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WHAT'S NEW IN INTENSIVE CARE

The 10 false beliefs in adult critical care nephrology

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1. Acute tubular necrosis is the main histopathologic finding in AKI

Acute tubular necrosis (ATN), a histological pattern observed after ischemic insult, is considered the most frequent cause of any form of acute kidney injury (AKI) despite the absence of extensive histological data. This belief derives from previous observations of ATN in biopsies of trauma patients. ATN is, however, uncommon in AKI (Fig. 1) and it does not accurately reflect the morphological changes during prolonged warm ischemia followed by reperfusion [1]. In the majority of cases, AKI in the critically ill patient is a complication of sepsis and major surgery. In such cases, ATN is uncommon (limited and sparse) and other pathophysiological non-ischemic mechanisms are involved as suggested by a lot of experimental data [2].

2. Decreased renal blood flow is the leading cause of AKI during sepsis

Renal hypoperfusion is considered one of the leading causes of AKI in sepsis via a mechanism of renal hypoxia but, although renal blood flow (RBF) is difficult to investigate in humans [3], data from animal models of hyperdynamic sepsis have shown that AKI occurs in the context of increased RBF and a reduction of renal conductance (renal vasodilatation) [4]. Available data in human sepsis are limited and often unreliable and, in many cases, RBF during sepsis does not correlate with renal function [5]. The increased RBF during hyperdynamic sepsis matches well with the paucity of ATN in septic AKI. In addition, microcirculatory dysfunction, including convective shunting of oxygen and decrease in capillary density, and filtration of inflammatory mediators (cytokines, chemokines, complement fragments) which may exert toxic effects on tubular cells, may contribute to renal dysfunction even in case of increased RBF [6].

3. Fluid challenge is always recommended in patients with oliguria

Fluids are commonly administered to ICU patients to improve hypotension, hypoperfusion, and oliguria in the process of hemodynamic optimization. Renal failure secondary to factors compromising renal perfusion was previously identified as pre-renal AKI, which today has to be considered a significantly flawed pathophysiologic concept [7]. In fact, renal hypoperfusion can be secondary to decreased renal arterial flow due to inadequate cardiac preload (i.e., hypovolemia) or to impairment of cardiac function (i.e., heart failure, HF). These two conditions, characterized by poor renal perfusion (and then theoretically "pre-renal" by definition) differ by a crucial point: one is fluid responsive [increase of cardiac output after fluid loading, for which central venous pressure (CVP) is a poor predictor] while the other is not. On the contrary, fluids administered in conditions where the CVP is increased, such as diastolic heart failure or right ventricular failure, are likely to compromise renal function through systemic venous congestion (congestive kidney failure). When congestion is present, fluid loading and positive fluid balance are predictors of kidney dysfunction compromising the transrenal pressure gradient [8]. Thus, treatment should be adjusted to individual conditions prior to start fluid administration and CVP may help the clinician to suspect the venous contribution to AKI. A fluid bolus should not represent the single "one size fits all" response to AKI.

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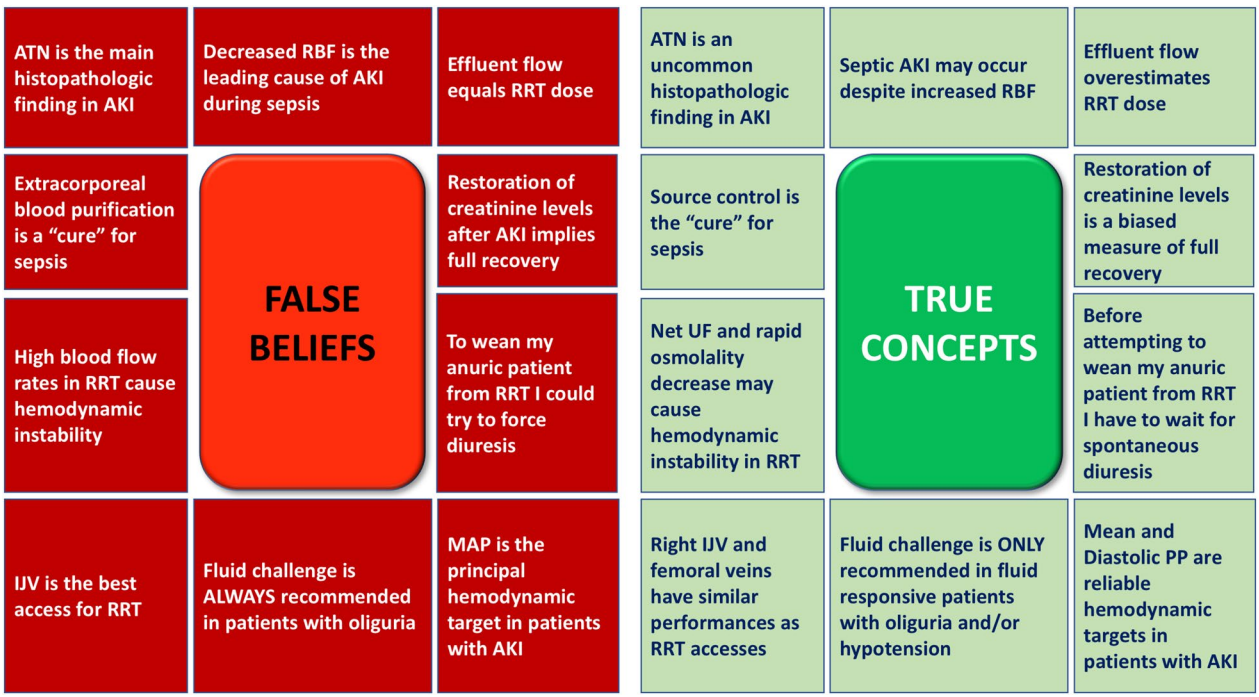

Fig. 1 Graphic representation of false beliefs and true concepts. ATN acute tubular necrosis, AKI acute kidney injury, RBF renal blood flow, MAP mean arterial pressure, UF ultrafiltration, RRT renal replacement therapies, IJV internal jugular vein, PP perfusion pressure

4. Mean arterial pressure is the principal hemodynamic target in patients with AKI

Despite large randomized trials suggesting to target mean arterial pressure (MAP) of 65 mmHg after fluid resuscitation in patients with septic shock [9] in order to guarantee organ perfusion pressure, there is little evidence that MAP adequately represents kidney perfusion. It has been demonstrated that, in terms of perfusion pressure, diastolic perfusion pressure (DPP), calculated as diastolic arterial pressure (DAP) − CVP, is associated with the development of AKI. Low DAP, high CVP [10], and low mean perfusion pressure (MPP = MAP − CVP) were associated with septic AKI while MAP was not [11]. Elevation of CVP, and/or decrease in DAP, seems to be a key determinant of kidney dysfunction. Moreover, the change in DAP is believed to correlate with alteration of vascular tone. In this light, since decreased DAP is associated with AKI, vasopressors may be considered for its prevention/treatment.

5. Creatinine level restoration after AKI implies full renal recovery

Full recovery from AKI is generally defined as the return of serum creatinine (sCr) below the threshold of AKI according to the KDIGO criteria [12]. This definition has important limitations. Baseline sCr is required to distinguish non-recovery from pre-existing chronic kidney disease. Most recent sCr preceding acute illness or its back-calculation with formulas can be inaccurate. SCr at ICU admission is frequently altered by the dilution effect of volume resuscitation. Tubular secretion of creatinine, also affected by drugs, may contribute to the overestimation of glomerular filtration rate. Most importantly, SCr is influenced by muscle mass and protein intake, liver disease, and rhabdomyolysis. Muscle mass frequently decreases, especially in patients with prolonged ICU stay, and causes a significant bias between sCr values and actual measured creatinine clearance [13].

6. High blood flow rates in extracorporeal therapies cause hemodynamic instability

Extracorporeal therapies (ET) may impact hemodynamics in different ways. Priming the extracorporeal circuit with patient's blood without reinfusing the priming solution causes a relative hypovolemia. Net ultrafiltration rate exceeding the rate of intravascular refilling leads to hypovolemia [14]. Vasoactive drugs dilution/removal during ET may decrease serum concentration and therapeutic effect. Sudden decrease in blood osmolality during intermittent hemodialysis has been shown to be a risk factor for hemodynamic worsening. Blood flow rate is never responsible for hemodynamic instability since blood runs in a veno-venous closed circuit. At steady state, the amount of blood withdrawn by the machine is reinfused to the patient in the same time unit.

7. Jugular vein is the best access for renal replacement therapy

According to KDIGO guidelines, the right internal jugular vein (IJV) should be the first-choice access for renal replacement therapy (RRT) [15]. Catheters in the right IJV have a straight short course into the right brachiocephalic vein and cavo-atrial junction, likely allowing the best rheological performance. Catheters positioned in the left IJV may have a curved shape and they need to be longer to reach the right atrium: the flow performance (especially when blood is drawn from left brachiocephalic vein) might be inadequate. However, bedside practice and some available literature [16] suggest that, in non-obese patients, femoral cannulation for RRT could be similar to right IJV in terms of infection, dysfunction, or side effects.

8. Effluent equals ET dose

When a small solute's sieving coefficient equals 1, and full saturation of dialysate occurs during dialysis, the effluent flow equals treatment dose (or clearance (K)) only in case of post-dilution continuous veno-venous hemofiltration and low flow continuous veno-venous hemodialysis. In all other cases (intermittent hemodialysis or slow extended dialysis, predilution hemofiltration, or hemodiafiltration) and for solutes with molecular weight higher than 500 Da the statement is incorrect and effluent rate may overestimate delivered dose. Furthermore, the concept of RRT dose should include both "instantaneous K" and the effective time in which this is applied. Downtime may in fact create a mismatch between prescribed and delivered treatment dose.

Hence, by slightly overprescribing the RRT dose based on effluent flow rate (i.e., 30 ml/kg/h), the target dose actually delivered to the patient (i.e., 20 ml/kg/h) can be reliably achieved [17].

9. ET is a "cure" for sepsis

In spite of several positive experimental observations, no clinical trials have shown significant effects of ET on mortality in patients with sepsis and multiple organ failure [18]. The rational to remove "bad" solutes (mediators, cytokines, etc.) restoring the *milieu intérieur* is the basis for a variety of ET. The vast heterogeneity of pathogens, hosts, and their interaction may, however, explain the difficulty to find an effective ET in the general population. Different techniques should be adapted to specific patients along the lines of precision medicine. However, with the exception of endotoxin, removal of mediators by ET is still completely unspecific. The adverse effects of unselective removal of mediators (which may be good or bad) are still insufficiently investigated. While ET can only be considered "adjunctive therapies" aiming to affect the immune system during sepsis [19], antibiotic therapy and infection's source control remain the mainstay of sepsis treatment. The control of acidosis and fluid balance are probably the main clinical targets when ET are prescribed to septic patients with anuria. The most effective ET will never be effective in the presence of an uncontrolled source of infection.

10. I want to wean my anuric patient from RRT: let's stop the treatment, give volume, and administer a big bolus of loop diuretic

When the multiple organ dysfunction of a critically ill patient with severe AKI supported by ET improves (e.g., vasopressor support and mechanical ventilation are not needed anymore, and temperature and laboratory analyses are normalized), anuria may still be persistent. Since effective dialysis weaning protocols have never been described and concern about the evolution of AKI into a chronic renal condition is a major question, several attempts to "force" restoration of urine output can be seen in clinical practice. As a matter of fact, there is not a specific "deadline" for the kidneys to recover and no available therapeutic strategy. The only variables retrospectively associated with successful interruption of ET in the ICU are the recovery of a spontaneous urine volume (during dialytic treatment) above 400 ml/day in the absence of diuretic therapy, a 2-h creatinine clearance within 12 h of RRT cessation above 23 ml/min, and 24-h urinary creatinine excretion (despite diuretic use) of at least 5.2 mmol [20]. Further prospective studies should be conducted in RRT weaning.

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Compliance with ethical standards

Conflicts of interest

All authors state that they have no conflict of interests.

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