill patients who had undergone fluid resuscitation and found that the peripheral and normalized hematocrits identified the same patients provided that the patients were normovolemic or mildly hypovolemic. However, the peripheral hematocrit overdiagnosed anemia in 54.5% of the hypervolemic patients. This has important implications for treatment of trauma, as hemorrhage is the leading cause of preventable death in trauma victims. It is therefore important to be able to monitor ongoing blood loss. It has long been known that the peripheral hematocrit does not reflect a patient's true red blood cell volume – particularly in patients with volume derangements (Valeri et al. *Transfusion* 2006; 46:365-371; Takanishi et al. *Anesth Analg.* 2008; 106:1808-1812). Despite the fact that the peripheral hematocrit has proven inadequate in

estimating red cell volume, it remains the primary tool for estimating red cell volume in many clinical encounters. Dr. Schreiber's findings demonstrate that the peripheral hematocrit does not adequately represent red blood cell volume (RBCV) in hypervolemic patients. Use of the blood volume analyzer-100 (BVA-100) to directly assess red cell volume and to correct the peripheral hematocrit for volume derangements may help to distinguish true anemia from hemodilution, potentially preventing unnecessary interventions.

The following investigators were involved in this study: Philbert Van, MD, S. David Cho, MD, Samantha Underwood, MS, GJ Hamilton, BS, Bruce Ham, MD, and Martin Schreiber, MD. Further details about this study can be obtained from the presentation, which will soon be made available on Daxor's website at www.daxor.com/wta2010.asp.

Changes in Blood Volume Throughout Cardiac Surgery

Mark Nelson, MD, is the Principal Investigator at the Virginia Commonwealth University for a study which examines changes in total blood volume (BV) and red blood cell volume (RBCV) in patients undergoing elective cardiac surgery. The peripheral blood hematocrit is commonly used as a measure of red cell volume and is used to guide transfusion decisions during cardiopulmonary bypass and valve replacement/repair surgeries. A series of blood volume measurements was performed on all patients: (1) before surgery; (2) immediately after surgery; and (3) two hours after transfer to the intensive care unit (ICU).

47 of 50 patients have been enrolled into this study to date. The preliminary findings from this study will be exhibited as two poster presentations at the upcoming Society of Cardiovascular Anesthesiologists Annual Meeting in New Orleans on April 24-28, 2010. The following investigators are involved in this study: Mark Nelson, MD, MEd, Bruce Spiess, MD, John Kearney, MD, Pingle Reddy, MD, Jeff Green, MD, Derek Brinster, MD, Patricia Nicolato, DO and Vigneshwar Kasirajan, MD.

TEAM-HF Study

Stuart Katz, MD, is the Director of the Heart Failure program at the New York University Langone Medical Center. Dr. Katz performed some of the seminal work in blood volume analysis of heart failure patients when he was an Investigator at the Columbia University Medical Center. He and his colleagues showed that heart failure patients with expanded blood volumes had significantly increased mortality relative to heart failure patients with normal or contracted blood volumes (Androne AS et al, *Am J Cardiol.* 2004; 93:1254-1259). Dr. Katz will continue to pursue this line of research as

Principal Investigator for a multicenter trial which will investigate whether use of blood volume measurements in addition to existing standards of care can reduce rehospitalization and mortality in acute decompensated heart failure patients. The **T**reating to **E**uvolemia (Normovolemia) by Clinical **A**ssessment and **M**easured Blood Volume in **H**eart **F**ailure (TEAM-HF) Study will enroll 300 heart failure patients at the time of hospital discharge. To date, the following sites and Investigators have committed to participating in the trial:

Site:	TEAM-HF Site Principal Investigator(s)
(1) NYU Langone Medical Center (NY)	Stuart D. Katz, MD & Alex Reyentovich, MD
(2) Columbia-Presbyterian Medical Center (NY)	Mathew S. Maurer, MD
(3) ChristianaCare Health System (DE)	Mitchell T. Saltzberg, MD
(4) Allegheny General Hospital (PA)	George G. Sokos, DO & Srivinas Murali, MD
(5) Forsyth Medical Center (NC)	David L. Smull, DO
(6) Pacific Cardiology, LLC (HI)	Gregg Yamada, MD & Calvin Wong, MD
(7) St. Luke's Regional Heart Center-Bethlehem (PA)	Darren Traub, MD & Prasanna Sugathan, MD
(8) Temple University Hospital (PA)	James T. Fitzpatrick, MD & Lazaros Nikolaidis, MD
(9) The Valley Hospital (NJ)	John E. Strobeck, MD, PhD
(10) VA Maryland Health Care System - Baltimore (MD)	Stephen S. Gottlieb, MD
(11) Rush University Medical Center (IL)	Barbara A. Pisani, DO and Jose C. Mendez, MD