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Noninvasive Tissue Oxygen Saturation Measurements Identify Supply Dependency

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Background. **Hemorrhagic shock can lead to multiple organ failure and death. We have previously shown that noninvasive measurement of tissue oxygen saturation (StO_2) has predictive value for outcomes in patients suffering hemorrhagic shock. Our study objectives were twofold: (1) to compare invasive and noninvasive measurements of local and systemic tissue hemoglobin oxygenation and (2) to compare the effects of various physiologic conditions seen in patients in hemorrhagic shock on tissue hemoglobin oxygenation.**

Materials and Methods. **We studied pigs in controlled conditions mimicking shock induced by one of the following: hypothermia, isovolemic hemodilution, or manipulations of vascular tone. We obtained both invasive and noninvasive measurements in a hind limb of StO_2, tissue hemoglobin index, femoral artery and venous flows, blood pressures, temperature, pH, pO_2, pCO_2, oxygen saturation, lactate, hemoglobin, and base excess. In all cases, we measured baseline values in both experimental and control hind limbs.**

Results. **We found that tissue hemoglobin oxygenation did not vary significantly over relevant physiologic temperatures. Under all physiologic conditions tested, we found supply-dependent oxygen consumption at oxygen levels less than 7 mL O_2/min/kg. Similarly, we found that local oxygen delivery in animals subjected to varying degrees of isovolemic hemodilution or altered vascular tone was correlated with supply-dependent oxygen consumption, as measured by local noninvasive StO_2.**

Conclusions. **Noninvasive StO_2 measurements are valid and durable over a wide range of physiologic conditions and correlate with invasively-measured oxygen delivery.**

Key Words: **tissue oxygenation; StO_2; vasoactive treatment; anemia; animal model.**

INTRODUCTION

Tissue oxygen saturation (StO_2) measurements are derived from optical techniques using noninvasive near-infrared spectroscopy (NIRS). NIRS measures relative amounts of oxyhemoglobin and deoxyhemoglobin to determine overall tissue saturation of hemoglobin; this differs from standard pulse oximetry measurements in that hemoglobin saturation of the small vessels of the arterial and venous systems as well as the capillaries within sampled tissue is assessed [1]. Clinically, NIRS offers the advantage of continuous, noninvasive, peripheral bedside monitoring of oxygenation compared with standard techniques [2].

In critically ill patients or patients suffering from trauma and hemorrhagic shock, circulatory failure results in decreased global oxygen delivery (DO_2) with redistribution of blood flow *via* alterations in vascular tone [3]. Furthermore, tissue oxygen consumption (VO_2), which is normally constant with adequate DO_2 becomes "supply dependent" at low levels of DO_2 or in certain disease states such as septic shock, reflecting inadequate tissue oxygenation. Figure 1 shows local tissue oxygen consumption, which is dependent both on the global and local oxygen delivery. Under conditions of adequate DO_2, VO_2 is constant and independent of DO_2. However, when DO_2 falls below a critical point,

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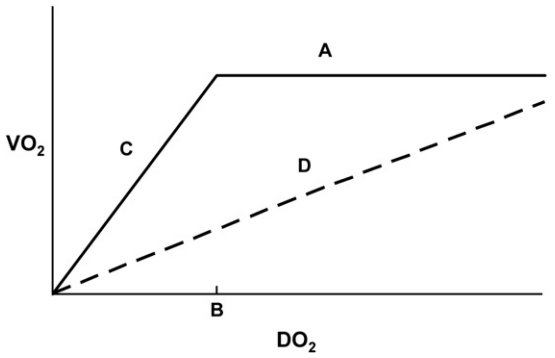

FIG. 1. The relationship between oxygen consumption (VO_2) and oxygen delivery (DO_2). Under normal physiologic conditions, VO_2 is constant even if DO_2 is increased (reflected by the "supply independent" plateau, [solid line (A)]. However, below a critical level of DO_2 [point (B)], VO_2 changes in a linear fashion proportional to DO_2 (represented by the "supply dependent" slope, [solid line (C)]. Furthermore, in certain disease states resulting in severe systemic inflammation (such as sepsis, burns, and trauma), oxygen extraction is blunted and VO_2 increases with less magnitude per unit increase in DO_2 [represented by the smaller slope, dotted line (D)].

VO_2 is affected and also begins to fall, reflecting a progressive failure of adequate tissue oxygenation, and leading to further deleterious sequelae [4].

Initial noninvasive measurements in critically ill patients do not provide an adequate assessment of tissue oxygenation and therefore, invasive tests are routinely used to provide a more complete profile. Noninvasive peripheral monitoring of tissue oxygenation by StO_2 is appealing in that it may allow earlier identification of inadequate tissue oxygenation, thereby increasing the subsequent opportunity for early intervention and treatment. Increasing reports describing the use of *in vivo* NIRS and StO_2 monitoring in pathophysiologic conditions such as sepsis, traumatic shock, acute respiratory distress syndrome (ARDS), and peripheral vascular disease indicate the potential value of adding this noninvasive technique to augment standard care [5–9]. Measurements using NIRS have been shown to correlate with multiple organ failure in patients with sepsis [10], and to be predictive of outcome after septic shock and severe traumatic injury [6, 11].

In our study, we sought to compare both systemic and local tissue oxygenation measurements obtained by invasive and noninvasive methods in pigs in which various physiologic conditions were manipulated to simulate those seen in patients, including hypothermia, anemia, and alterations in vascular tone.

MATERIALS AND METHODS

Animal Preparation

We used 15 juvenile male Yorkshire pigs weighing between 25 and 30 kg for this study. After the pigs had fasted for at least 12 h, we gave them subcutaneous buprenorphine (0.03 mg/kg) for analgesia. We used ketamine (10 mg/kg IM) and propofol (2 to 6 mg/kg i.v. to effect) to anesthetize the pigs, which we then intubated. We maintained mechanical ventilation throughout the experiment (Adult Star 2000; Infasonics Inc., San Diego, CA). We maintained anesthesia with 60% inhaled nitrous oxide and propofol, and all pigs were supine during the experiment. We conducted all experiments in accordance with protocols approved by the Institutional Animal Care and Use Committee of the University of Minnesota.

Surgical Technique

We placed and advanced a pulmonary artery catheter (PAC) in the internal jugular vein and then placed an arterial line in the carotid artery. We exposed the femoral vein and artery of the experimental hind limb (right) and fitted the limb with annular ultrasonic transducers for blood flow measurements (TS420; Transonic Systems, Inc., Ithaca, NY). We placed noninvasive near-infrared spectroscopy (NIRS) tissue oxygenation (StO_2) sensors on the experimental (right) and control (left) hind limb (InSpectra 650; Hutchinson Technologies, Hutchinson, MN).

We performed the following surgical procedures on the pigs: laparotomy, Foley catheter placement, splenectomy, and placement of vessel loops around the infrarenal vena cava, aorta, and right common iliac vein. After surgery, the pigs entered a stabilization period of variable duration until serum lactate levels fell below 2.0 mmol/L. At this time, we obtained baseline measurements. Next, we randomized pigs to the hypothermia, hemodilution, or vasopressor groups of the experiment. All pigs within a group were included in each of the experimental conditions. We euthanized pigs in all groups at the end of the experiment, with Beuthanasia D (1.0 mL/10 kg i.v.).

Measurements and Calculations

During the experiments, we recorded blood pressure, heart rate, temperature, cardiac output (CO), pH, pO_2, pCO_2, oxygen saturation (SaO_2), local and systemic venous oxygenation (SvO_2), lactate, hemoglobin, and base excess. Additionally, StO_2 and femoral artery and venous blood flows from both hind limbs were continuously displayed and recorded using Labview 7 Express (National Instruments, Austin, TX). We analyzed blood gases using a Gen Premier 3000 (Instrumentation Laboratories, Chicago, IL).

We calculated oxygen delivery (DO_2), oxygen consumption (VO_2), and oxygen extraction ratios (ERO_2) using the following equations:

$$DO_2(mL\ O_2/\min/kg) = [CO \times Hg\ concentration \times SaO_2 \times (constant)]/weight$$

$$Systemic\ VO_2(mL\ O_2/\min/kg) = [CO \times Hg\ concentration \times (SaO_2 - SvO_2) \times (constant)]/weight$$

$$Local\ VO_2(mL\ O_2) = CO \times Hg\ concentration \times (SaO_2 - SvO_2) \times (constant)$$

$$Systemic\ ERO_2(\%) = (systemic\ VO_2/DO_2) \times 100\%$$

$$Local\ ERO_2(\%) = (local\ VO_2/DO_2) \times 100\%$$

We calculated systemic VO_2 measurements using SvO_2 obtained from blood taken from the proximal port of the PAC while calculating the local VO_2 using SvO_2 from blood taken from the femoral vein of the experimental limb. We did not index local VO_2 values by weight of the pigs.