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Research state of early fluid resuscitation and volume management in sepsis-associated acute kidney injury

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Abstract: Sepsis-associated acute kidney injury (SA-AKI) is a common and serious complication in patients with sepsis. Its pathogenesis is complex, involving multiple pathophysiological processes such as immune dysregulation, microcirculatory disturbances, and energy metabolism imbalances, with a clinical mortality rate of 35% to 67%. Current treatment strategies focus on early fluid resuscitation and precise volume management, although there is still controversy regarding these approaches. Research has shown that crystalloid fluids (especially balanced electrolyte solutions) may reduce the incidence and short-term mortality of SA-AKI. However, large-scale randomized controlled trials have not demonstrated significant differences compared to normal saline. Albumin, as a colloid solution, may improve tissue perfusion, but its concentration choices and suitable patient populations still require further verification. Hydroxyethyl starch and dextran injections have not been recommended due to safety concerns. In terms of volume management, traditional goal-directed fluid resuscitation (such as the 30 mL/kg fluid infusion) lacks clear survival benefits. However, fluid overload is closely related to adverse outcomes. Restrictive fluid strategies may reduce the risk of renal congestion but can increase the need for vasopressor drugs. Existing evidence does not support strictly limiting the initial resuscitation volume. Point-of-care ultrasound techniques offer a non-invasive tool for dynamically assessing venous congestion status (such as VExUS scoring), potentially reducing the risk of SA-AKI through optimized fluid management. Future approaches should combine biomarkers with multimodal monitoring to create individualized fluid management plans, balancing the need for early resuscitation against the risks of volume overload, to improve outcomes for patients with SA-AKI. This article provides a brief review on fluid resuscitation and volume management in SA-AKI patients.

Keywords: Sepsis; Acute kidney injury; Fluid resuscitation; Volume management; Vasoactive agents

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Sepsis-associated acute kidney injury (SA-AKI) is a heterogeneous syndrome of acute kidney injury directly caused by sepsis or indirectly by iatrogenic factors during sepsis treatment [1-2]. According to incomplete statistics, 25% to 45% of sepsis patients develop SA-AKI [3], and the mortality of patients with SA-AKI ranges from 35% to 67% [4].

The exact pathogenesis of SA-AKI remains unclear. It can occur in sepsis patients even without obvious hypoperfusion and hemodynamic instability [5]. Differences in the individual's underlying susceptibility to tissue and organ damage may determine the distinct pathophysiological mechanisms of SA-AKI. Therefore, scholars have proposed various theories to explain the

dissociation between structural and functional abnormalities observed in SA-AKI. The latest consensus currently recommends classifying SA-AKI into 5 types based on pathophysiological mechanisms and biomarkers [3]. Type I is caused by abnormal immune regulation, characterized by systemic and renal inflammation as well as complement activation [6]; type II involves activation of the renin-angiotensin-aldosterone system and mitochondrial dysfunction [7]; type III is related to the energy metabolism adaptation mechanism [8]; both type IV and type V are associated with microcirculatory dysfunction and changes [9], with slight differences in biomarkers. These injury mechanisms act on glomeruli, renal tubules, and podocytes, ultimately leading to the development of SA-AKI. Clinically, SA-AKI is divided into 3 phenotypes based on the body's tolerance. Type I is usually Kidney Disease Improving Global Outcomes (KDIGO) stage 1 with or without biomarker detection; type II is KDIGO stages 2-3 without biomarker detection; type III is KDIGO stages 2-3 with biomarker detection [3,10-11]. Novel biomarkers can assist in the early diagnosis of SA-AKI and prediction of its progression, facilitating the timely initiation of effective interventions to improve patient prognosis [2].

Currently, the prevention and treatment of SA-AKI include early fluid resuscitation and volume management, source control of infection, application of vasoactive agents, targeted drug therapy, and renal replacement therapy (RRT). This article aims to focus on the latest research status of early fluid resuscitation and volume management in SA-AKI prevention strategies.

1 Early fluid resuscitation

Early fluid resuscitation is crucial for preserving the microcirculation and macrocirculation in patients with sepsis. Currently, the crystalloids used clinically for resuscitation are mainly balanced crystalloids and normal saline. Colloids include albumin, synthetic colloids (e.g., hydroxyethyl starch) and dextran.

1.1 Choice of resuscitation fluids——crystalloids

Crystalloids are the first-line agents for sepsis resuscitation, which can improve circulation and increase tissue perfusion by enhancing cardiac output. In previous studies, patients resuscitated with normal saline had higher serum chloride levels and a significantly increased incidence of hyperchloremic metabolic acidosis [12]. Therefore, recent studies on fluid resuscitation have mainly focused on balanced crystalloids and normal saline. A meta-analysis evaluating the relationship between crystalloids and outcomes in critically ill patients showed that the balanced crystalloids group had lower in-hospital and 28/30-day mortality rates and incidence of acute kidney injury (AKI), but there was no difference in progression to requiring RRT. For most critically ill adult patients, balanced crystalloids should be preferred over normal saline [13]. Another meta-analysis also suggested that balanced crystalloids were more likely to reduce in-hospital mortality [14]. However, in a randomized controlled trial involving 10,520 critically ill patients, resuscitation with balanced crystalloids did not significantly reduce the 90-day mortality rate in critically ill patients [15]. In a 2022 multicenter randomized controlled trial published in the New England Journal of Medicine, there was no evidence that resuscitation with normal saline increased mortality or the incidence of AKI [16].

In studies on sepsis, some literature reported that resuscitation with balanced crystalloids reduced the incidence of sepsis-associated acute kidney injury (SA-AKI) [12], and the risk of major adverse renal events within 30 days was lower with balanced crystalloids than with normal saline [13]. Early use of balanced crystalloids in sepsis resuscitation may have a greater impact on survival, but the beneficial effects of balanced crystalloids were only observed in patients who started using them in the emergency department [17]. A secondary analysis of the Isotonic Solutions and Major Adverse Renal Events Trial (SMART) also suggested that sepsis patients resuscitated with balanced crystalloids had lower 30-day mortality [18]. Recently, patients resuscitated with balanced crystalloids were associated with better renal function recovery in a study of community-acquired SA-AKI [19]. However, the results of a 2024 single-center randomized controlled trial on fluid resuscitation in sepsis showed that there was no statistically significant difference in the incidence of major adverse renal events and other secondary outcomes within 28 days between sepsis patients resuscitated with balanced crystalloids or normal saline [20]. Thus, there is no consensus on which crystalloid to choose for resuscitation, and this remains a key research focus for SA-AKI in the future.

1.2 Choice of resuscitation fluid – albumin

During the body’s inflammatory process, the endothelial glycocalyx is damaged, vascular permeability changes, and a large amount of fluid extravasates. Supplementing crystalloids alone cannot achieve effective resuscitation and may further aggravate tissue edema. High-molecular-weight colloids induce selective expansion of the intravascular space via osmotic pressure, maintaining effective circulating blood volume. Previous studies have indicated that albumin use—whether as initial resuscitation fluid or as a supplement to crystalloid resuscitation—is associated with lower mortality [21]. Compared with crystalloid resuscitation, fluid resuscitation using albumin of different concentrations (especially 20% albumin) significantly reduces the 90-day mortality of sepsis patients and improves the prognosis of septic shock patients [22]. Albumin administration during resuscitation in sepsis patients better ameliorates tissue hypoperfusion [23]. A single-center retrospective study found that among septic shock patients, early albumin use did not differ in the number of vasopressor days compared to non-use, but

significantly shortened mechanical ventilation duration [24]. A meta-analysis including 58 studies suggested that albumin combined with crystalloids reduced sepsis mortality more effectively than hydroxyethyl starch combined with crystalloids [25]. Thus, the consensus report of the 28th Acute Disease Quality Initiative Working Group recommends albumin as the first choice if large-volume fluid therapy and colloid supplementation are required [3].

However, a UK-based multicenter sepsis-related study showed that crystalloid-only resuscitation had lower mortality than albumin plus crystalloids, with no benefit from early albumin application [26]. A recent multicenter, retrospective, inverse probability of treatment weighting cohort study found that 25% albumin use in patients with SA-AKI at admission may be associated with increased composite outcomes of RRT or in-hospital mortality, while 5% albumin did not elevate such risks [27]. Clearly, there is no consensus on albumin concentration, and further research is needed. Internationally, a multicenter randomized controlled trial verifying albumin's efficacy in early septic shock treatment is ongoing—setting 30 g/L albumin as the phased resuscitation target—whose results may guide future therapy [28].

1.3 Choice of resuscitation fluid – synthetic colloids and dextran

Although debate persists about resuscitation fluid types, hydroxyethyl starch and dextran have been identified to show a clearly link with allergic reactions, coagulopathy, and drug-induced AKI, which are no longer recommended for fluid resuscitation in sepsis patients [29].

2 Management of resuscitation volume

Fluid resuscitation is the cornerstone of sepsis treatment. While it can improve tissue perfusion and reduce the risk of prerenal AKI, it may also cause edema of organs and peripheral tissues. Intestinal edema impairs the intestinal mucosal barrier, leading to bacterial translocation, intra-abdominal infection, and damage to distant organs—thus accelerating the progression of sepsis. Pulmonary edema is associated with fluid overload, increased vascular permeability, and downregulation of Na^+-K^+ pump and aquaporin levels during AKI. It is prone to induce ventilator-associated lung injury (VALI), and even complicated by atelectasis, pneumonia, and acute respiratory distress syndrome (ARDS) [30]. Therefore, volume management is of critical importance.

2.1 Bundle strategy for fluid resuscitation (BUNDLE)

Previous studies have found that goal-directed fluid resuscitation therapy cannot reduce the need for renal replacement therapy (RRT) or improve mortality in patients with septic shock [31]. Thus, the Surviving Sepsis Campaign Guidelines 2021 [32] recommend implementing 1-hour and 3-hour BUNDLE: patients with hypotension or lactate ≥4 mmol/L should receive 30 mL/kg fluid resuscitation within 3 hours [32]. A recent single-center retrospective cohort study showed that completing 30 mL/kg fluid resuscitation within 2 hours may be associated with early shock reversal and lower 28-day mortality [33]. In a database-based cohort study, the survival group better implemented the 1-hour BUNDLE and used vasoactive agents to maintain blood pressure [34]. However, in a multicenter study involving 23 emergency departments in France and Spain for suspected sepsis patients, good implementation of the 1-hour BUNDLE (with 30 mL/kg fluid resuscitation) did not reduce in-hospital mortality [35]. The application of the 1-hour BUNDLE also did not benefit the survival rate of patients with cirrhosis complicated by septic shock [36].

2.2 Restrictive fluid eesuscitation and standard resuscitation strategy

Currently, the possible mechanism underlying SA-AKI is thought to involve redistribution of intrarenal blood flow, leading to local tissue ischemia and hypoxia in the kidney [37]. Higher fluid volumes may cause fluid overload, resulting in renal congestion and exacerbation of damage, which adversely impacts prognosis. Studies have shown that fluid overload is associated with poorer outcomes, significantly increasing 28-day mortality [38]. Each 1 L increase in fluid balance raises the risk of death by 1.19-fold [39]. A study included sepsis patients who had completed 6-hour resuscitation volumes, dividing them into a restrictive fluid group (fluid therapy given only when hypoperfusion signs appeared) and a liberal fluid group (continuous fluid therapy). Results indicated that the restrictive group had significant benefits in indicators such as 90-day severe adverse renal events, 90-day survival rate, and days without mechanical ventilation or RRT—suggesting that volume overload may influence the development and progression of SA-AKI [40]. Thus, some scholars have proposed restrictive fluid resuscitation strategies for sepsis. However, restrictive fluid resuscitation did not reduce 90-day mortality compared to standard resuscitation in a study of adult sepsis patients [41]. Another randomized controlled trial enrolled 1,563 sepsis patients, assigning them to restrictive or liberal fluid groups. The restrictive group used vasopressors earlier, more frequently, and for longer durations, but again showed no reduction in 90-day mortality [42]. Therefore, although evidence supporting 30 mL/kg fluid resuscitation is weak and primarily from observational studies, existing research does not support limiting initial resuscitation volume to below 30 mL/kg [43]. In conclusion, the optimal fluid management plan for sepsis patients remains uncertain. Clinicians should weigh the risks and benefits of fluid management at each stage for critically ill patients,

avoiding insufficient early resuscitation and fluid overload in the stable phase [44].

2.3 Volume management via bedside color Doppler ultrasound may reduce the incidence of SA-AKI

Bedside color Doppler ultrasound is widely used in the diagnosis and treatment of critically ill patients due to its advantages of non-invasiveness, rapidity, real-time monitoring, dynamic observation, and repeatability—especially in early resuscitation monitoring and optimization of fluid therapy regimens. The combination of inferior vena cava width, hepatic vein blood flow, portal vein pulsatility index, and renal vein impedance index is called the venous excess ultrasound score (VExUS), which has good diagnostic accuracy for renal and prerenal AKI [45]. VExUS score can accurately reflect venous congestion, with accuracy comparable to that of selective right heart catheterization measurements. An increase in VExUS score is clearly associated with the development of AKI in hospitalized patients [46]. A study performed bedside ultrasound examinations 3-6 hours after initial fluid resuscitation for sepsis. According to the KDIGO guidelines, the sepsis group was divided into AKI group and non-AKI group, and the AKI group was further divided into 3 subgroups. The results showed that VExUS score can evaluate the venous congestion status of sepsis patients after initial resuscitation. The combination of VExUS score and Sequential Organ Failure Assessment (SOFA) score has the highest predictive value for SA-AKI, while SOFA score and AKI stage are independent risk factors for 28-day mortality in SA-AKI patients [47]. Another study confirmed a significant correlation between changes in VExUS score and fluid balance as well as AKI stage: as renal function improves, VExUS score decreases accordingly. VExUS score can reliably indicate venous congestion and help guide the timing of clinical fluid negative balance management [48]. These studies suggest that early optimization of fluid resuscitation volume via VExUS score may reduce the incidence of SA-AKI.

3 Conclusion

To summarize, early fluid resuscitation and volume management in sepsis are closely related to the development and progression of SA-AKI. Crystalloids are the first-line treatment option for sepsis resuscitation. Although findings from studies on initial resuscitation with albumin are inconsistent, guidelines still recommend considering albumin for treatment. Despite weak evidence, existing studies do not support limiting the early resuscitation volume to below 30 mL/kg. Clinicians should weigh the risks and benefits of fluid management at each stage for critically ill patients, avoiding insufficient early resuscitation and fluid overload in the stable phase. VExUS scoring via bedside color Doppler ultrasound can optimize fluid resuscitation volume and reduce the incidence of SA-AKI.

Conflict of interest None

Reference

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·学术前沿·

脓毒症相关性急性肾损伤早期液体复苏和容量管理的研究现状

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摘要： 脓毒症相关性急性肾损伤(SA-AKI)是脓毒症患者常见的严重并发症，其发病机制复杂，涉及免疫调控异常、微循环障碍及能量代谢失衡等多重病理生理过程，临床死亡率为35%~67%。目前治疗核心包括早期液体复苏与精准容量管理，但其策略仍存在争议。研究表明，晶体液(尤其是平衡盐液)可降低SA-AKI发生率及短期病死率，但大规模随机对照试验未显示出其与生理盐水的显著差异；白蛋白作为胶体液可能改善组织灌注，但其浓度选择及适用人群仍需进一步验证，而羟乙基淀粉与右旋糖酐注射液因安全性问题已不推荐。容量管理方面，尽管传统目标导向液体复苏(如30 mL/kg液体输注)缺乏明确生存获益，但液体过负荷与不良预后密切相关。限制性液体策略虽减少肾脏充血风险，却可能增加血管活性药物需求，现有证据不支持严格限制初始复苏量。床旁超声技术通过动态评估静脉淤血状态(如VExUS评分)，为优化液体管理提供无创工具，可能降低SA-AKI发生风险。未来需结合生物标志物与多模态监测，制定个体化液体管理方案，平衡早期复苏与容量过负荷的矛盾，以改善SA-AKI患者预后。本文就SA-AKI患者的液体复苏及容量管理作一综述。

关键词： 脓毒症；急性肾损伤；液体复苏；容量管理；血管活性药物

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Research state of early fluid resuscitation and volume management in sepsis-associated acute kidney injury

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Abstract: Sepsis-associated acute kidney injury (SA-AKI) is a common and serious complication in patients with sepsis. Its pathogenesis is complex, involving multiple pathophysiological processes such as immune dysregulation,

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microcirculatory disturbances, and energy metabolism imbalances, with a clinical mortality rate of 35% to 67%. Current treatment strategies focus on early fluid resuscitation and precise volume management, although there is still controversy regarding these approaches. Research has shown that crystalloid fluids (especially balanced electrolyte solutions) may reduce the incidence and short-term mortality of SA-AKI. However, large-scale randomized controlled trials have not demonstrated significant differences compared to normal saline. Albumin, as a colloid solution, may improve tissue perfusion, but its concentration choices and suitable patient populations still require further verification. Hydroxyethyl starch and dextran injections have not been recommended due to safety concerns. In terms of volume management, traditional goal-directed fluid resuscitation (such as the 30 mL/kg fluid infusion) lacks clear survival benefits. However, fluid overload is closely related to adverse outcomes. Restrictive fluid strategies may reduce the risk of renal congestion but can increase the need for vasopressor drugs. Existing evidence does not support strictly limiting the initial resuscitation volume. Point-of-care ultrasound techniques offer a non-invasive tool for dynamically assessing venous congestion status (such as VExUS scoring), potentially reducing the risk of SA-AKI through optimized fluid management. Future approaches should combine biomarkers with multimodal monitoring to create individualized fluid management plans, balancing the need for early resuscitation against the risks of volume overload, to improve outcomes for patients with SA-AKI. This article provides a brief review on fluid resuscitation and volume management in SA-AKI patients.

Keywords: Sepsis; Acute kidney injury; Fluid resuscitation; Volume management; Vasoactive agents

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脓毒症相关性急性肾损伤(sepsis-associated acute kidney injury,SA-AKI)是一种由脓毒症直接导致或由脓毒症治疗期间医源性因素间接导致的急性肾脏损伤的异质性综合征[1-2]。据不完全统计,脓毒症患者并发SA-AKI的几率为25%~45%[3],并发SA-AKI的患者死亡率为35%~67%[4]。

SA-AKI的确切发病机制仍不清楚,即使在没有明显的低灌注和血流动力学不稳定的脓毒症患者中也会发生[5]。个体对组织和器官损伤的基础易感性的不同,可能决定了SA-AKI不同的病理生理机制。因此,为了解释SA-AKI中观察到的结构异常与功能异常的脱节,学者们提出了多种理论。目前最新的共识建议将SA-AKI依据病理生理机制和生物标志物分为5种类型[3]。Ⅰ型是免疫调控异常所致,表现为全身和肾脏炎症以及补体激活[6];Ⅱ型为肾素-血管紧张素-醛固酮系统激活和线粒体功能障碍[7];Ⅲ型为能量代谢适应机制[8];Ⅳ型和Ⅴ型均为微循环的功能障碍和变化[9],因生物标志物而略有区别。上述损伤机制作用于肾小球、肾小管和足细胞,最终可导致SA-AKI的发生。根据机体耐受程度的不同,临床上将SA-AKI分成3个表型。Ⅰ型通常为改善全球肾病预后组织(Kidney Disease Improving Global Outcomes,KDIGO)分期1期,有/无生物标志物检出;Ⅱ型为KDIGO 2~3期,无生物标志物检出;Ⅲ型为KDIGO 2~3期,有生物标志物检出[3,10-11]。新型生物标志物能协助早期诊断SA-AKI并预测进展程度,有助于及时启动有效干预措施,从而改善患者预后[2]。

目前SA-AKI的预防和治疗包括早期液体复苏和容量管理、感染源的控制、血管活性药的应用、针对性药物治疗和肾脏替代治疗(renal replacement therapy,RRT)。本文旨在重点介绍SA-AKI预防策略中早期液体复苏和容量管理的最新研究现状。

1 早期液体复苏

早期液体复苏对于挽救脓毒症患者的微循环和宏观循环非常重要。目前临床用于复苏的晶体液主要为平衡盐液和生理盐水。胶体液包括白蛋白、合成胶体(如羟乙基淀粉)和右旋糖酐。

1.1 复苏液体的选择——晶体液 晶体液是脓毒症复苏的一线手段,可以通过增加心输出量改善循环,增加组织灌注。既往研究中,接受生理盐水复苏患者的血清氯离子水平更高,高氯性代谢性酸中毒的发生率明显增加[12]。因此,最近液体复苏的研究主要围绕平衡盐液和生理盐水展开。一项评估晶体液与重症患者结局关系的荟萃分析提示,平衡盐液组的住院和28/30 d病死率以及急性肾损伤(acute kidney injury,AKI)发生率更低,但进展至需要RRT的情况无差异;对于大多数危重症成年患者,应优先使用平衡晶体液而非生理盐水[13]。一项荟萃分析也提示,平衡盐液降低住院死亡率的可能性更高[14]。然而,在一项包含10 520例重症患者的随机对照研究中,使用平衡盐液复苏没有显著降低重症患者90 d病死

率[15]。2022年新英格兰杂志的一项多中心随机对照研究中，也没有任何证据表明使用生理盐水复苏会增加病死率和AKI的发生率[16]。

在脓毒症的研究中，有文献报道使用平衡盐液复苏能降低SA-AKI的发生率[12]，使用平衡盐液复苏30 d内发生严重肾脏不良事件的几率低于生理盐水[13]。在脓毒症复苏早期使用平衡盐液可能对生存的影响更大，不过平衡盐液的有益效果仅在急诊抢救室就开始应用的患者中观察到[17]。等渗溶液和主要肾脏不良事件试验（isotonic solutions and major adverse renal events trial，SMART）的二次分析也提示脓毒症患者使用平衡盐液复苏有更低的30 d病死率[18]。最近，一项社区获得性SA-AKI的研究中，使用平衡盐液进行复苏的患者与较好的肾脏功能恢复相关[19]。然而，2024年一项单中心脓毒症液体复苏的随机对照研究结果表明，使用平衡盐液或生理盐水对脓毒症患者28 d内发生主要肾脏不良事件和其他次要结局的影响均无统计学差异[20]。由此可见，到底选择哪种晶体液复苏尚无定论，未来仍是SA-AKI的研究重点。

1.2 复苏液体的选择——白蛋白 机体炎症过程中内皮糖萼受损，血管通透性发生改变，大量液体外渗，仅补充晶体无法有效复苏，且可能进一步加重组织水肿，高分子量的胶体通过渗透压的作用引起血管内空间的选择性扩张，维持有效循环血量。既往研究提示，使用白蛋白无论是作为初始复苏液还是晶体液复苏的补充，都与较低的死亡率相关[21]。与晶体液复苏相比，使用不同浓度白蛋白，尤其是20%白蛋白进行液体复苏，可显著降低脓毒症患者90 d病死率并改善脓毒性休克患者预后[22]。脓毒症患者复苏时使用白蛋白，能更好地改善组织灌注不足[23]。在一项单中心回顾性研究中，脓毒性休克患者早期使用白蛋白组与未使用白蛋白组相比，使用升压药的天数无差异，但机械通气的时间明显缩短[24]。一项纳入了58项研究的荟萃分析提示，白蛋白联合晶体液复苏组比羟乙基淀粉联合晶体液复苏组更能降低脓毒症患者的病死率[25]。因此，第28届急性疾病质量倡议工作组共识报告建议，如果需要大量的液体治疗并补充胶体，可以将白蛋白作为首选[3]。

然而，英国的一项与脓毒症相关的多中心研究显示，单纯晶体液复苏与白蛋白联合晶体液相比的病死率更低，没有发现白蛋白早期应用带来益处[26]。近期一项多中心、回顾性、基于治疗概率倒数加权队列的研究发现，入院时存在SA-AKI的患者使用25%白蛋白可能与RRT或住院死亡率的复合结局增加相关，而5%白蛋白未增加上述风险[27]。可见，使用白蛋白的浓度尚无统一意见，仍需要进一步研究。国际上，一项验证白蛋白在脓毒性休克患者早期治疗有效性的多中心随机对照研究正在进行中，该研究以白蛋白30 g/L为阶段复苏目标，其结果可能会指导未来的治疗[28]。

1.3 复苏液体的选择——合成胶体和右旋糖酐 虽然目前用于复苏的液体类型仍存在争论，但是羟乙基淀粉和右旋糖酐与过敏反应、凝血功能障碍和药物诱导的AKI明确相关，已经不推荐用于脓毒症患者的液体复苏[29]。

2 复苏容量的管理

液体复苏是脓毒症治疗的基石，虽然可以改善组织灌注，降低肾前性AKI的风险，但也会导致器官和外周组织水肿。肠道水肿损害肠黏膜屏障，引起肠道细菌易位，导致腹腔内感染及远隔器官损害，加速脓毒症的进展。肺水肿与液体过负荷、血管通透性增加、AKI过程中钠-钾泵和水通道蛋白水平的下调有关，易引起呼吸机相关性肺损伤，甚至并发肺不张、肺炎和急性呼吸窘迫综合征[30]。因此容量管理至关重要。

2.1 液体复苏的集束化策略（BUNDLE） 既往研究发现，基于目标导向的液体复苏治疗不能降低脓毒性休克患者RRT需求和改善病死率[31]。因此，拯救脓毒症运动指南建议实施1 h和3 h的BUNDLE，其中出现低血压或者乳酸≥4 mmol/L的患者3 h内应给予30 mL/kg的液体进行复苏[32]。最近一项单中心回顾性队列研究发现，2 h内完成30 mL/kg液体复苏量，可能与早期休克逆转和较低的28 d病死率有关[33]。一项基于数据库的队列研究中，生存组更好地执行了1 h的BUNDLE和使用血管活性药维持血压[34]。然而，在法国和西班牙23个医院急诊科疑似脓毒症患者的多中心研究中，良好实施1 h的BUNDLE给予30 mL/kg液体复苏并没有降低院内病死率[35]。1 h的BUNDLE应用对肝硬化合并脓毒性休克患者的生存率也没有带来益处[36]。

2.2 限制性液体复苏和标准复苏策略 目前认为，导致SA-AKI的可能机制是肾内血流的重新分布，引发肾脏局部组织缺血和缺氧[37]，较高的液体量可能会造成液体过负荷，导致肾脏充血并加重损害，对预后造成不良影响。有研究指出液体过负荷与更差的预后相关，明显增加28 d病死率[38]；液体平衡

每增加1 L,死亡风险增加1.19倍[39]。一项研究纳入了已经完成6 h复苏量的脓毒症患者,根据后续液体治疗策略分为限制性液体组(出现低灌注迹象予以液体治疗)和自由液体组(持续液体治疗)。结果提示,限制性液体组在90 d发生严重肾脏不良事件、90 d生存率、未进行机械通气和RRT的天数等指标均有明显获益;提示容量过负荷可能影响SA-AKI的发生和发展[40]。由此,部分学者提出限制性液体复苏策略治疗脓毒症。然而,在一项成年脓毒症患者的研究中,限制性液体复苏策略和标准复苏策略相比,没有降低90 d病死率[41]。另一项随机对照研究中,1 563名脓毒症患者分为限制性液体组和自由液体组。结果提示,限制性液体组使用升压药的时间更早、更普遍且更长,同样没有降低90 d病死率[42]。因此,尽管支持30 mL/kg液体复苏的证据薄弱且主要来自观察性研究,但现有的研究并不支持将初始复苏量限制在30 mL/kg以下[43]。总之,脓毒症患者的最佳液体管理方案目前仍不确定,临床医生应考虑重症患者每个阶段液体管理的风险和益处,避免早期复苏不足和稳定期液体过负荷[44]。

2.3 通过床旁彩超进行容量管理可能减少SA-AKI的发生 在早期复苏监测并优化液体治疗方案中,床旁彩超因具备无创、快速、实时、动态和可重复的优势,广泛应用于重症患者的诊疗。下腔静脉宽度、肝静脉血流、门静脉脉动指数和肾静脉阻抗指数相结合,被称为静脉充盈超声评分(venous excess ultrasound score,VExUS),对肾性和肾前性AKI有较好的诊断准确性[45]。VExUS评分能准确反映静脉淤血情况,其准确性与选择性右心导管检查测量结果相当,分值的升高与住院患者发生AKI明确相关[46]。有研究在脓毒症液体初始复苏治疗后3~6 h行床旁超声检查,按照KDIGO指南将脓毒症组分为AKI组和非AKI组,并将AKI组分为3个亚组。结果显示,VExUS评分可评估脓毒症患者初始复苏后静脉淤血状态,VExUS评分和序贯器官衰竭评估(Sequential Organ Failure Assessment,SOFA)评分的联合对SA-AKI的预测价值最高;SOFA评分和AKI分期是SA-AKI患者28 d死亡的独立危险因素[47]。另一项研究也证实VExUS评分的变化与液体平衡和AKI分期之间存在显著相关性,随着肾功能的改善,VExUS评分也有所下降;VExUS评分能够可靠地显示静脉淤血,并有助于指导临床进行液体负平衡管理的时机[48]。以上研究提示,通过VExUS评分早期优化液体复苏量,可降低SA-AKI的发生率。

3 结 语

综上所述,脓毒症早期液体复苏和容量管理与SA-AKI的发生和发展密切相关。晶体液是脓毒症复苏的一线治疗选择,尽管白蛋白进行初始复苏的研究结果不一致,指南仍建议可以考虑使用白蛋白进行治疗。尽管证据薄弱,但现有的研究并不支持将早期复苏量限制在30 mL/kg以下。应考虑重症患者每个阶段液体管理的风险和益处,避免早期复苏不足和稳定期液体过负荷。床旁彩超进行VExUS评分可优化液体复苏量,降低SA-AKI的发生率。

利益冲突 无

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