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A QUANTITATIVE ANALYSIS OF CLINICAL END POINTS OF RESUSCITATION AFTER MASSIVE BLOOD TRANSFUSION

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INTRODUCTION: The integration of massive transfusion protocols (MTP) in the contemporary management of hemorrhagic shock is associated with improved survival. Given the rapid infusion of blood products over a relatively short period of time, it is unclear if traditional endpoints of resuscitation (bedside hemodynamic parameters and laboratory values) accurately reflect total intravascular blood volume (BV) measured quantitatively. The aim of this study was to perform a comparative analysis of BV status, assessed clinically and quantitatively, after subject stabilization following use of MTP, to determine if endpoints of resuscitation can be further refined in this setting.

METHODS: A retrospective chart review was conducted to identify critically-ill surgical subjects from 2016 to 2018 who had MTP implemented and, once clinically stabilized, a BV analysis. BV was measured using an FDA-approved device (BVA-100, Daxor Corporation, NY, USA) which uses I-131-radiolabled-albumin injected into the peripheral circulation with timed serial blood samples to calculate BV. Hypovolemia, euvolemia, and hypervolemia are defined as <0%, 0-16%, and >16% deviation from predicted norms, respectively.

RESULTS: 25 subjects formed the study group. Subject characteristics were mean age 45±20 years; 21 males:4 females; median APACHE II 25 (IQR 23-29); median hospital length of stay 31.5 days (IQR 13.6-72.7). Median total RBC units transfused was 11 (IQR 6-22); median hemoglobin at the time of MTP was 7 (IQR 6.1-8.5) and at the time of BV analysis 9.4 g/dL (IQR 8.7-10.7). Median lactate at the time of MTP was 6.8 (IQR 4.2-9.4) and at the time of BV analysis 1.6 mmol/L (IQR 1.2-2.7); 22 subjects survived to hospital discharge (88%). After completion of MTP and clinical stabilization, BV analysis showed hypovolemia in 6 (24%), euvolemia in 5 (20%), and hypervolemia in 14 (56%) subjects, respectively (95% CI for euvolemia: 0.07 – 0.41).

CONCLUSIONS: Traditional endpoints of resuscitation after implementation of MTP may not accurately reflect true BV. Only 20% of subjects in this study were euvolemic, with 24% demonstrating hypovolemia, despite meeting traditional clinical surrogates indicative of euvolemia. If validated in a larger study use of BV analysis may have the potential to refine our approach to use of MTP.

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INVESTIGATION OF HEMODYNAMIC PARAMETERS USING A PORCINE HEMORRHAGE AND VOLUME OVERLOAD MODEL

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INTRODUCTION: Accurately measuring fluid status during intraoperative hemorrhage is challenging, and quantification of fluid overload can be far more difficult. In this investigation, a porcine model of hemorrhage followed by over-resuscitation is used to determine which hemodynamic parameters optimally detect volume status. We hypothesize that central hemodynamic parameters will correlate to volume loss and overload better than vital signs.

METHODS: Eight pigs were anesthetized and cannulated with an arterial line and a pulmonary artery catheter. Pigs were hemorrhaged at 30 mL/min to a total blood loss of 400 mL. After each 100 mL of hemorrhage, vital signs (heart rate, systolic blood pressure, mean arterial pressure, diastolic blood pressure, pulse pressure, pulse pressure variation) and centrally obtained hemodynamic parameters (mean pulmonary artery pressure [MPAP], pulmonary capillary wedge pressure [PCWP], central venous pressure [CVP] and cardiac output [CO]) were obtained. Blood volume was restored, and the pigs were over-resuscitated with 2,500 mL of crystalloid, collecting all parameters after each 500 mL bolus. Hemorrhage and resuscitation phases were analyzed separately using one-way ANOVA with Tukey's post-hoc test to determine whether there were differences among each parameter over the range of volume. Conformity of parameters during the range of hemorrhage or over-resuscitation was assessed using simple linear regression.

RESULTS: Systolic, diastolic and mean arterial blood pressure significantly decreased with increasing volume of hemorrhage, changes significant by the first 100 mL of blood removal ($P<.05$). MPAP, PCWP and CVP significantly decreased over the course of hemorrhage ($P<.05$), first realized at hemorrhage volumes of 200 mL, 200 mL, and 300 mL, respectively. Centrally obtained parameters best demonstrated linear conformity with hemorrhage ($R2\geq0.98$). Conversely, only central hemodynamic parameters CVP, MPAP, CO and PCWP changed during over-resuscitation ($P<.0001$). As with hemorrhage, PCWP demonstrated the highest R2 value during over-resuscitation (0.98).

CONCLUSIONS: Pulmonary capillary wedge pressure is the most accurate parameter to trend in the detection of both hemorrhage and over-resuscitation, demonstrating the unmet clinical need for a less-invasive PCWP equivalent.