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New markers for acute renal failure

In developed countries acute renal failure (ARF) has mainly iatrogenic or ischemic causes; whereas in a population that is poor, young and with no comorbidities, infection is the most frequently encountered cause.

The stages of ARF are defined, either by AKIN criteria (Acute Kidney Injury Network), or by RIFLE criteria (Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, End stage renal disease) elaborated from populations of patients suffering from tubular necrosis, functional ARF, obstructive ARF and severe CRF (Chronic renal failure).

AKIN criteria

(Metha RL et al. Crit Care 2007; 11:R31)

CRITERION	CREATININE	URINARY OUTPUT
Stage 1	1.5 times the "reference" value or › 127 micro moles/L	Less than 0.5 mL/kg/h over 6 hours
Stage 2	2 times the "reference" value	Less than 0.5 mL/kg/h over 12 hours
Stage 3 NB: transplant patients are considered as stage 3	3 times the "reference" value or › 354 micro moles/L	Less than 0.3 mL/kg/h over 24 hours or anuria for 12 hours

RIFLE criteria

(Bellomo R, et al. Crit Care 2004 ;8 :R204-12)

CRITERION	CREATININE OR GLOMERULAR FILTRATION (GF)	URINARY OUTPUT
At risk	Creatinine x 1.5 or GF decreased by 25%	Less than 0.5 mL/kg/h over 6 hours
Lesion	Creatinine x 2 or GF decreased by 50%	Less than 0.5 mL/kg/h over 12 hours
Insufficiency	Creatinine x 3 or GF decreased by 75% or creatinine › 354 µmol/L	Less than 0.3 mL/kg/h over 24 hours or anuria for 12 hours
Loss	Complete loss of renal function for more than 4 weeks	

A certain number of confounding factors related to these criteria, which determine the severity of the renal condition using the creatinine concentrations, must be taken into account:

- the stability of the creatinine release during the diurnal cycle;
- in case of a sudden change in GFR, accumulation of creatinine in total water content (plasma concentration only increases progressively).

These considerations are behind the proposition of new markers that hopefully have a better diagnostic and analytical performance in: early diagnosis, diagnosis of established renal insufficiency and the establishment of a prognosis.

Research has focused equally on both urinary markers and serum markers.

Below is a summary of the four "new" main characteristic markers:

1. Cystatin C (serum or plasma)

- Early marker (increases between 8 and 12 hours after an intervention);
- ARF prediction between 24 and 48 hours before the increase in creatinine (better sensitivity and specificity in resuscitation patients);
- better sensitivity with GFR variations;
- no differential diagnosis between the different types of ARF;
- a standardised and automated test exists.

2. NGAL (neutrophil-gelatinase associated lipocalin) (urines)

- very promising early marker (increases 2 hours after an intervention: cardiac surgery, kidney transplant or following injection with iodine contrast products);
- detection of kidney failure 24 to 48 hours earlier with a sensitivity of 80 - 90%;
- in the case of pre-existent ARF or infections, interpretation difficulties;
- requires thorough and careful urine collection;
- interpretation takes into account the urinary output;
- automated test.

3. KIM-1 (Kidney Injury Molecule-1) (urine)

- increase in concentrations 24 hours after heart surgery in 100% of patients who go on to develop ARF;
- the marker is sensitive to ischemia;
- differential diagnosis with pre-renal lesions and CRF;
- poor sensitivity in the case of induced ARF by contrast products;
- unfavourable prognostic marker (death or put on dialysis);
- stratification of risk;
- ELISA test is available.

4. IL-8 (urine)

- increase in urine concentrations 6 hours after heart surgery in children going on to develop ARF;
- earlier rise seen compared to creatinine in ARF;
- beneficial for the differential diagnosis (increases in established ARF, for example in the case of tubular necrosis), but not in CRF, urinary tract infections, nephrotic syndrome and prerenal obstructions;
- predictive marker of mortality in children and transplant rejection;
- ELISA test is available.

Other markers have been put forward, such as carbamylated haemoglobin, MMP-9, NHE-3, CD11b, retinol-BP and N-acetyl-β-D-glucosaminidase (NAG): they can be useful in the diagnosis of established ARF, early detection or in providing a prognosis.

Conclusion

Confronted with this abundance of markers, several points need further clarification before elaborating these recommendations any further: studies on a wider range of populations to further define the decision thresholds and to specify the best moment to perform testing following a stressful situation, define the associated markers relative to the objectives (diagnostic or prognostic) and optimise the performance of the reagents to allow for routine clinical use.

For more information:

Liotier J. Biomarqueurs et insuffisance rénale aiguë. Le praticien en anesthésie-réanimation 2012 ;16(1):9-18.

Jacques Ingrand, analysis of a conference by Laurence Piéroni, Pôle de biologie médicale, Centre hospitalier Avignon (Avignon University Hospital), during the 29th CORATA Conference - Lille 13-15 June 2012