What is the evidence of utility for intraosseous blood transfusion in damage-control resuscitation?

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Intraosseous (IO) access is an old technique for gaining entrance to the systemic circulation, which has received a general resurgence in the last 30 years. IO access takes advantage of the vascularity of cancellous bone, the spongy bone inside the hard outer compact bone. Cancellous bone is composed of a lattice work of spicules or trabeculae and hematopoietic red marrow, creating a porous framework. Clinically relevant cancellous bone used for IO access is located at the ends of long bones, such as the humerus, femur, and tibia, and the sternum. Originally, IO access was recommended for use in the resuscitation of critically ill children with difficult intravenous (IV) access. Over time, the clinical use of IO access increased, and its status of use has been elevated by such prestigious organizations as the American Heart Association Committee on Advanced Cardiac Life Support. IO access is now recommended as a rescue technique to treat all critically ill patients regardless of age, when peripheral IV access is difficult or impossible.[1]

Damage-control resuscitation (DCR) is the mainstay of modern combat resuscitation of the injured soldier[2] and has been extended to civilian casualty care.[3]

DCR differs from previous resuscitation methods by emphasizing a blood and coagulation factor resuscitation strategy. In this strategy, blood is preferred over crystalloid for volume replacement, and coagulation factor therapy is aggressively begun early in the resuscitation process to head off the lethal triad of coagulopathy, acidosis, and hypothermia. The rate-limiting step for rapid implementation of this transfusion strategy as part of DCR is satisfactory IV access. Standard advanced trauma life support (ATLS) guidelines emphasize the need for the rapid placement of multiple large bore peripheral IV catheters. When that placement is difficult or impossible, ATLS recommends the use of IO access for infusions of crystalloid or blood until alternative venous access is achieved.[3] The recommendation of IO access for blood transfusion is found not only in ATLS guidelines but also in recommendations from the Infusion Nurses Society (INS).[4] In line with these recommendations, IO access is used as a rescue access in the prehospital implementation of DCR in the combat setting.[5]

The scientific and clinical evidence for the use of IO access is voluminous, as evidenced by the Scientific Bibliography provided by VidaCare,[6] one of the large manufacturers of IO devices, and available in any routine literature search. However, direct scientific and/or clinical data to support the use of IO access for the purpose of blood transfusion in adult humans are very limited to anecdotal reports. For example, in one case report on an injured soldier, six attempts were required to place four IO catheters that were reportedly used to transfuse 2 U of packed red blood cells (pRBCs).[7] A civilian report of successful blood transfusion by the IO route in a 79-year-old female cannot be used to establish a foundation for the general use of the technique in the adult population since the nature of the bone varies greatly by age, sex, and ethnicity.[8] In this era of evidence-based medicine, the absence of good evidence supporting the use of IO access for the very critical function of blood transfusion in DCR places existing recommendations for its use in question. This lack of evidence is compounded by the clinical experience of the lead author. Multiple attempts to use IO access for blood transfusion, both in the civilian adult emergency setting and in combat casualty care, have repeatedly been unsuccessful. These attempts were made by highly experienced clinicians using specific manufacturers' guidelines for IO infusion. In all cases, at best, flow rates totally insufficient for resuscitation with blood products were established. The procedures were aborted because the pressure required to achieve even these rates exceeded the tolerance of the infusion system at its connections. This incongruity between field experience and existing recommendations by the leading authorities has initiated this review.

DISCUSSION

Blood flow in the body is generally modeled by Poiseuille's Law, which describes laminar flow through a hollow tube. Because of the structure of trabecular bone and the IO space, blood flow through the IO space is better modeled by Darcy's Law, which describes flow through a porous media.[9–11] The equation that follows is the Darcy's Law.

$$\text{Darcy's Law}\, Q = \frac{\left(kA(P_f - P_O)\right)}{\mu L}$$

Darcy's law describes the relationship of flow rate, Q, as directly proportional to intrinsic permeability, k (a measure of the ability of a porous material to allow fluids to pass through it), the cross sectional area, A, and pressure difference, ΔP, and inversely proportional to fluid viscosity, μ, and length, L.

Since rapid flow rates are the sine qua non of blood component resuscitation in DCR, let us examine the potential for rapid infusion of blood through the IO space based on the parameters of the Darcy's Law. Regarding the area parameter, the IO catheter itself is not the rate-limiting area for flow rate of

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blood products since it is in the same gauge range as IV catheters used successfully in DCR. Therefore, other features of the IO space define this area parameter. We will not address the contribution of length changes to flow rate, as we conclude that it is a minor effect with limited variability among adults. This leaves two critical parameters that will determine the required pressure to maintain a desired flow rate, namely, the solution viscosity and the intrinsic bone permeability.

First, we note that there is an inverse relationship between flow rate and the viscosity of the fluid. While there is significant support for the use of IO lines for fluid delivery, it should be noted that current medical standards use saline-based solutions with viscosities close to 1 cP; however, the viscosity of pRBCs used in DCR is estimated to be greater than 10 cP.[12] Since pRBCs are 10+ times more viscous than crystalloid solutions, it will require at least 10+ times the pressure to obtain the same flow rate as crystalloid in IO infusion.

Second, the intrinsic permeability factor is directly related to flow rate, so that as intrinsic permeability increases, flow rate increases. Conversely, lower intrinsic permeability lowers flow rate. To better understand the effects of intrinsic permeability on flow rates, we must establish the range of intrinsic permeability in our target population. The scientific community has established that there is a linear relationship between bone density and bone porosity and an exponential relationship between bone porosity and intrinsic permeability.[9,10]

The bone mineral density increases with age up to a peak density occurring in the early 20s. The soldier population is aged right at the peak of bone density for all races and sex. Beginning by 45 years of age, bone density decreases in all categories. Figure 1 plots the bone density changes as a function of age using data collected by the US Department of Health and Human Services, Center for Disease Control and Prevention.[13]

Since bone mineral density is easy to measure clinically and, as previously mentioned, there is a well-established linear relationship between mineral density and bone porosity, as seen in Figure 2,[14] we next need to establish the relationship between porosity and intrinsic permeability. We found two studies in the literature that describe the relationship using both experimental and theoretical models. Figure 3 was generated using results from both published reports[9,10] relating bone porosity to intrinsic permeability.

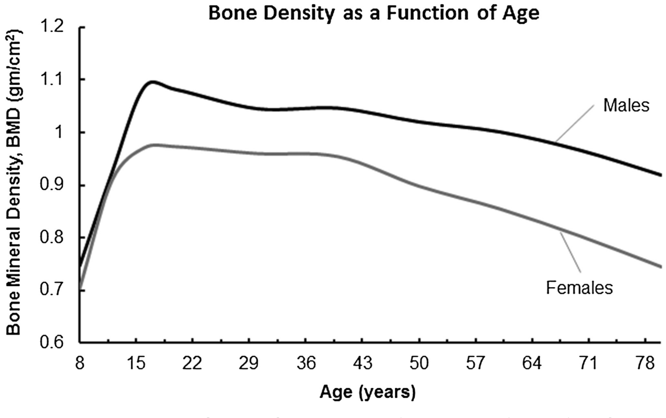

Figure 1. Average bone density as a function of age for the US population. The data for this graph was provided by the Center for Disease Control and Prevention. It is critical to note that most published research in animals and clinical studies for the delivery of blood product focuses on either the elderly (>75 years) or very young (<8 years). The bone density of those populations is at least 30% less than for 20-year-old to 34-year-old adults who make up the bulk of the military population.

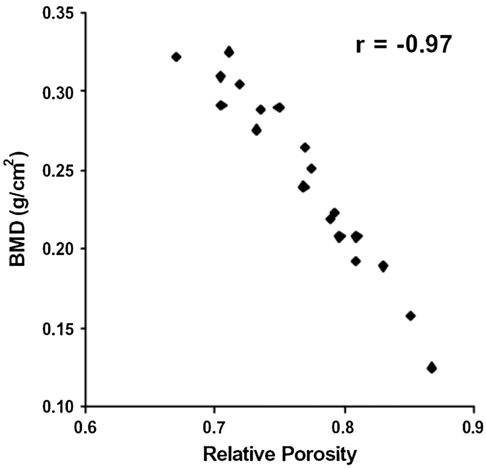

Figure 2. Established linear relationship between bone mineral density and bone porosity.

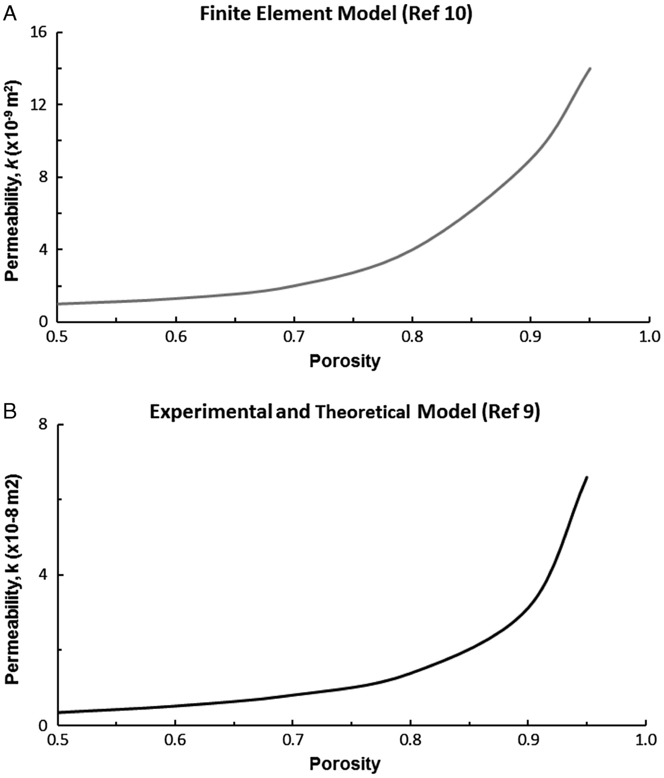

Figure 3. *A*, The relationship of permeability as a function of porosity developed using a finite element model.[10] *B*, The relationship of permeability as a function of porosity developed experimental values and theoretical models.[9]

Both the theoretical results and the experimental results show agreement in the shape of the curve. Although there is significant variability in the permeability ranges, previous studies have also reported large ranges in measured permeability.[11] Most importantly, the relationship between bone porosity and intrinsic permeability is exponential over the relevant human ranges. This exponential relationship and the relationship between bone density and bone porosity means that small increases in bone density can cause exponential decreases in intrinsic permeability. In adults, cancellous bone density can vary from 50% to 95%,[15] and the porosity of bone in the human femur is expected to double between the ages of 40 years and 80 years.[16] These changes of porosity and the relationship in Figure 3 indicate that there could be a greater than 10-fold decrease in permeability in military age casualties compared with the elderly.

Based on the Darcy's Law, the only parameter a medical practitioner has to adjust to increase flow rate in an IO system in DCR is pressure. Increases in pressure not only strain the connections in the infusion system itself but also increase shearing forces in the fluid. Shearing forces may cause hemolysis of the transfused blood, loss of oxygen carrying capacity, and consequent development of rhabdomyolysis. Presently, we are aware of only two studies that address this concern in IO blood transfusion.[17,18] In both studies, no hemolysis was seen, but the research model was an immature swine, and the bone density of immature swine in no way approximates the bone density of young adult humans.

CONCLUSION

DCR is the new paradigm for trauma resuscitation in both military and civilian populations. As of 2013, the key national organizations that set trauma resuscitation and vascular access guidelines recommend the use of IO access for transfusing blood when IV access cannot be established. Extrapolation from animal studies and undue generalization from human case reports at the extremes of age seem to form the basis for the recommendations. Two of the major manufacturers of IO technology also recommend the use of IO access for blood transfusion. In one case, the company's chief scientific officer, acknowledging the total lack of available scientific evidence, stated that IO use for blood transfusion is "better than nothing in most cases" (Philbeck T. personal communication, 2012). We disagree with this comment and go further to say that it actually could be far worse than nothing.

Based on the Darcy's Law and the resulting low flow rates of blood transfused into the IO space, nothing of substance can be achieved by transfusing blood via the IO route in DCR. Analysis of flow dynamics in the appropriate theoretical model of porous media reveals that flow rates through IO access can be markedly limited by the viscosity of the blood products and the permeability of cancellous bone in the IO space. Permeability creates an even greater obstacle to flow in the military-aged population. These limits push the pressure needed to attain flow rates adequate for DCR above the pressure levels tolerated by the infusion system and risk causing hemolysis.

Consequently, it would make much more sense to take notice of the 2006 and 2010 recommendations of the INS and have all medical personnel trained in the use of light or sound technologies to facilitate successful peripheral IV access and to avoid the IO route entirely when blood transfusion is required.

Based on clinical observation, the lack of clinical evidence in the medical literature, and the factors discussed herein, we postulate that maximum flow rates attainable for transfusion of blood products used in DCR via the IO route are simply inadequate for successful resuscitation.

Until studies in a representative population show the clinical success of the IO technique in DCR, current recommendations for the use of IO access for blood transfusion by ATLS and the INS should be modified to better reflect this scientific uncertainty.

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