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EDITORIAL

Does this critically ill patient with oliguria need more fluids, a vasopressor, or neither?

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Introduction

Oliguria is often viewed as an alarming sign of renal "hypoperfusion". It frequently triggers hemodynamic interventions such as fluid and vasopressor therapy with the aim of improving systemic hemodynamics and restoring renal perfusion and eventually renal function. However, oliguria does not always point to renal hypoperfusion. Faced with an oliguric patient, intensive care unit physicians should answer the following questions: Is oliguria related to renal hypoperfusion? Will the patient respond to fluids or a vasopressor and which treatment is most appropriate? Can undue treatment cause harm?

Understanding the cause of oliguria

Various physiologic or pathophysiologic mechanisms have been proposed for acute oliguria, including: (1) a stress response with increased release of antidiuretic hormone unrelated to kidney perfusion or damage and with maintained glomerular filtration rate (GFR), (2) reversible renal hypoperfusion due to low cardiac output (hypovolemia or myocardial dysfunction) or due to vasoplegic hypotension (below the autoregulatory threshold or with disturbed autoregulation), (3) established/ongoing renal damage resulting from ischemia, inflammation, mitochondrial dysfunction, cell cycle arrest, or (4) a combination of these [1]. In the setting of experimental hyperdynamic sepsis, Langenberg et al. reported large reductions in GFR and urine output despite elevated renal blood flow (RBF), pointing to renal dysfunction that is not related to a perfusion problem [2]. Also in patients with established acute kidney injury (AKI) there appears to be a dissociation between RBF and GFR [3].

In view of the absence of reliable bedside measurements of RBF and GFR, identifying the cause of oliguria in clinical practice is mainly based on the clinical context. The cause of oliguria can be obvious in some typical situations of overt fluid losses or heart failure in which the choice of adequate intervention appears evident. In critically ill patients, however, the complexity of the mechanisms underlying oliguria generally requires clinical judgment (Fig. 1).

When to give fluids?

After hypotension, oliguria is the second-most frequent trigger of fluid challenges (FC) [4]. However, fluids are only useful if the patient's circulation is fluid-responsive (i.e., when the administration of fluids will lead to an increase of cardiac output) and if the kidney is also still fluid-responsive (i.e., when reversible hypoperfusion with increased tubular reabsorption is the cause of the oliguria) (Fig. 1). Over recent years, several indices of fluid-responsiveness have been validated and introduced into clinical practice. However, determining whether the kidney is fluid-responsive may be more difficult.

The use of urinary biochemical indices is often quoted in textbooks as a means to identify reversible AKI due to hypoperfusion. However, the performance of such indices to predict the reversibility of AKI and consequently the usefulness of further hemodynamic optimization in critically ill patients have proved to be disappointing [5]. Legrand et al. studied the usefulness of urinary indices measured at the time of oliguria to predict renal response

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Tweet Careful clinical adjudication is required before giving fluids or vasopressors to reverse oliguria in critically ill patients.

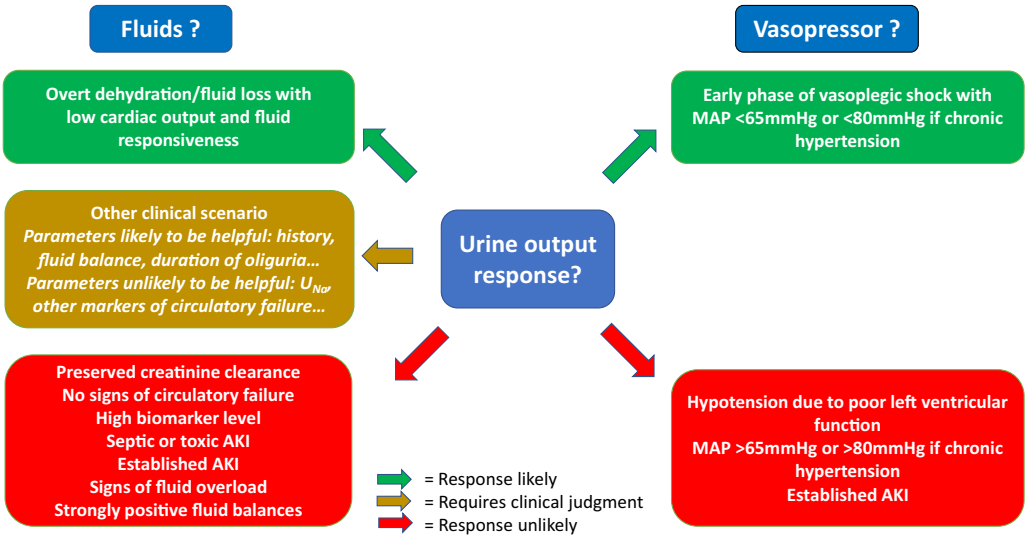

Fig. 1 Parameters of clinical judgment for the management of critically ill patients with acute oliguria. *AKI* Acute kidney injury, *MAP* mean arterial pressure, U_{Na} Urine sodium

to FC among critically ill patients [6]. These authors reported that FC reversed oliguria in only one-half of the patients and that neither urinary sodium or fractional excretion of sodium or urea were good predictors of renal response to FC [6].

Several published studies illustrate the dissociation between systemic and renal hemodynamics and the difficulty in predicting renal responses [increase in urine output (UO)] to fluid administration from systemic hemodynamic responses [6–9]. A systematic analysis of studies comparing different approaches to guide resuscitation (mainly in surgical patients) shows that the use of UO as an hemodynamic target results in a paradoxical higher incidence of AKI [7]. In the "PROCESS" trial, patients managed with early goal-directed therapy or standard protocolized care received more fluids and more vasopressors and/or dobutamine [10]. Although they achieved a significant higher mean arterial pressure (MAP) at the end of resuscitation, the incidence of AKI was not reduced compared to a control group [10].

It should be acknowledged that none of the above-mentioned studies predicting/evaluating renal responses to fluids have been performed in the rescue phase of shock, when responses to fluid may be different. However, outside the initial resuscitation phase, the administration of fluids should only be considered if they have the potential to increase cardiac output and if the presence of reversible kidney hypoperfusion can be assumed. The latter assumption may require substantial clinical adjudication (Fig. 1).

When to give a vasopressor?

The importance of perfusion pressure for kidney function is suggested by several large observational trials showing an association between the duration and severity of hypotension and subsequent development of AKI. Because RBF and GFR are normally autoregulated they can be maintained in the presence of decreased renal perfusion pressure. The lower limit of autoregulation of RBF in humans has not been clearly established, but it is increased in patients with chronic arterial hypertension. It is also not clear whether autoregulation is maintained in critically ill patients and what the impact is of vasoactive drugs on the mechanisms underlying autoregulation.

Vasopressors are often administered to patients with vasodilatory hypotension. Variable renal responses have been observed in vasodilatory shock, including no change in UO [11, 12], increase in UO but not in the GFR [13], and increase in both UO and GFR [14–16]. The renal response to an increased MAP probably depends on the baseline MAP. Studies reporting a positive effect of vassopressors on kidney function started at lower MAP, i.e., below the lower autoregulatory threshold. Of note, none of these studies showed that renal function is further enhanced by increasing MAP to >75 mmHg. A large randomized trial indeed did not establish a survival or renal benefit from increasing MAP to 80–85 mmHg in septic shock patients, except in the subgroup of patients with chronic hypertension for whom a significant renal benefit was found [17]. It should be acknowledged that most of the patients

in the lower MAP target (65–70 mmHg) group had a MAP of >70 mmHg. The trial therefore does provide evidence that a MAP of 65–70 mmHg is safe for the kidney [17].

When not to give fluids or a vasopressor to oliguric patients?

The dissociation between systemic hemodynamics and UO suggests a predominant role of non-hemodynamic causes of decreased kidney function, particularly in sepsis. Potential underlying mechanisms include intrarenal shunting, inflammation with impaired microcirculation, mitochondrial dysfunction, and cell cycle arrest. High levels of biomarkers of kidney damage may be helpful in confirming or refuting these non-hemodynamic causes [18]. In patients with oliguria based on these pathophysiologic mechanisms, further fluid resuscitation will not benefit the kidney. Thus, in patients with overt septic AKI and after the initial fluid resuscitation, further fluid boluses are not warranted. On the contrary, unnecessary fluids may even be deleterious for the kidney [19], and signs of fluid overload should be followed closely (Fig. 1). The targeting of higher MAP with vasopressors may also cause harm (cardiac arrhythmia or excessive vasoconstriction) [17].

Consequences for clinical practice

Oliguria is an overused parameter to guide resuscitation and must always be interpreted within the clinical context (Fig. 1). Of note, the 2016 version of the "Surviving Sepsis Campaign" no longer mentions a UO of ≥0.5 mL/kg/h as a goal of resuscitation [20]. Isolated oliguria without signs of vasoplegia, hypovolemia, or low cardiac output is unlikely to be explained by a systemic hemodynamic cause and must not evoke the administration of additional fluids or vasopressors. Oliguria should also not trigger further hemodynamic interventions in the clinical setting of established AKI. In all other patients, deciding on fluid challenges in response to oliguria will require a careful integration of the patient's history, systemic hemodynamics, fluid responsiveness, signs of dehydration or fluid overload, information on antecedent fluid losses and fluid balances, and duration of oliguria [1]. Oliguria resulting from vasodilatory hypotension should preferably be treated with a vasopressor. However, a MAP of 80–85 mmHg as target does not seem to be a beneficial strategy, except in patients with chronic hypertension.

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Compliance with ethical standards

Conflicts of interest
The authors declare that they have no conflicts of interest to declare.

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