Oliguria and Fluid Overload

Thomas Rimmelé · John A. Kellum

The CRISMA (Clinical Research, Investigation, and Systems Modeling of Acute Illness) Laboratory,
Department of Critical Care Medicine, University of Pittsburgh Medical Center, Pittsburgh, Pa., USA

Abstract

Oliguria is a very common clinical situation that is also often difficult to interpret since it may represent either the expression of a disease or the normal response of the kidneys to extracellular volume depletion or decreased renal blood flow. In patients with acute kidney injury, oliguria is independently associated with mortality. Fluid overload is a complication of the impaired sodium and water excretion observed in patients with oliguric acute kidney injury. Fluid overload leads not only to cardiopulmonary complications such as congestive heart failure and pulmonary edema requiring mechanical ventilation but also to several others such as delayed wound healing, tissue breakdown, and impaired bowel function. The aim of this short review is to point out the deleterious effects of these two related clinical situations emphasizing their pathophysiology.

Oliguria

Oliguria is one of the most common clinical situations encountered by physicians. Its interpretation is often difficult since it may represent either the expression of a disease or the normal response of the kidneys to extracellular volume depletion or decreased renal blood flow. In terms of epidemiology, the Acute Dialysis Quality Initiative group has defined oliguria as urine output less than 0.3 ml/kg/h for at least 24 h. However, since any delay in treatment can lead to a dangerous progression of the acute kidney injury (AKI), early clinical recognition of oliguria appears to be crucial. Thus, oliguria should rather be suspected when the urine flow rate is <0.5 ml/kg/h for two consecutive hours. Indeed, 69% of ICU patients who developed AKI in one study were oliguric [1], and these patients represent a subgroup of AKI patients with poor prognosis. Many epidemiologic studies have found the presence of oliguria, in the context of AKI, to
be independently associated with mortality [1–3]. Although not all severe forms of AKI are characterized by oliguria [4], the association of oliguria and mortality is explained at least partially by the fact that oliguria represents a surrogate for a more significant injury or greater severity of AKI [5]. The fact that nonoliguric AKI is reported to have a better prognosis compared with oliguric AKI is important because it probably partially explains why many ICU practitioners want to preserve or increase urine flow by using loop diuretics [6, 7].

Urine output is a function of glomerular filtration and tubular secretion and reabsorption. Glomerular filtration is directly dependent on renal perfusion, which is a function of 3 determinants: circulating blood volume, cardiac output and renal perfusion pressure which depends on arterial pressure and renal vascular resistances. The intra-renal vasculature is capable of preserving glomerular filtration rate (GFR) in the face of varying systemic pressure through important neurohumoral autoregulating mechanisms that affect the afferent and efferent arterioles modulating the renal perfusion pressure. The renin-angiotensin-aldosterone system is perhaps the most significant one (fig. 1).

The relationship between urine output and renal function is complex: oliguria may indeed be more profound when tubular function is intact [8]. When volume depletion and hypotension occur, vasopressin secretion is strongly stimulated and, as a consequence, the distal tubules and collecting ducts become fully permeable to water. Concentrating mechanisms in the inner medulla are also aided by low flow through the loops of Henle and thus, urine volume is minimized and urine concentration maximized (>500 mosm/kg). Conversely,

![Network of effects and feedback loop for the renin-angiotensin-aldosterone system](image-url)
Oliguria and Fluid Overload

when the tubules are injured, maximal concentrating ability is impaired and urine volume may even sometimes be normal (nonoliguric AKI). These physiologic effects form the basis of clinical rules to distinguish prerenal from renal oliguria (table 1). As described, a high urine osmolality coupled with a low urine Na in the face of oliguria and azotemia is strong evidence of intact tubular function. However, this situation should definitely not be interpreted as ‘benign’ or even as ‘prerenal azotemia’ since intact tubular function may also be seen with various forms of disease such as glomerulonephritis. Sepsis, the most common condition associated with AKI in the ICU [9], may also alter renal function without any characteristic changes in urine indices [10, 11].

Oliguria indicates either an important reduction in GFR related to a decreased renal perfusion or a mechanical obstruction to urine flow.

Reduction in GFR linked to decreased renal perfusion can be related to the following conditions:

a Absolute decrease in blood volume due to trauma, hemorrhage, burns, diarrhea or sequestration of fluid as in pancreatitis or abdominal surgery.

b Relative decrease in blood volume in which the primary disturbance is an alteration in the capacitance of the vasculature due to vasodilatation. This is commonly encountered in sepsis, hepatic failure, nephrotic syndrome, and use of vasodilatory drugs including anesthetic agents.

c Decreased cardiac output that can happen in many clinical situations (e.g. cardiogenic shock, cardiac tamponade).

d Decreased renal perfusion pressure that may be due to structural causes such as thromboembolism, atherosclerosis, dissection, inflammation (vasculitis

| Table 1. Biochemical indices useful to distinguish prerenal from intrarenal oliguria |
|---------------------------------|------------------|------------------|
|                                 | Oliguria          |                  |
|                                 | prerenal         | intrarenal       |
| Urine osmolality, mosm/kg       | >500             | <400             |
| Urine Na, mM                    | <20              | >40              |
| Serum urea/serum creatinine     | >0.1             | <0.05            |
| Urine/serum creatinine          | >40              | <20              |
| Urine/serum osmolality          | >1.5             | ≤1               |
| Fractional excretion of Na, %   | <1               | >2               |
| Fractional excretion of urea, % | <35              | >35              |

Fractional excretion of Na = [(urine Na/serum Na)/(urine creatinine/serum creatinine)] ×100. Except for Fe urea, these indices are unreliable once the patient has received diuretic or natriuretic agents (including dopamine and mannitol)
especially scleroderma) affecting either the intra- or extrarenal circulation. Although renal arterial stenosis presents as subacute or chronic renal dysfunctions, renal atheroembolic disease can present as AKI with acute oliguria. Renal atheroemboli (usually due to cholesterol emboli) usually affects older patients with a diffusive erosive atherosclerotic disease. It is most often seen after manipulation of the aorta or other large arteries during arteriography, angioplasty or surgery [12]. This condition may also occur spontaneously or after treatment with heparin, warfarin or thrombolytic agents. Drugs such as cyclosporine, tacrolimus and ACE inhibitors cause intrarenal vasoconstriction resulting in reduced renal plasma flow. Rarely, decreased renal perfusion may also occur as a result of an outflow problem such as a renal vein thrombosis or abdominal compartment syndrome which is a symptomatic organ dysfunction that results from an increase in intra-abdominal pressure. Abdominal compartment syndrome leads to AKI and acute oliguria mainly by directly increasing renal outflow pressure, thus reducing renal perfusion. Other possible mechanisms decreasing renal perfusion pressure include direct parenchymal compression and arterial vasoconstriction mediated by stimulation of the sympathetic nervous and renin-angiotensin systems (renin-mediated arterial vasoconstriction) by the fall in cardiac output related to decreased venous return. However, emerging evidence suggests that the rise in renal venous pressure, rather than the direct effect of parenchymal compression, is the primary mechanism of renal dysfunction. Generally, intra-abdominal pressures >15 mm Hg can lead to oliguria and pressures >30 mm Hg usually lead to anuria [13].

Acute tubular necrosis which is often an end result of the above factors. It may also be due to direct nephrotoxicity of agents like antibiotics, heavy metals, solvents, contrast agents, crystals like uric acid or oxalate.

Reduction in GFR can also be related to mechanical obstruction to urine flow. This can be due to complete or severe partial bilateral ureteral obstruction (caused by stones, papillary sloughing, crystals or pigment), urethral or bladder neck obstruction (blood at the urethral meatus or urethral disruption after trauma, prostatic hypertrophy or malignancy, recent spinal anesthesia) or simply due to malpositioned or obstructed urinary catheter. Rarely, urine volume can be increased in cases of partial obstruction due to pressure-mediated impairment of urine concentration. Rapid increases in serum blood urea nitrogen and creatinine (especially more than double every 24 h) is a particularity of urinary obstruction.

**Fluid Overload**

Fluid overload is an obvious complication of the impaired sodium and water excretion observed in oliguric AKI. In addition, critically ill patients with
Oliguric AKI are at increased risk for fluid imbalance due to widespread systemic inflammation, reduced plasma oncotic pressure and increased capillary leak [5]. All these phenomena make these patients very good candidates for rapid and severe fluid overload states leading to cardiopulmonary complications such as congestive heart failure, pulmonary edema requiring mechanical ventilation, pulmonary restrictive defects and reduced pulmonary compliance.

Fluid overload is also implicated (at least indirectly) in the occurrence of other complications such as leaking of surgical anastomoses, sepsis, bleeding requiring transfusion, wound infection or dehiscence. These associations are supported by studies evaluating different strategies of administration of perioperative fluid therapy during surgical procedures. Brandstrup et al. [14] randomized 172 patients undergoing colorectal surgery to either a goal-oriented replacement of measured fluid losses or a standard intraoperative and postoperative regimen which is known to greatly exceed the fluid losses leading to an excess of 3–7 kg in weight in the early postoperative period [15]. Postoperative complications described above were dramatically reduced for patients receiving the restrictive regimen (33% vs. 51%, p = 0.01) [14]. Another study confirmed these findings in 152 patients undergoing elective major gastrointestinal surgery [16].

As stated above, patients with oliguric AKI are particularly at risk of fluid overload and therefore a restrictive strategy of fluid administration should be used in these patients when possible. This is probably even of greater importance when considering recent changes in ICU practice worldwide with early goal-directed therapy meaning administration of large volumes of fluid therapy [17–20]. Indeed, intensivists are now more likely to try first to give additional fluid therapy during resuscitation rather than initiating vasopressors, and this may further compound fluid overload in oliguric AKI patients. While underresuscitation should be avoided, fluid accumulation can be associated with harm [21–24]. In a small cohort of sepsis-induced AKI patients, Van Biesen et al. [23] reported that additional fluid therapy leading to positive fluid balance failed to impact kidney function while reducing lung function and oxygenation. Other studies have shown that a high positive cumulative fluid balance is an independent risk for hospital mortality [21, 22, 25]. More recently, the ARDS Clinical Trials Network reported a randomized trial comparing restrictive and liberal strategies for fluid management after complete resuscitation in 1,000 ICU patients with acute lung injury, of which most were septic [24]. Although no difference in the primary outcome of death at 60 days was found between the strategies (25.5% for restrictive vs. 28.4% for liberal, p = 0.3), the restrictive strategy had showed improved lung function, increased ventilator-free days, reduced ICU length of stay, no increase in the rate of nonpulmonary organ failure or shock and a trend for reduced need for RRT [24]. Thus, the practice of giving additional fluid in excess of the measured losses (resulting
References


In fluid overload) is not supported by evidence especially for patients that are not responsive to fluid [5, 21, 23, 24]. Conversely, there is emerging evidence that positive fluid accumulation in ICU patients can adversely impact outcomes [5, 21–25].


John A. Kellum
604 Scaife Hall, The CRISMA Laboratory Critical Care Medicine, University of Pittsburgh
3550 Terrace Street
Pittsburgh, PA 15261 (USA)
Tel. +1 412 647 7125, Fax +1 412 647 8060, E-Mail Kellumja@ccm.upmc.edu