Citation	Schetz M, Hoste E, (2016), Understanding oliguria in the critically ill Intensive Care Med. 2016 Sep 12 (Epub ahead of print)
Archived version	Final publisher's version / pdf
Published version	http://dx.doi.org/10.1007/s00134-016-4537-7
Journal homepage	http://link.springer.com/journal/134
Author contact	greet.vandenberghe@med.kuleuven.be + 32 (0)16 344021
IR	https://lirias.kuleuven.be/handle/123456789/552682

(article begins on next page)

UNDERSTANDING THE DISEASE

Understanding oliguria in the critically ill

Miet Schetz^{1*} and Eric Hoste^{2,3}

© 2016 Springer-Verlag Berlin Heidelberg and ESICM

Physiologic and pathophysiologic determinants of urine output

The three determinants of urine output (UO) are glomerular filtration, net tubular reabsorption, and/or the patency of the tubular lumen and the postrenal urinary tract.

1. Tubular reabsorption

UO is predominantly determined by tubular reabsorption in the distal tubules mediated by vasopressin (ADH), although activation of the sympathetic nervous system and the renin–angiotensin–aldosterone system and changes in hydrostatic and oncotic forces in the peritubular capillaries may also contribute. Non-osmotic stimuli for ADH release such as anxiety, pain, hypoxemia, hypercapnia, nausea, vomiting, postoperative states, and some drugs may induce oliguria without affecting glomerular filtration rate (GFR). Intraoperative oliguria indeed appears a poor predictor of postoperative acute kidney injury (AKI) [1]. In addition, oliguria due to increased tubular reabsorption may also be an adequate physiologic response to a reduction in extracellular volume and renal blood flow (RBF), while maintaining GFR through afferent vasodilation and efferent vasoconstriction.

2. Glomerular filtration

Oliguria in ICU patients is often the first sign of a decreased GFR (=AKI), although non-oliguric AKI has also been described, especially when nephrotoxicity is implicated. The classical distinction between prerenal and renal AKI is increasingly being questioned and both can probably co-exist in the same

patient. However, the concept of mainly functional versus mainly structural (tubular damage) AKI may help clinicians in the management of the patient with oliguria [2]. Oliguria of functional AKI is mainly due to renal hypoperfusion, secondary to hypovolemia or low cardiac output, and increased tubular reabsorption (preserved tubular function). A reduction of renal perfusion pressure below the lower limit of autoregulation or in patients with impaired autoregulation may also result in a reduction of RBF and GFR with oliguria.

“Renal” AKI is characterized by tubular damage mainly resulting from ischemia and inflammation. The mechanisms underlying a decrease of GFR and UO in acute tubular damage are less clear. Depending on the underlying etiology persistent hypoperfusion (direct or via activated tubuloglomerular feedback), altered glomerular hemodynamics, intrarenal shunting, heterogeneity of intrarenal blood flow due to impaired microcirculation and/or tubular obstruction and backleak have been implicated [3]. Some authors have suggested that the reduced GFR (and oliguria) is a protective mechanism to reduce the filtered solute load and thus the required energy for reabsorption.

3. Obstruction of the urinary tract is another reversible cause of oliguria that, however, is less frequent in ICU patients.

Oliguria as a part of the AKI-KDIGO definition

Although oliguria does not always point to a reduced GFR, it is part of the current KDIGO consensus definition [4]. In this definition AKI is diagnosed and staged according to creatinine (AKI-Cr) and/or urine output (AKI-UO) criteria with the most sensitive stage 1 being defined as UO less than 0.5 ml/kg/h for a period of at least 6 h. UO criteria of AKI have been reported in up to 65 % of adult ICU patients [5]. Compared with the Scr criteria the UO criteria mostly result in an earlier

*Correspondence: marie.schetz@uzleuven.be

¹ Clinical Department and Laboratory of Intensive Care Medicine, Division of Cellular and Molecular Medicine, KU Leuven University, Herestraat 49, B3000 Louvain, Belgium

Full author information is available at the end of the article

diagnosis (not in the least because of the more frequent assessment compared with serum creatinine) and increase the incidence of AKI [5, 6], implying that many patients with oliguria will not develop AKI-Cr (because of recovery or death?).

Diagnostic assessment of oliguria

The differential diagnosis of oliguria in critically ill patients is difficult because of the lack of real-time measurements of GFR and/or RBF. Every episode of oliguria should therefore be interpreted in the clinical context (shock, sepsis, surgery, nephrotoxicity...) (Fig. 1). Oliguria requires a diagnostic work-up that should minimally include an evaluation of kidney function (short-term creatinine clearance), volume status, cardiac output, perfusion pressure, and identification of other potentially reversible causes (e.g., postrenal causes or nephrotoxic drugs). Several tools have been evaluated to diagnose the etiology of oliguria. Urine sediment and proteinuria may indicate renal causes of oliguria. Urine biochemistry, including fractional excretion of sodium or urea, is often used, but has very low diagnostic accuracy to distinguish transient (more often functional) from persistent (more often tubular damage) AKI [7]. Postrenal causes of oliguria can easily be ruled out by bedside ultrasound. Foley catheter dysfunction should be excluded. Although not yet generally accepted, biomarkers of kidney damage may help distinguish between damage and functional AKI [8].

Oliguria as trigger for clinical intervention

Oliguria is frequently a trigger for fluid loading [9, 10] but on the other hand it also predisposes to fluid overload, which is associated with worse outcomes [11] and may require diuretics. In addition, the decision to start RRT is frequently driven by the presence of oliguria [12]. Whether or not to give fluids to an oliguric patients requires a careful integration of several elements, including the patient's history, hemodynamic parameters, fluid responsiveness, signs of dehydration or fluid overload, information on antecedent fluid losses and fluids balances and duration of oliguria. In the decision whether or not to give fluids it is also important to realize that fluid responsiveness of the systemic circulation does not necessarily correspond to fluid responsiveness in the kidney. The few studies that evaluated the impact of fluid boluses on UO found a poor correlation between the effect on hemodynamic parameters (cardiac index, perfusion pressure) and the effect on UO [13].

Oliguria as a result of vasodilatory hypotension should preferentially be treated with a vasopressor, which may paradoxically result in renal vasodilation through a baroreflex-mediated decrease of sympathetic tone and increase GFR and UO [14]. It should also be noted that although RBF and GFR are normally autoregulated, this is not the case for UO. An increase of perfusion pressure with a vasopressor may thus increase UO independent from an effect on GFR.

Association of oliguria with worsening of AKI, RRT, and mortality

Many short episodes of oliguria are not followed by AKI-Cr and more stringent UO criteria to predict the subsequent development of AKI-Cr have been suggested [6]. In most ICU patients the development of oliguria is a bad sign. Oliguria is indeed part of many illness severity and prognostic scores. Oliguria without AKI-Cr has a higher mortality than the absence of any AKI [5, 6]. Furthermore, the addition of oliguria to the creatinine criteria increases prognostic accuracy [5, 6], possibly because patients die or receive RRT before the creatinine criteria are reached. Both severity and duration of oliguria are associated with mortality and need for RRT [5, 6]. Worst outcomes are seen when both UO and Scr criteria are met [5, 6]. Reversal of oliguria with diuretics (furosemide stress test) may help to predict worsening of early stages of AKI [15].

Author details

¹ Clinical Department and Laboratory of Intensive Care Medicine, Division of Cellular and Molecular Medicine, KU Leuven University, Herestraat 49, B3000 Louvain, Belgium. ² Intensive Care Unit, Ghent University Hospital, Ghent University, De Pintelaan 185, 9000 Ghent, Belgium. ³ Research Foundation-Flanders (FWO), Egmontstraat 5, 1000 Brussels, Belgium.

Compliance with ethical standards

Conflicts of interest

None.

Received: 2 July 2016 Accepted: 31 August 2016

Published online: 12 September 2016

References

1. Goren O, Matot I (2015) Perioperative acute kidney injury. *Br J Anaesth* 115(Suppl 2):ii3–ii14
2. Lameire N, Van Massenhove J, Van Biesen W (2012) What is the difference between prerenal and renal acute kidney injury? *Acta Clin Belg* 67:309–314
3. Gomez H, Ince C, De Backer D, Pickkers P, Payen D, Hotchkiss J, Kellum JA (2014) A unified theory of sepsis-induced acute kidney injury: inflammation, microcirculatory dysfunction, bioenergetics, and the tubular cell adaptation to injury. *Shock* 41:3–11
4. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group (2012) KDIGO clinical practice guidelines AKI: AKI definition. *Kidney Intern Suppl* 2:19–36
5. Kellum JA, Sileanu FE, Murugan R, Lucko N, Shaw AD, Clermont G (2015) Classifying AKI by urine output versus serum creatinine level. *J Am Soc Nephrol* 26:2231–2238
6. Vaara ST, Parviainen I, Pettilä V, Nisula S, Inkinen O, Uusaro A, FINNAKI Study Group (2016) Association of oliguria with the development of acute kidney injury in the critically ill. *Kidney Int* 89:200–208
7. Perazella MA, Coca SG (2012) Traditional urinary biomarkers in the assessment of hospital-acquired AKI. *Clin J Am Soc Nephrol* 7:167–174
8. Singer E, Elger A, Elitok S, Kettritz R, Nickolas TL, Barasch J, Luft FC, Schmidt-Ott KM (2011) Urinary neutrophil gelatinase-associated lipocalin distinguishes pre-renal from intrinsic renal failure and predicts outcomes. *Kidney Int* 80:405–414
9. Boulain T, Boissrame-Helms J, Ehrmann S, Lascarrou JB, Bouglé A, Chiche A, Lakkhal K, Gaudry S, Perbet S, Desachy A, Cabasson S, Geneau I, Courouble P, Clavieras N, Massanet PL, Bellec F, Falquet Y, Réminiac F, Vignon P, Dequin PF, Meziani F (2015) Volume expansion in the first 4 days of shock: a prospective multicentre study in 19 French intensive care units. *Intensive Care Med* 41:248–256
10. Cecconi M, Hofer C, Teboul JL, Pettilä V, Wilkman E, Molnar Z, Della Rocca G, Aldecoa C, Artigas A, Jog S, Sander M, Spies C, Lefrant JY, De Backer D, FENICE Investigators, ESICM Trial Group (2015) Fluid challenges in intensive care: the FENICE study. A global inception cohort study. *Intensive Care Med* 41:1529–1537
11. Prowle JR, Kirwan CJ, Bellomo R (2014) Fluid management for the prevention and attenuation of acute kidney injury. *Nat Rev Nephrol* 10:37–47
12. Gaudry S, Hajage D, Schortgen F, Martin-Lefevre L, Pons B, Boulet E, Boyer A, Chevrel G, Lerolle N, Carpentier D, de Prost N, Lautrette A, Bretagnol A, Mayaux J, Nseir S, Megarbane B, Thirion M, Forel JM, Maizel J, Yonis H, Markowicz P, Thiery G, Tubach F, Ricard JD, Dreyfuss D, AKIKI Study Group (2016) Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit. *N Engl J Med* 375:122–133
13. Lammi MR, Aiello B, Burg GT, Rehman T, Douglas IS, Wheeler AP, deBoisblanc BP, National Institutes of Health, National Heart, Lung, and Blood Institute ARDS Network Investigators (2015) Response to fluid boluses in the fluid and catheter treatment trial. *Chest* 148:919–926
14. Redfors B, Bragadottir G, Sellgren J, Sward K, Ricksten SE (2011) Effects of norepinephrine on renal perfusion, filtration and oxygenation in vasodilatory shock and acute kidney injury. *Intensive Care Med* 37:60–67
15. Koyner JL, Davison DL, Brasha-Mitchell E, Chalikonda DM, Arthur JM, Shaw AD, Tumlin JA, Trevino SA, Bennett MR, Kimmel PL, Seneff MG, Chawla LS (2015) Furosemide stress test and biomarkers for the prediction of AKI severity. *J Am Soc Nephrol* 26:2023–2031