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Review

Oliguria in critically ill patients: physiological or pathological?

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ABSTRACT

Urine output (UO) is a major clinical sign, available at the bedside for all patients, all over the world. Currently, oliguria is defined according to the KDIGO guidelines as a UO < 0.5 mL/kg/h over 6 h. The threshold was originally selected by expert consensus and has since been associated with adverse outcomes. However, the optimal cut-off remains uncertain and its bedside relevance is regularly challenged by clinicians. Observational studies have suggested that transient or mild oliguria may not consistently be associated with adverse outcomes. Indeed, mild oliguria may capture episodes of physiological water retention rather than pathological kidney injury with structural damage. However, oliguria remains one of the main triggers for fluid or diuretic administration in intensive care units.

Improving the understanding of oliguria at the bedside and its influence on clinical decisions requires a thorough knowledge of the physiological mechanisms underlying urine formation and the pathophysiology of oliguria. In this review, we describe the process of urine formation and explain the different physiological and pathological mechanisms leading to oliguria. We further discuss how pathological and physiological oliguria can be differentiated at the bedside, highlighting the role of clinical tools, biomarkers and imaging techniques. Finally, we examine how this distinction may inform clinical decision making, and guide interventions.

Background

Urine output (UO) is a major clinical sign, readily available at the bedside for all patients, all over the world. Low UO, or oliguria, can inform on illness severity and prognosis as demonstrated by its inclusion in most commonly used severity scores such as SOFA-2 or SAPS-II [1,2]. Oliguria is reported in up to 75% of critically ill patients and commonly triggers medical interventions such as fluid or diuretic administration [3,4].

For many decades, oliguria definition was not consensual but a urine output <400–500 ml within 24 h was generally considered pathological. This threshold came from small studies conducted on healthy volunteers in the mid-20th century [5,6]. In those studies, subjects were submitted to prolonged fasting and water deprivation while undergoing repeated assessment of urine and plasma osmolality. Maximal urine osmolality was 1200–1400 mOsm/kg and under conditions of maximal water retention, the minimal urine volume required to excrete the daily solute load was 500 ml/day. Because this threshold relied on an assumed minimal solute load in healthy fasting subjects, it cannot be directly extrapolated to critical illness. Over the following decades this daily value was replaced by an hourly value normalized to body weight allowing to identify AKI earlier, in real-time, and to apply the definition in a paediatric population [7]. In 2004, the Acute Dialysis Quality Initiative (ADQI) consortium, proposed the first consensus definition of acute kidney injury (AKI) and oliguria. In this definition, oliguria was defined as a UO < 0.5 mL/kg for 6 h [7]. This weight-based hourly threshold was not equivalent to the previous definition: 0.5 ml/kg/h corresponds to 960 ml/day in an 80 kg adult. Subsequent iterations of this definition have left that threshold unchanged [8,9]. Thus, the current definition for oliguria is not primarily derived from prognostic studies or pathophysiological data obtained in critically ill patients and its bedside relevance to predict outcomes or pathophysiological mechanism is regularly questioned by clinicians. Supporting this view, observational studies have suggested that transient or mild oliguria may not consistently be associated with adverse outcomes, such as mortality or long-term renal dysfunction [4,10,11]. Indeed, mild (<0.5 mL/kg/h for 6–12 h)

Abbreviations: AKI, Acute kidney Injury; GFR, Glomerular Filtration Rate; KDIGO, Kidney Disease Improving Global Outcomes; ICU, Intensive Care Unit; RRT, Renal Replacement Therapy; UO, Urine output.

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oliguria may capture episodes of physiological water conservation rather than pathological kidney injury.

To improve the understanding of oliguria at the bedside and its implications for clinical decision making, a thorough knowledge of the physiological mechanisms governing urine formation and the pathophysiology of oliguria is essential. In this review, we describe the physiological processes underlying urine formation and explain the mechanisms leading to oliguria. Building on a previous narrative review [12], we propose a more detailed and updated approach for distinguishing pathological from physiological oliguria at the bedside. We also propose a three-level framework linking clinical triggers, systemic responses and renal consequences, recognizing that mechanisms may coexist and interact and that physiological and pathological oliguria are not mutually exclusive states. Finally, we discuss how this framework may inform therapeutic actions.

Physiological determinants of urine output

The production of urine by the kidneys involves two main steps that occur within the nephrons: glomerular filtration and tubular reabsorption (Fig. 1).

Glomerular filtration takes place within the glomeruli, where plasma water and small solutes are filtered through the glomerular filtration membrane into the Bowman's chamber. The glomerular filtration membrane consists of three layers: the glomerular endothelial wall including the glycocalyx layer and the fenestrated endothelial cells, the glomerular basement membrane, and the podocytes with their interdigitating foot processes [13]. The filtrate is referred to as *primary urine* [14]. This filtrate is iso-osmotic to plasma and has a composition that closely resembles that of plasma except for large proteins and blood cells, whose passage is restricted by the glomerular filtration membrane. The rate of this filtration process, known as the glomerular filtration rate (GFR), is determined by hydrostatic and oncotic pressures within the glomerular capillaries and urinary tract, and by integrity of the filtration membrane. Whole-kidney GFR is the sum of filtration across functioning nephrons. At the single-nephron level, the determinants of the GFR can be described by the following equation:

$$SNGFR = k \times S \times ((PGC - PBC) - \pi I\Psi - \pi B\Psi)$$

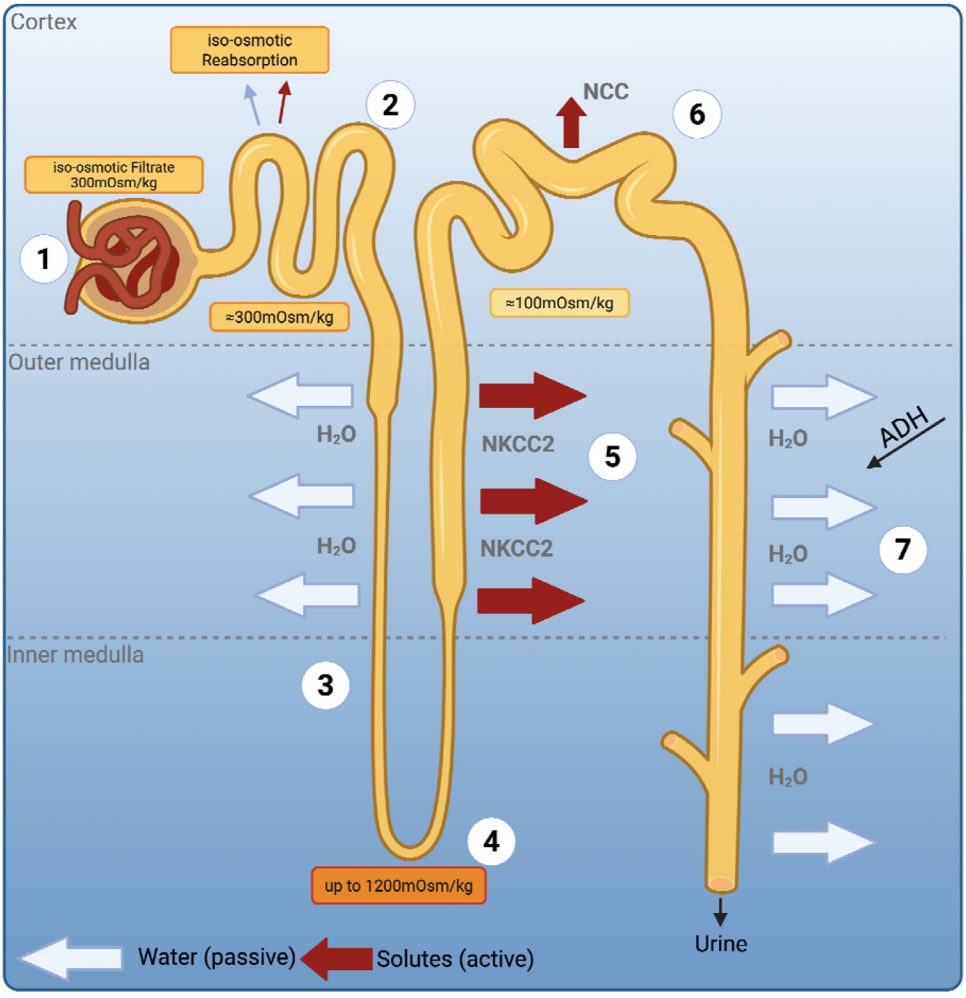


Fig. 1. Determinants of urine formation along the glomerulus and nephron.
Glomerular ultrafiltration (1) is maintained relatively constant despite changing physiological conditions. It generates an iso-osmotic filtrate (~300 mOsm/kg) in Bowman's space. In the proximal tubule (2), ~65% of filtered solutes and water are reabsorbed proportionally, maintaining iso-osmolarity. In the descending thin limb of the loop of Henle (3), water passively exits into the increasingly hyperosmotic medullary interstitium, concentrating tubular fluid until its maximum at the medullar tip of the loop (4) (up to ~1200 mOsm/kg). In contrast, the thick ascending limb (diluting segment) (5) actively reabsorbs Na^+, K^+, and Cl^- (via NKCC2 pump) but is impermeable to water, thereby reducing tubular osmolality and contributing to the corticomedullary gradient establishment. The early distal tubule (6) continues this dilution via NaCl reabsorption (NCC), with tubular fluid reaching ~100 mOsm/kg. Final urine concentration is determined in the collecting ducts (7), where water reabsorption depends on vasopressin (ADH): in its absence, the ducts remain impermeable, producing dilute urine (50–100 mOsm/kg), whereas in its presence, aquaporin-2 channels allow water reabsorption into the hyperosmotic medulla, producing concentrated urine (up to 1200 mOsm/kg). Created in BioRender.

Where:

- SNGFR is the single-nephron glomerular filtration rate
- k is the hydraulic permeability coefficient of the glomerular filtration membrane
- S is the surface area available for filtration
- P_{GC} and P_{BC} are the hydrostatic pressures in the glomerular capillary (P_{GC}) and Bowman's chamber (P_{BC}) respectively

$\pi I\Psi$ and $\pi B\Psi$ are the oncotic pressures in the glomerular capillary ($\pi I\Psi$) and bowman chamber ($\pi B\Psi$) respectively. In physiological states, $\pi B\Psi \approx \Gamma$ because the membrane markedly restricts the passage of plasma proteins in a size- and charge-selective manner. Low-molecular-weight proteins are freely filtered before being reabsorbed in the proximal tubule, while only very small amounts of albumin enter the filtrate. Several regulatory mechanisms contribute to maintaining a relatively constant GFR despite changing physiological conditions, primarily through modulation of afferent and efferent arteriolar resistance [15]. The first intrinsic mechanism of autoregulation is the myogenic response of afferent arterioles [16]. Through the myogenic response, afferent arterioles constrict in response to increased intraluminal pressure, and dilate when intraluminal pressure decreases. The second intrinsic mechanism is the tubuloglomerular feedback. It involves the sensing of intratubular sodium chloride by the macula densa, a specialized group of cells located in the distal convoluted tubule, adjacent to the glomerulus [17,18] (Fig. 2). When GFR increases or tubular sodium reabsorption decreases, a greater amount of sodium chloride reaches the macula densa and is sensed by its cells. In response, the macula densa signaling leads to local adenosine release, which induces afferent arteriolar vasoconstriction and suppresses renin secretion. This leads to decreased hydrostatic pressure in the glomerular capillaries (P_{GC}) and ultimately decreases GFR [19,20]. Conversely, when GFR decreases and sodium chloride delivery to the macula densa is reduced, the feedback mechanism is attenuated, resulting in afferent arteriolar vasodilation. Finally, the third regulatory mechanism involves activation of the renin-angiotensin-aldosterone system (RAAS). Reduced renal perfusion leads to the release of renin by juxtaglomerular cells. Renin catalyzes the conversion of angiotensinogen to angiotensin I, which is subsequently converted to angiotensin II by angiotensin-converting enzyme. Angiotensin II preferentially constricts the efferent arteriole, thereby preserving glomerular capillary hydrostatic pressure and maintaining GFR despite reductions in systemic blood pressure [21].

Tubular reabsorption: determinants and regulation

On average, 180 liters of primary urine are produced by filtration each day. Under normal conditions GFR has only a limited effect on urine volume and composition, which are primarily determined by tubular reabsorption and secretion processes.

Tubular reabsorption is the second step of urine formation. This process involves the reabsorption of most of the glomerular filtrate (up to 99%) allowing the excretion of 1–2 liters of urine per day while precisely regulating water and solute balance. This process occurs along the different specialized segments of the renal tubule and is largely determined by the anatomical and functional structure of the nephron (Fig. 1). In particular, the hairpin structure of the loop of Henle, together with the surrounding vasa recta vessels enables the generation and maintenance of a corticomedullary interstitial osmotic gradient which is crucial for urine concentration. Reabsorption mechanisms vary throughout the tubule [23]. In the proximal tubule, most filtered sodium is reabsorbed through active transport driven by the basolateral Na^+/K^+ ATPase. Water follows passively through

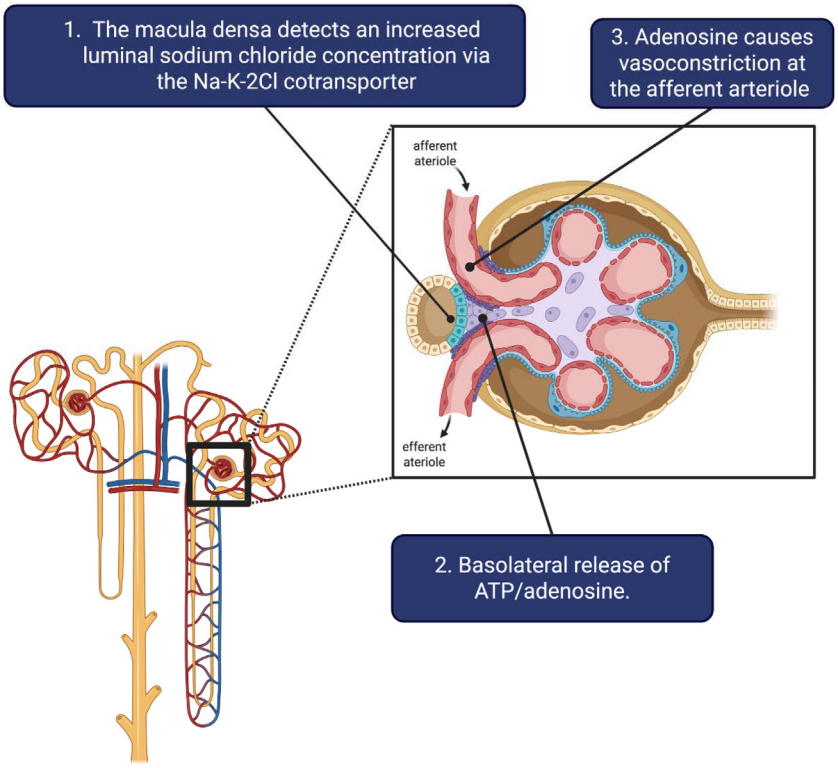


Fig. 2. Simplified representation of the tubuloglomerular feedback (TGF) mechanism.
The macula densa, located at the point where the distal tubule contacts the vascular pole of its own glomerulus, first registers the elevated luminal chloride/sodium chloride concentration via the apical Na-K-2Cl cotransporter (NKCC2) (1). This triggers the basolateral release of ATP, which is rapidly converted to adenosine (2). Adenosine, acting through an adenosine receptor, subsequently causes vasoconstriction of the afferent arteriole (3), thereby lowering glomerular capillary pressure and reducing renal blood flow to return the filtration rate toward its set point. ATP, adenosine triphosphate. Adapted from Mayerhöfer et al. [22] Created in BioRender.

aquaporin-1 channels and leaky intercellular junctions, maintaining near iso-osmolarity in the intratubular fluid [24]. In the descending thin limb of the loop of Henle, which is highly permeable to water owing to abundant aquaporin-1 expression, water passively diffuses into the hyperosmotic interstitium. As a result, tubular fluid becomes progressively concentrated, reaching its highest concentration at the tip of the loop [25]. In contrast, the thick ascending limb actively reabsorbs Na^+, K^+, and Cl^- via Na + - K + -2Cl cotransporter (NKCC2) while remaining impermeable to water. This process dilutes the tubular fluid and contributes to the establishment of the interstitial corticomedullary osmotic gradient [26]. The early distal tubule, also referred to as the "diluting segment", reabsorbs an additional 5–10% of filtered Na^+ through the NaCl cotransporter (NCC). Because this segment has a low permeability to water, tubular fluid becomes further diluted as its osmolality decreases [27]. Thus, urine is hypo-osmolar when entering the collecting duct where final adjustments of urine volume and osmolarity occur under the regulation of antidiuretic hormone (ADH). In the presence of ADH, aquaporin-2 channels are inserted into the apical membrane of collecting duct cells, increasing water permeability and allowing water reabsorption down the osmotic gradient generated by the hyperosmotic medullary interstitium. This results in the production of concentrated urine. In the absence of ADH, the collecting ducts remain water-impermeable, limiting water reabsorption and leading to the excretion of dilute urine [28]. Urea recycling also contributes to the osmotic gradient in the inner medulla: ADH increases urea permeability in the inner medullary collecting duct via UT-A1 and UT-A3 transporters, promoting urea reabsorption and accumulation in the medullary interstitium [25,29]. In light of this, how altered urea production and handling affect medullary concentrating mechanisms and urine output remains incompletely understood and warrants further investigation [30]. This is particularly relevant in critically ill patients, as they experience catabolic states and AKI.

Several neurohormonal and feedback systems finely regulate urine volume and concentration at the tubular level (Table 1). As previously described, the RAAS is activated in response to a decrease in renal perfusion pressure or reduced sodium chloride delivery to the macula densa. In addition to its effects on the efferent arteriole, angiotensin II promotes sodium reabsorption in the proximal tubule and aldosterone secretion from the adrenal cortex. Aldosterone enhances sodium reabsorption in the distal convoluted tubule and collecting ducts by increasing epithelial sodium channels (ENaC) activity and upregulating Na^+/K^+-ATPase, leading to sodium reabsorption and water retention. The overall effect of RAAS activation is the retention of sodium and water, a reduction in urine volume, and the preservation of circulatory homeostasis [31].

Antidiuretic hormone, also known as vasopressin, is the principal determinant of urine volume and concentration. ADH is secreted by the posterior pituitary gland in response to increased plasma osmolality, decreased effective circulating volume, and various non-osmotic stimuli including pain, nausea and stress. In addition, several drugs can also stimulate its release. ADH binds to V2 receptors on collecting duct epithelial cells, triggering the insertion of aquaporin-2 channels into the apical cellular membranes and thereby increasing water permeability, allowing osmotic equilibration with the hyperosmotic medullary interstitium. Vasopressin also increases urea permeability in the inner medullary collecting duct, contributing to the medullary osmotic gradient. Together, these effects concentrate urine by promoting water reabsorption, resulting in reduced urine volume [32].

Other hormones and regulatory systems also contribute to a lesser extent to renal water conservation. In particular, the sympathetic nervous system enhances tubular sodium and water reabsorption during stress or hypovolemia. Conversely, atrial natriuretic peptide (ANP), released in response to atrial stretch, promotes afferent arteriolar dilation, efferent arteriolar constriction, and inhibition of renin and aldosterone secretion. These effects increase GFR and urinary sodium and water excretion [33].

Finally, although tubular secretion contributes substantially to the composition and excretion of selected solutes, its direct contribution to urine volume is usually smaller; changes in the excreted solute load can nevertheless influence urine volume through osmotic effects.

Determinants of oliguria

Low urine output does not necessarily indicate structural injury. In many patients it reflects the ability of intact kidneys to preserve volume and osmotic homeostasis through coordinated RAAS and ADH activation. This adaptive response, historically termed "renal success", represents a physiological attempt to maintain circulatory and fluid balance [34].

In the presence of structural damage, the mechanisms underlying oliguria are highly heterogeneous and may vary according to the nature of the primary insult.

Glomerular causes of pathological oliguria include mesangial contraction, endothelial dysfunction, and loss of effective filtration surface, all leading to a decrease in glomerular filtration rate. In addition, profound alterations of systemic hemodynamics that exceed the capacity of renal autoregulatory mechanisms may also lead to a GFR drop and the development of oliguria. Such hemodynamic dysfunction, although not initially associated with structural damage,

Table 1
Neurohormonal determinants of urine output.

Hormone/system	Trigger	Site of action	Main effect	Impact on urine output
Renin–Angiotensin–Aldosterone System (RAAS)	↓ Renal perfusion pressure (hypotension, hypovolemia), ↓ NaCl delivery to macula densa, ↑ Sympathetic activity	- Ang II: efferent arteriole, proximal tubule - Aldosterone: distal tubule, collecting duct	- Ang II: efferent vasoconstriction (↑ glomerular pressure), ↑ Na^+ and water reabsorption - Aldosterone: ↑ ENaC and Na^+/K^+-ATPase activity: ↑ water reabsorption	↓ Urine volume, ↑ Na^+ reabsorption (concentrated urine if ADH present)
Arginine Vasopressin (ADH)	↑ Plasma osmolality, ↓ Arterial pressure or effective circulating volume, stress, pain, nausea, drugs*	Collecting duct cells (apical membrane)	Insertion of aquaporin-2 channels, ↑ water reabsorption	↓ Urine volume, ↑ urine osmolality (concentrated urine)
Sympathetic Nervous System	↓ Arterial pressure, hypovolemia, stress (pain, hypoxia, shock)	Renal vasculature, proximal tubule	Afferent vasoconstriction, ↑ Na^+ and water reabsorption	↓ Urine volume, ↓ Na^+ excretion
Atrial Natriuretic Peptide (ANP)	↑ Atrial stretch (volume expansion, increased venous return)	Glomerular arterioles, collecting duct	Afferent dilation, efferent constriction (↑ GFR), ↓ Na^+ reabsorption, inhibition of renin/aldosterone	↑ Urine volume, ↑ Na^+ excretion (dilute urine)
Prostaglandins & Nitric Oxide	Local hypoxia, shear stress, excessive vasoconstrictor stimulation (Ang II, catecholamines)	Renal vasculature, collecting duct	Vasodilation, counteract excessive vasoconstriction, maintain medullary perfusion	Preserve GFR and urine output under stress

Ang II: Angiotensin II, GFR glomerular filtration rate, *drugs that increase release of ADH: Fluoxetine, sertraline, paroxetine, venlafaxine, duloxetine, amitriptyline, imipramine, haloperidol, risperidone, olanzapine, carbamazepine, oxcarbazepine, cyclophosphamide, vincristine, morphine, tramadol, ecstasy (MDMA).

is nevertheless pathological and may compromise renal perfusion and oxygenation, ultimately leading to cellular damage if prolonged or severe.

At the tubular level, impaired sodium reabsorption in the thick ascending limb would be expected to reduce the corticomedullary osmotic gradient and impair urine-concentration ability, thereby favoring polyuria, as observed in genetic disorders or following pharmacological inhibition of sodium transport by loop diuretics. However, in the setting of acute tubular injury, oliguria results from the interplay of several pathophysiological mechanisms. First, damage to tubular epithelial cells (particularly in the proximal tubule) results in the accumulation of cellular debris, sloughed cells, and tubular casts within the tubular lumen. This intratubular obstruction increases hydrostatic pressure within the upstream tubules and Bowman's space, thereby reducing the net filtration pressure in the glomerulus, the GFR and ultimately UO [35]. Second, impaired proximal tubular sodium reabsorption increases NaCl delivery to the macula densa, activating tubuloglomerular feedback and promoting afferent arteriolar vasoconstriction, which further reduces GFR. Third, disruption of epithelial cell polarity and tight junctions integrity increases tubular permeability, allowing filtrate to leak back into the interstitium and peritubular circulation. This phenomenon, often referred to as backleak, reduces the amount of filtrate ultimately excreted as urine and thereby contributes to oliguria [36]. Inflammation, interstitial oedema and cell swelling may further impair tubular flow by narrowing or obstructing the tubular lumen [37]. Experimental evidence supports these latter mechanisms: in a murine model of endotoxemia studied using intravital microscopy, selective accumulation of lipopolysaccharide (LPS) within proximal tubular epithelial cells was associated with reduced tubular flow and, after 24 h, the development of luminal obstruction caused by swollen epithelial cells [38].

Other important contributors to the pathophysiology of oliguria include renal venous congestion and renal interstitial oedema. Indeed, an elevated central venous pressure (CVP) reduces renal perfusion pressure gradient (mean arterial pressure – CVP) and interstitial oedema directly increases interstitial and intratubular pressures. Together these effects reduce net glomerular filtration pressure and contribute to a decline in GFR [39]. Clinical and experimental studies have consistently shown that elevated CVP is associated with reduced urine output and poorer clinical outcomes, independently of cardiac output or arterial blood pressure [40,41]. Raised intra-abdominal pressure is another potentially reversible cause of oliguria. It can increase renal venous and interstitial pressures and reduce the pressure gradient available for glomerular filtration [42]. It can be observed in patients with abdominal pathology, major surgery or trauma, fluid accumulation, or reduced abdominal compliance. Importantly, oliguria in this context does not necessarily reflect hypovolemia and may even be exacerbated by additional fluid administration, highlighting the importance of careful hemodynamic assessment.

Differentiating physiological and pathological oliguria at bedside

Considering different thresholds and dynamics of oliguria

As already mentioned, the current KDIGO definition of oliguria was initially adopted by consensus but has subsequently been associated with adverse outcomes. A systematic review highlighted that, across a wide range of clinical settings, low urine output was associated with both AKI and mortality [43]. However, short-lived or mild episodes of oliguria (e.g., $\leq$ 6 h) are frequently reversible and appear to carry limited prognostic significance. In contrast, more prolonged and severe oliguria (e.g., $<$0.3 mL/kg/h or $<$0.1 mL/kg/h sustained for several hours) has been shown to be more strongly associated with subsequent AKI, the need for RRT, and increased mortality [11,44]. In the FINNAKI study, distinct patterns of oliguria severity and duration were associated with stepwise increases in the risk of AKI and mortality. These observations suggest that duration and severity of urine output reduction may provide more clinically relevant information than a single dichotomous threshold and that a sustained fall in urine output should warrant reassessment even before a formal threshold is crossed.

However, if a single threshold had to be retained, several observational studies including critically ill or perioperative patients have challenged the conventional threshold of 0.5 mL/kg/h. Most of them found that lower thresholds (particularly $<$ 0.3 mL/kg/h and $<$ 0.1 mL/kg/h sustained for several hours) were more strongly associated with AKI and mortality [44–49]. However, these retrospective threshold-optimisation analyses are hypothesis-generating and susceptible to overfitting and optimistic estimates of predictive performance, particularly when thresholds are derived and evaluated in the same cohort [46,47]. In contrast, in patients undergoing elective major abdominal surgery in the RELIEF trial, lowering the intraoperative urine-output threshold from $<$0.5 to $<$0.3 mL/kg/h did not identify a further increase in postoperative AKI risk. However, the positive predictive value of intraoperative oliguria at the $<$0.5 mL/kg/h threshold remained very low, at 25.5%. Interestingly, a small randomized trial of 40 patients undergoing elective colectomy, without AKI risk factors, found that targeting a minimal urine output of 0.2 mL/kg/h during surgery was non-inferior to the conventional target of 0.5 mL/kg/h with respect to renal biomarkers, while permitting a more restrictive fluid management strategy [50]. To date, these findings have not been replicated in a population of critically ill patients.

Persistent AKI is defined by the Acute Disease Quality Initiative (ADQI) 16 consensus as the fulfillment of AKI criteria, including UO, beyond 48 h [51]. This is supported predominantly by creatinine-based studies and does not establish 48 h of isolated oliguria as an independently validated prognostic cut-off. Previous studies in critically ill patients consistently found that prolonged oliguria is associated with worse outcomes, but most of them assessed durations up to 12 or 24 h as the upper threshold [11,39,44].

Finally, the assessment of oliguria presents several challenges. Classification depends on how urine volume is computed over time (e.g. whether an averaged or a sustained reduction over the specified time windows is considered) and which body weight is used for normalization. Both choices alter its incidence and prognostic association [52,53]. Diuretics may mask low spontaneous output, and extracorporeal ultrafiltration may affect fluid balance and thus urine production. Collection delays, catheter obstruction and spontaneous voiding may all lead to measurement error and require attention.

Whether addressing the intensity or the duration of oliguria, studies challenging the current definition have primarily sought to identify the cut-offs with the greatest prognostic value. However, prognostic discrimination does not necessarily reflect underlying pathophysiology; therefore, even if a definition with stronger outcome prediction were adopted, it would not necessarily allow to distinguish physiological from pathological oliguria with certainty. To date, this distinction likely requires an integrated assessment combining clinical context, physiological parameters, and, possibly, biomarkers.

Clinical evaluation and context

The clinical context may provide some clues for distinguishing among the various causes of oliguria (Fig. 3).

First, oliguria may result from non-osmotic ADH secretion triggered by stimuli such as pain, stress or nausea [54,55]. This has been proposed as an evolutionarily conserved mechanism that forms

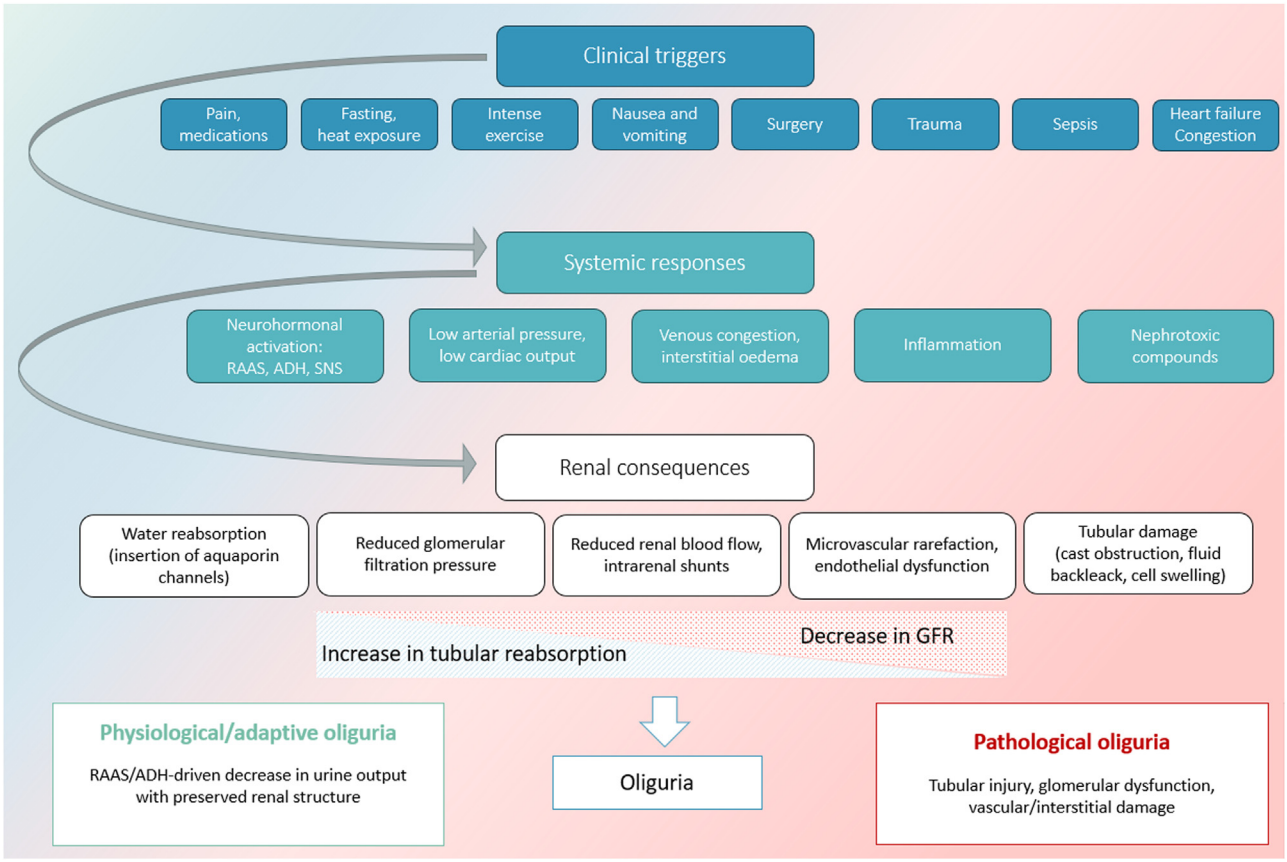


Fig. 3. Causes and pathophysiological mechanisms of oliguria.
Common clinical triggers for oliguria include sepsis, trauma, surgery, fasting, nausea and vomiting, intense exercise, pain, medications, and conditions associated with venous congestion such as heart failure and abdominal compartment syndrome. Each trigger can induce one or more systemic responses such as neurohormonal activation (RAAS, ADH, sympathetic nervous system(SNS)), arterial hypotension or low cardiac output, venous congestion and interstitial edema, inflammation, or exposure to nephrotoxic compounds. These systemic alterations lead to intrarenal adaptive or pathological mechanisms, including increased tubular water reabsorption via aquaporin-2 insertion, sympathetic and RAAS activation, reduced glomerular perfusion and filtration pressure, tubular obstruction by casts, and filtrate backleak due to epithelial damage. Oliguria can be a physiological/adaptive response (RAAS/ADH-driven decrease in urine output with preserved renal structure, e.g., fasting, dehydration, postoperative ADH surge, or exercise) or a pathological response (acute kidney injury with tubular, glomerular, or vascular/interstitial damage, e.g., septic or ischemic shock, tubular cell injury with backleak, or rhabdomyolysis with pigment casts).

part of the broader neuroendocrine response to stress. This situation might be encountered in post-operative and trauma patients and can be particularly challenging as it can lead to clinical uncertainty [56–58]. Several drugs including antidepressants, antipsychotics, anti-epileptics, chemotherapeutics and opioids, as well as the recreational drug MDMA, can also induce or potentiate ADH secretion [59]. In these situations, effective circulating volume is generally preserved and fluid administration is therefore unlikely to be beneficial. Nevertheless, close clinical monitoring and removal of offending triggers, if possible, remain warranted until urine output returns to normal.

Second, oliguria may reflect a physiological renal adaptation to altered body homeostasis (such as dehydration, hypovolemia or hypernatremia). In these situations, activation of neurohormonal systems, particularly RAAS and ADH systems, promotes sodium and water conservation, resulting in a reduction in urine output. This adaptive response constitutes an appropriate kidney response, even when urine output meets KDIGO criteria for AKI. In such situations, prompt restoration of intravascular volume through appropriate fluid administration is essential to reverse renal hypoperfusion, restore homeostasis and prevent progression to structural kidney injury. For instance, oliguria in ultra-endurance athletes is often considered a physiological adaptation. However, studies have reported concomitant increases in biomarkers of tubular damage despite adequate hydration during exercise, suggesting that physiological oliguria and subclinical kidney stress or damage may coexist [60,61]. Similarly, gastrointestinal fluid losses may induce adaptive oliguria through activation of the RAAS and ADH pathways. However, if fluid deficits are not promptly corrected, renal hypoperfusion may lead to structural damage [12].

Finally, oliguria may result from overt structural kidney damage accompanied by a loss of renal function.

Biomarkers

At the bedside, traditional urinary biochemistry has long been used to differentiate functional (“prerenal”) causes of oliguria from intrinsic kidney injury. Indices such as the fractional excretion of sodium (FENa) or urea (FEUrea) are readily available at the bedside and provide insight into the tubular handling and reabsorption of filtered Na^+ and urea. In the setting of hypovolemia, intact renal tubules increase sodium and water reabsorption as an adaptive response aimed at restoring fluid homeostasis. Consequently, FENa and FEUrea are low (generally $<$ 1% and 35%, respectively). However, these indices perform poorly in critically ill patients, especially in the presence of chronic kidney disease, prolonged ICU stay, or diuretic exposure as demonstrated in a recent meta-analysis [62]. More recently, biomarkers of renal stress or tubular damage have emerged as promising tools to identify and characterize AKI. In 2020, an ADQI consensus proposed combining damage and functional

biomarkers, along with clinical information, to improve the diagnostic accuracy of AKI, to recognize the different pathophysiological processes, to discriminate AKI etiology, and to assess AKI severity [63]. To date, no studies have evaluated the added value of these biomarkers to differentiate physiological from pathological oliguria in patients with isolated oliguria. Neutrophil Gelatinase-Associated Lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and liver fatty acid binding protein (L-FABP) rise rapidly after tubular damage and have been associated with adverse renal and clinical outcomes [64]. However, these biomarkers are not specific of kidney injury and can also rise in other situations such as sepsis or liver dysfunction. The product of tissue inhibitor of metalloproteinase-2 and insulin-like growth factor-binding protein 7 ([TIMP-2]·[IGFBP7]), a biomarker of kidney stress, reflecting tubular cell-cycle arrest has demonstrated strong predictive value for the development of severe AKI in ICU populations [65]. Among patients with oliguria, increased urinary [TIMP-2]·[IGFBP7] concentrations are associated with a higher risk of adverse outcomes including RRT requirement or death. In contrast, patients with low or negative biomarker level appear to have a substantially lower risk of these events [64]. Urinary dickkopf-3 is another candidate of tubular-stress marker, but its value for discriminating adaptive from pathological oliguria in unselected ICU patients has not been established yet [66]. Urinary C–C motif chemokine ligand 14 (CCL14) predicts persistent severe AKI in critically ill patients with established KDIGO stage 2–3 AKI and may complement functional markers when assessing the likelihood of renal recovery [67].

In the specific context of oliguria, the interpretation of urinary biomarkers may be affected by low urine flow rates and highly concentrated urine. For example, urinary [TIMP-2]·[IGFBP 7] is measured as an absolute concentration product rather than normalized to urine creatinine. In an oliguric patient with maximally concentrated urine, the value can be high even in the absence of tubular stress, leading to a false-positive result. To improve comparability across patients and biomarkers performance, some authors have proposed normalizing biomarker concentrations to urinary creatinine or estimating biomarker excretion rates, thereby accounting for variations in urine dilution and flow [68,69]. However, to date, neither is fully validated for dynamic ICU decisions.

In selected patients with established early AKI, a standardized furosemide stress test can provide prognostic information about progression to AKI stage 3, provided volume status and contra-indications are considered [70]. It has not been validated as a diagnostic test to distinguish adaptive from pathological oliguria, and its use should complement but not replace assessment of perfusion, congestion and other causes of reduced urine output.

Point-of-care imaging

Beyond laboratory assays, point-of-care imaging may provide valuable additional information in the assessment of oliguria. In particular, the renal resistive index (RRI), measured by doppler ultrasonography, offers an indirect estimate of renal vascular resistance. However, it is influenced by several factors, including arterial pulse pressure and compliance, heart rate, venous and interstitial pressure, intra-abdominal pressure, and vasopressor support [71]. Its diagnostic accuracy, specificity and clinical utility in the evaluation of oliguria, remain subjects of ongoing debate [72,73]. More recent approaches include the Venous Excess Ultrasound (VExUS) score, which integrates Doppler assessment of hepatic, portal, and intrarenal venous flow patterns to identify systemic venous congestion, an increasingly recognized contributor to oliguria and kidney dysfunction [74]. Contrast-enhanced ultrasound (CEUS) enables real-time assessment of renal cortical perfusion and microvascular blood flow. Although it has not been specifically evaluated in patients with oliguria, studies in AKI suggest that it may detect perfusion deficits and provide prognostic information regarding renal outcomes during AKI [75–77].

Clinical management of oliguria

Based on the clinical evaluation and the suspected causes of oliguria an individualized management approach can be proposed (Fig. 4).

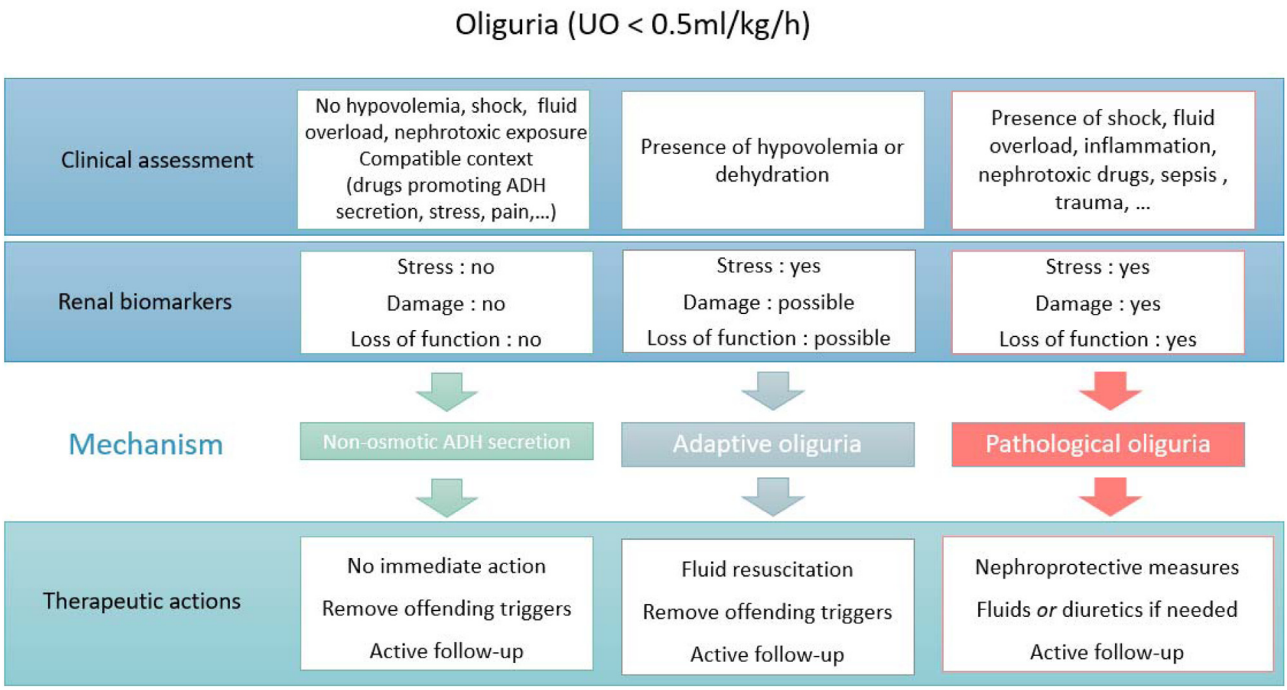


Fig. 4. Conceptual Proposal for Clinical Approach to Oliguria.
Based on a meticulous clinical assessment (including patient medical history and context review, complete hemodynamic evaluation, review of renal insults) and the possibly guided by renal biomarkers profile, 3 situations associated with oliguria could be differentiated. Therapeutic actions result from the situation suspected.

Volume management in oliguria

Fluid administration remains the most commonly used first-line intervention for oliguria in the ICU [78]. However, as discussed at length above, oliguria does not necessarily reflect hypovolemia and is a poor predictor of fluid responsiveness [79]. Only one pilot trial, the RESPONSE trial, prospectively evaluated the effect of volume administration on outcomes in haemodynamically stable oliguric ICU patients [80]. In this study, a 500 mL crystalloid bolus increased UO more frequently than observation, but the effect was modest and transient and was accompanied by a more positive fluid balance; effects on clinically important kidney outcomes remain uncertain. In the absence of better evidence, any decision to administer fluids should be embedded in a structured hemodynamic assessment, integrating dynamic indices of preload responsiveness, markers of venous congestion, lactate kinetics and tissue perfusion parameters. Only oliguria accompanied by clear evidence of dehydration, hypovolemia, renal hypoperfusion and preload responsiveness should prompt fluid administration. This is a physiologically grounded, individualized approach rather than a validated oliguria-specific intervention proven to improve patient-centered outcomes.

Conversely, in euvolemic or hypervolemic patients, additional fluid administration may exacerbate venous congestion, impair renal perfusion, and worsen outcomes [81]. Bedside tools such as venous Doppler (e.g., VExUS), CVP measure or estimation, focused cardiac ultrasound, and passive leg raising maneuvers can help distinguish true hypovolemia from congestion and support individualized hemodynamic management. The same principle applies to diuretic therapy: loop diuretics should not be initiated solely in response to oliguria but rather reserved for patients with evidence of fluid overload or venous congestion.

Importantly, severe hypotonic hyponatremia can develop from SIADH, which requires removal of reversible triggers where possible and fluid restriction according to symptoms and severity. Vasopressin antagonists, such as tolvaptan, have been proposed as second-line treatments but their practical use is complicated by their unpredictable impact on sodium change and their high risk of overcorrection [82,83].

Nephroprotective bundle-of-care

In patients with oliguria associated with overt kidney injury or with evidence of kidney stress identified by biomarkers, implementing a nephroprotective bundle to minimize further insults represents a rational and widely accepted approach. This is particularly important because recurrent or sustained injury may promote maladaptive repair processes, leading to fibrosis, loss of functional nephron mass and the development of chronic kidney disease [84,85]. Such nephroprotective bundles usually combine repeated assessment of hemodynamic status, avoidance of nephrotoxic medications and unnecessary contrast exposure, appropriate medication dose adjustment, glycemic monitoring and close follow-up of kidney function, including serum creatinine and urine output. Several RCTs conducted in selected postoperative patients have demonstrated that the implementation of nephroprotection bundles can reduce the incidence of AKI in patients at high risk of kidney injury [86,87]. However, to date, these bundles have not been evaluated in large, unselected, populations of oliguric ICU patients.

Continuous automated urinary output monitoring

New devices now allow to monitor urine output continuously at the bedside. These continuous or high-frequency electronic urine output monitoring systems have demonstrated the ability to detect oliguria and KDIGO-defined AKI earlier than serum creatinine criteria, with reported lead times of up to 30–40 h in selected postoperative and cardiac surgery populations [88,89]. In the surgical theater, they also showed better agreement with the reference method than measurements obtained by nurses [90]. Traditional methods of urine measurements may delay the recognition of clinically relevant trends. In contrast, continuous monitoring systems may facilitate earlier detection of oliguria and targeted interventions, although their impact on patient-centered outcomes remains to be established.

Conclusions

Oliguria remains one of the most frequent yet challenging clinical signs encountered in critical care. It may represent a physiological, adaptive response to stress and neurohormonal activation aimed at preserving circulatory homeostasis, or a pathological manifestation of structural kidney injury and impaired renal function. The challenge for clinicians lies in distinguishing between these distinct states, as they share common triggers and may coexist. Integrating clinical context, kidney biomarkers, bedside imaging and meticulous hemodynamic assessment is essential to interpreting oliguria and guiding individualized management.

Authors contributions

CM conceptualization, Visualization, Writing-Original draft, Review & Editing.

TM Visualization, Writing - Review & Editing.

AS Writing - Review & Editing.

MJ Supervision, Writing - Review & Editing.

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During the preparation of this work, the author(s) used ChatGPT for language editing. The author(s) reviewed and edited the output as needed and take full responsibility for the content of the published article.

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