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Direct markers of organ perfusion to guide fluid therapy: When to start, when to stop

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Up until now, the discussion in the literature as to the choice of fluids is almost completely restricted to the composition, with little to no attention paid to the importance of hemodynamic end points to achieve a desired optimal volume. The determination of fluid volume is left to the discretion of the attending physician with only surrogate markers as guidance the initiation and cessation of fluid therapy. In this article, we aim to discuss the available literature on existing clinical and experimental criteria for the initiation and cessation of fluid therapy. Furthermore, we present recent data that have become available after the introduction of direct in vivo microscopy of the microcirculation at the bedside, and discuss its potential influence on the existing paradigms and controversies in fluid therapy.

Introduction

For many years, fluid therapy has been a cornerstone in perioperative management and intensive care medicine to maintain organ function in a large variety of disease states [1,2]. The motives for fluid administration are diverse and include supplementation for fluid or blood loss, compensation for increased resistance to venous return with subconsequent reduction of preload, and maintenance of perfusion pressure under conditions of reduced vasomotor tone. Apart from supplementation of chemical components such as electrolytes and protein (-like) substances, the central idea behind fluid

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administration has always been the conceived restoration of cell homeostasis, in order to maintain organ function. In this concept, the final place of action of fluid therapy is assumed to be in the microcirculation, the vascular compartment where life-conditional processes, such as the exchange of oxygen and waste products, take place. It can be regarded as an organ representing a port way to the parenchymal cells.

However, due to practical limitations, the microcirculation remains elusive in clinical practice [3]. Instead, almost unrestrained efforts have been exerted to develop and validate surrogate end points for fluid resuscitation, based on the manipulation of systemic hemodynamic variables. Although such indirect end points have been successful to some extent, they have not been able to establish definitive start and stop criteria for fluid therapy [4]. This seems to be of utmost importance as both insufficient and excessive fluid administration have been associated with adverse outcome [5–7]. In addition to this view, the discussion in the literature as to the choice of fluids used for various categories of patients is almost entirely directed at the composition of these fluids, with little to no attention paid to the importance of hemodynamic end points to achieve a desired optimal volume. This issue has especially been a problem in recent large randomized trials where fluids are administered with no clear hemodynamic criteria for fluid administration and the determination of fluid volume is left to the discretion of the attending physician, an approach which is referred to in the literature as a pragmatic [8]. In this article, we aim to discuss the available literature on existing clinical and experimental criteria for the initiation and cessation of fluid therapy. Furthermore, we present recent data that have become available after the introduction of direct in vivo microscopy of the microcirculation at the bedside and discuss its potential influence on the existing paradigms and controversies in fluid therapy.

When do doctors start fluid therapy?

In general, there is a large variety of potential triggers that encourage doctors to start fluid administration.

"Clinical signs of impaired organ perfusion." Traditionally, clinical assessment of volume status is either based on macrocirculatory parameters, such as (orthostatic) hypotension and tachycardia, or parameters of peripheral circulatory perfusion, for example, capillary refill time, central-to-toe temperature gradient, and skin mottling [9–11]. Alternatively, clinicians observe perfusion-related organ function such as altered mental status, oliguria, and tachypnea. However, all of these clinical parameters lack specificity and may be explained by alternative causes, other than hypovolemia-related perfusion abnormalities. For example, tachycardia may be a sign of hypovolemia, but also be related to stress or sympathic overdrive.

"Laboratory markers." Elevated lactate levels are usually associated with an increased anaerobic metabolism and therefore a potential trigger for the restoration of perfusion deficits with fluid therapy. Although increased lactate is repeatedly associated with an inverse outcome, many alternative explanations other than hypoperfusion should be considered, for example, epinephrine-induced stimulation of the Na^+–K^+-ATPase pump, lipopolysaccharide-mediated enhanced lactate production or impaired lactate clearance [12]. Hemoconcentration, reflected by increased hematocrit, or protein concentration may also serve as a reason to initiate fluid administration.

"Static filling pressures." Over the past decades, static filling pressures have played a major role in the initiation of fluid therapy. Classically, pulmonary artery occlusion pressure and central venous pressure cutoff values have been advocated as a marker of left and right ventricular preload. Although more recent data have clearly demonstrated that this assumption appears to be erroneous, "optimizing" central venous pressure with fluid therapy is still part of current resuscitation guidelines [2,13,14].

"Dynamic indices." The use of dynamic indices is based on the assumption that the cardiac function of patients with impaired organ perfusion is on the steeper part of the Frank–Starling curve. Changes in these variables are established after a standardized fluid challenge or passive leg raise test. These indices include stroke volume optimization, reduction in stroke volume or pulse pressure variability (as a result of circulation–ventilation interaction), and changes in end-tidal carbon dioxide [15]. This is performed by transpulmonary thermodilution methods, noninvasive pulse-contour analysis of arterial wave forms, or by ultrasound. Although it is the assumption of the attending clinician that an increase