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Review Article

The Recent Development about Fluid Management in Patients under Surgical Stress

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ABSTRACT: In this narrative review, recent development about fluid management in surgical, trauma and critically ill patients are summarized. Fluid movement across vasculature has been described by Starling principle. However, classic Starling principle may not adequately account for the clinical data and revised Starling principle has been proposed. In this revised principle, transvascular fluid movement is significantly less than previously thought and is largely dependent on hydrostatic force and healthy glycocalyx. Previously, generation of non-functioning extravascular space (third space: 3rd space) has been implicated in the generation of surgery-induced hypovolemia. However, recent investigations clearly suggest that 3rd space does not exist and question the appropriateness of supplement 3rd space loss. Actually, restrictive fluid strategy disregarding 3rd space loss achived better patient outcome. Liberal administration of normal saline has been attributed to the development of hyperchloremic metabolic acidosis but recent data demonstrate that hyperchloremia may be cause renal damage. In this perspective, use of buffered solution is advocated.

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KEYWORDS: Starling principle, third space, hyperchloremia

Patients under surgical stress posed unique challenge to the attending physicians. These patients typically demonstrate hemodynamic instability that should be corrected in a timely manner. Understanding physiological rationale about circulatory physiology and fluid handling is indispensable for the proper management and recent investigations clearly demonstrate that part of the previous paradigm needs to be revised. In this narrative review, this author will focus on the new concepts about "Starling's hypothesis", "third space", and "chloride". The composition of commonly used fluid for surgical, trauma and critically ill patients is summarized in the Table 1 for reader's convenience.[1] Among them, there are two distinctive features; presence or non-presence of oncotically active particles and the composition of anions. Fluids containing oncotically active particles such as albumin and hydroxyethyl starch are summarized as colloid, while fluids without oncotically active particles are called either crystalloid or extracellular fluids. Crystalloids of which composition of anion are similar to plasma; chloride

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Table 1 Commonly used fluids for surgical, trauma and critically ill patients[1]

	Plasma	Colloid		Crystalloid	
		Natural colloid	Synthetic colloid	Unbalanced (unbuffered) solution	Balanced (buffered) solution
		4% albumin *	6% hydroxyethyl starch	0.9% NaCl	Lactate Ringer solution
Colloid oncotic pressure (mmHg)	25	25	25		
Osmolarity (mOsm)	291	250	308	308	281
Na (mmol/l)	135-145	148	154	154	131
K (mmol/l)	4.5-5.5				4
Ca (mmol/l)	2.2-2.6				2
Mg (mmol/l)	0.8-1.0				
Cl (mmol/l)	94-111	128	154	154	108
Bicarbonate (mmol/l)	28				
Lactate (mmol/l)	1-2				28

*: 5% albumin is available in Japan.[1]

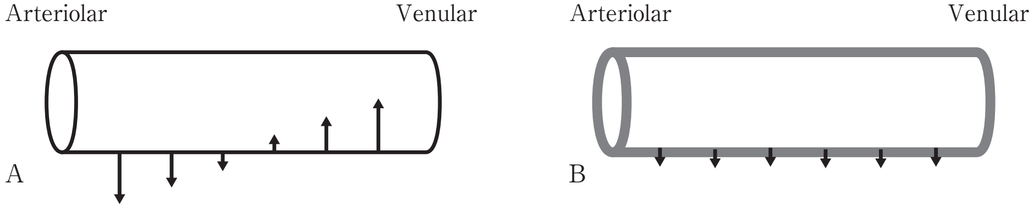

Fig. 1 Schematic presentation of original (A) and revised Starling principle (B).
Arrows indicate the direction and the quantity of fluid exchage across microvasculature. Thick line in the right panel represents glycocalyx.[7]

(Cl) and buffer anion such as bicarbonate, lactate or acetate, are called balanced solution or buffered salt solution. Zero point nine percent sodium Cl (normal saline: NS) solution corresponds to unbalanced or unbuffered salt (crystalloid) solution.

Revised Starling's hypothesis

The original Starling's formula describes the exchange of fluid across intravascular and extravascular space (Fig. 1A).[2]

$$Jv/A=Lp\ [(Pc-Pi)\ -\sigma\ (\pi c-\pi i)]$$

Jv: microvascular flow exchange, A: vascular surface area, Lp: Permeability index, Pc: capillary hydrostatic pressure, Pi: interstitial hydrostatic pressure, σ: osmotic reflection coefficient, πc: capillary oncotic pressure, πi: interstitial oncotic pressure.

Hydrostatic force comprises driving force for fluid filtration from intravascular to extravascular space and colloid osmotic pressure is the driving force for fluid reabsorption from extravascular space to intravascular space. Anatomically, fluid filtration is dominant at arteriolar side while fluid absorption is dominant at venular side due to the hydrostatic pressure gradient between arteriolar side to venular side. In this classic model, the distribution of fluid is dependent on its colloid osmotic pressure. Fluid without oncotic pressure (crystalloid) distributes throughout entire extracellular fluid space while fluid with same oncotic pressure to plasma (iso-oncotic colloid solution) distributes only in the intravascular space. Since interstitial space is about 3 times larger than intravascular space, only 25% of the crystalloid solution should remain in the intravascular space. Thus, the volume effect of crystalloid is supposedly 25% of iso-oncotic colloid solution under this paradigm.

However, such classic Starling principle can not address several important findings. First, the actual volume effect of crystalloid seems to be context-dependent and to exceed theoretical value in hypovolemic patients.[3] Actually, several studies indicated that the volume effect of colloid solution is only 1.5 times larger than crystalloid solution.[4, 5] Second, the corresponding anatomical features controlling permeability and osmotic reflection have not been elucidated in the classic Starling principle. Recent studies strongly indicate that endothelial glycocalyx, extracellular matrix on the luminal side of endothelial cells, serves as a barrier to the fluid exchange across microvasculature.[6]

To account for these advancements, revised Starling principle has been proposed (Fig. 1B).[7–9] As graphically presented in the Fig. 1, the net filtration is significantly smaller than the classic principle and occurs throughout the microvasculature. Such resistance is supposedly provided by healthy glycocalyx. Then, filtration is more dependent on the hydrostatic pressure and context-sensitivity of volume effect can be explained by this modification. Furthermore, colloid osmotic pressure dependent-fluid reabsorption has little effect on the total fluid exchange.

Although the clinical implications of revised Starling principle have not yet been established, several important suggestions have been proposed. First, hydrostatic pressure plays more important role than previously thought and unwarranted fluid administration may be less effective and possibly harmful. This issue is further discussed in the following chapter. Second, undisturbed glycocalyx is critical for the proper handling of fluid. Currently, several strategies have been proposed to protect glycocalyx against insults but remain in the experimental stage.[10] Further clinical studies are warranted to address this issue.

Third space

It has been well known that most surgical patients became hemoconcentrated after surgery. This finding clearly suggests intravascular volume is reduced. To account for this process, the concept of third space (3rd space) was proposed in the early 1960's by Shires and colleagues. They measured extracellular (fluid) volume (ECV) with tracer method and found that ECV was decreased.[11] Then, they divided ECV into intravascular space (first space: 1st space) and interstitial space (second space: 2nd space). As previously mentioned, clinical and experimental results suggest both 1st and 2nd space were decreased. Then, they conceptualized that surgical stress promotes the increase of non-functioning ECV and termed it "third space". The formation of 3rd space inevitably decrease the volume of functioning ECV and cause extensive shift from intravascular space to interstitial space (Fig. 2A). Under this paradigm, supplementation of decreased functioning ECV may attenuate the decrease of intravascular volume. Thus, crystalloid, which will distribute whole ECV, is liberally administered to compensate the reduction of circulating blood volume due to the 3rd space loss. The amount of 3rd space loss has never been quantitatively assessed, but it is assumed as high as 6 ml/kg/hr during upper abdominal surgery. This assumption is probably derived from the fact that such large quantity of crystalloid is necessary to achieve adequate urine output (1 ml/kg/hr) under traditional volatile agent-based anesthetic management. Consequentially, typical fluid balance during upper abdominal surgery without significant blood loss usually is 7–8 ml/kg/hr and cumulative fluid balance easily exceeds 5000 ml in extensive surgery.[10] Resultantly, such fluid is accumulated in the interstitial tissue and tissue edema is evident several days after surgery.

However, the existence of 3rd space and the rationale of liberal fluid strategy to supplement 3rd space has been recently questioned. First, previous studies that demonstrated decreased ECV had methodical flaws and recent studies using more technologically valid methods failed to demonstrate decreased ECV during surgery.[12] Contrarily, recent data convincingly demonstrated that the volume of ECV is highly proportional to the intraoperative fluid balance. Thus, reduced circulating blood volume may be balanced by the increased interstitial fluid and the evolution of the non-functioning of ECV is highly questionable (Fig. 2B).

Since the rationale of liberal fluid strategy using crystalloid was to supplement 3rd space loss, such practice may not be appropriate under our current knowledge. Furthermore, recent clinical data strongly suggest that positive fluid balance and increased interstitial fluid negatively affect the outcome of surgical patients.[13] From this perspective, it is quite understandable that the elimination of 3rd space supplementation by crystalloid may achieve better clinical outcome. Such strategy is termed as "restrictive fluid strategy" and the positive effects of such strategy on patient outcome after surgery have been reported ever since.[14, 15] This strategy also achieved

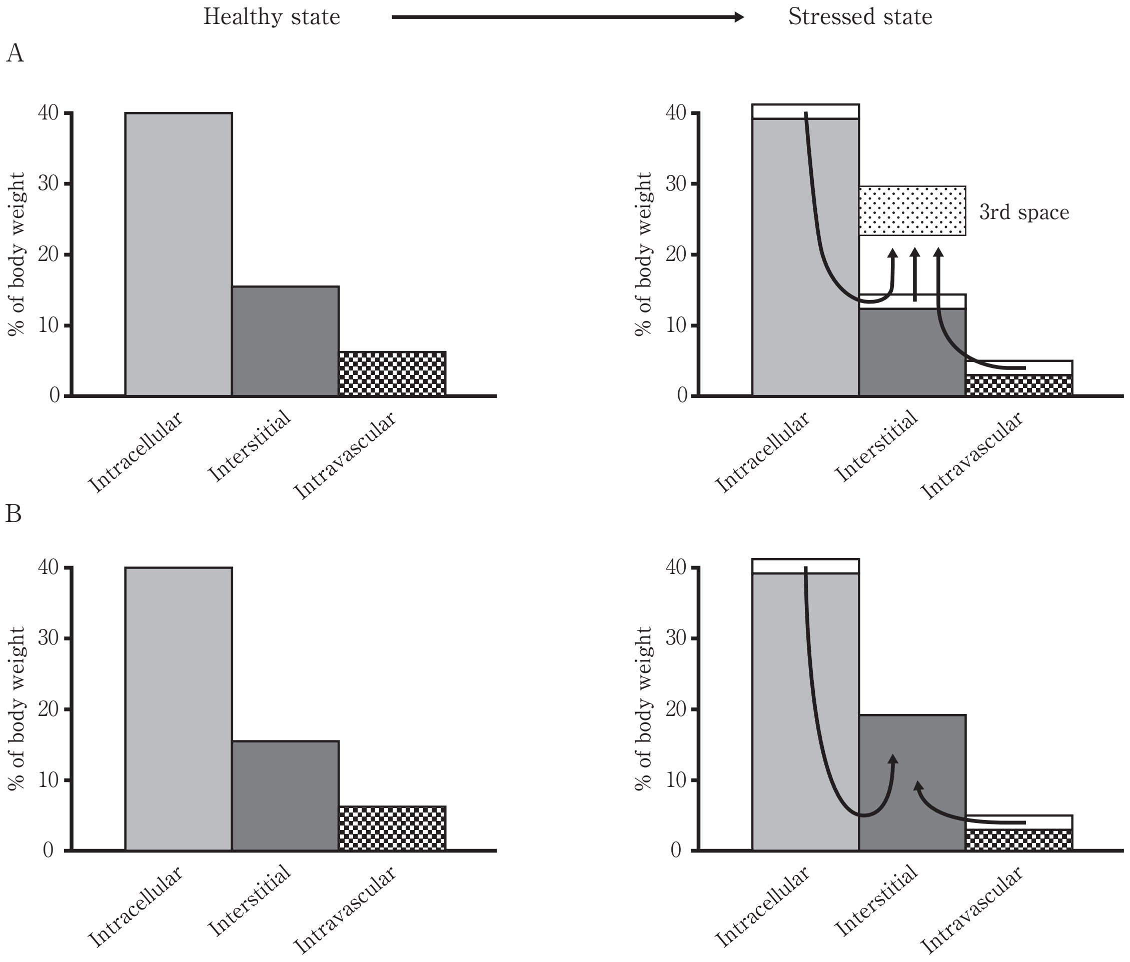

Fig. 2 Conventional (A) and current (B) understandings about the change of extracellular volume during surgical stress.
In each A and B, left and right figure represent healthy and stressed state, respectively. Curved arrows in the stressed state represent theoretical fluid movement between each fluid space.

improved outcome in critically ill patients with ventilatory support.[16] In conclusion, the existence of 3rd space is quite questionable and supplementation of such imaginary 3rd space with crystalloid lacks scientific validity. Recent evidence strongly suggests that the elimination of 3rd space supplementation improves outcome by reducing the edema-related complications.

Chloride

Traditionally, NS has been predominantly used for resuscitation. This is presumably based on the facts that NS is inexpensive, compatible with blood products because it lacks calcium and low risk of hyperkalemia because it does not contain potassium. However, the Cl concentration of NS is 154 mEq/l and exceeds the normal range of plasma Cl concentration. Thus, administration of large amount NS inadvertently causes hyperchloremia. Hyperchloremic metabolic acidosis has been acknowledged as a consequence of NS administration. This acid-base disturbance is best accounted for by physiochemical approach (Stewart approach).[17] In this approach, bicarbonate concentration is primarily determined by the balance between highly dissociable cations (Na, K, Ca, Mg) and anions (Cl and lactate). Such balance is represented by strong ion difference (SID) (Na+K+Ca+Mg-Cl-lactate) and the normal SID is approximately 40 mEq/l. On the contrary, SID of NS is zero and infusion of large amount of NS decreases SID and reduces the bicarbonate concentration and pH. However, most clinicians regard hyperchloremic acidosis as relatively harmless phenomenon and little attention has been paid to the negative consequences of un-physiological concentration of Cl.

However, recent investigations have demonstrated several important implications of excess administration of NS. For example, renal arterial blood flow velocity and cortical perfusion was significantly compromised after rapid infusion of 2 liter NS compared to balance solution in volunteers.18) Possible negative effects of NS administration or hyperchloremia are also demonstrated in the following four large retrospective studies.19–22) However, the prospective randomized trials about this issue provided mixed results.23, 24) Collectively, it may be prudent not to use NS exclusively to the patients who may be susceptible to renal damage and acid-base disturbances.

Many physicians may believe that NS is indicated in patients with end-stage renal disease. However, this notion is not sufficiently supported by the scientific evidence. Obviously, potassium increase due to exogenous source can be negated, however, plasma potassium may increase due to efflux of potassium from intracellular to extracellular space with concomitant influx of hydrogen ion when extracellular space becomes acidotic. In patients undergoing cadaveric renal transplantation, the serum potassium was comparable between patients who received saline and balanced solution containing potassium at least 4 hours after the start of these fluids.25) Although this finding may not always be applicable to all the patients who regularly undergo hemodialysis, proper balance between NS and balanced solution should be achieved when treating such special patient population.

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