	Advantage	Disadvantage	Current practice	Research questions
Electronic/automatic UO registration (1, 2)	- Automatically incorporated in the patient data management system. - Continuous registration of UO. - Automatic staging of AKI severity based upon UO criterion. - Integration of urinary electrolyte monitoring and intra-abdominal pressure.	- Additional costs for disposables and hard-/software.	- Not (yet) routinely applied in most ICUs. - Applied in selected patient populations in some ICUs.	- An ongoing study will evaluate the impact on errors and nursing workload (NCT03636113). - Does automatic UO registration and AKI staging improve clinical outcome? (NCT0523045)
Furosemide stress test (Urinary output in the two hours after furosemide 1 mg/kg in naïve patients, 1,5 mg/kg in pre-exposed patients)	- Accurate prediction of AKI 3 (AUROC 0,87) (3). - Accurate prediction of the need for KRT (4). - Furosemide frequently administered in AKI patients with fluid overload.	- May worsen kidney function in prerenal AKI. To minimize this risk, intravenous substitution with crystalloids at a rate of one ml for each ml UO per hour during the six hours after the FST was advised in the original study.	- Increasingly incorporated in general assessment in most ICUs but not always in the correct dose.	- Is the renal response to other doses of furosemide also informative?
Kidney biopsy	- Detailed insight in the pathological alterations in the glomeruli and tubules. - Improved insight in the underlying molecular mechanisms which may identify new biomarkers.	- Risk of bleeding and other complications.	- Only performed in specific indications, seldomly in critically ill patients. - Not routinely performed for septic or ischemic AKI.	- Risk-benefit needs to be further explored. - A multicentric prospective cohort study including all kidney biopsies for AKI is running (5).
Urine sediment (6)	- Clear association between the presence of renal tubular epithelial cells and granular casts and the progression of AKI. - Low costs.	- Performance of the test depends on experience. - Need for specific equipment. - Automated microscopy probably less performant	- Rarely performed in critically ill patients. - Studies done on subgroup of AKI patients, many not critically ill (selection by nephrologist consult)	- Can automated microscopy add information in the assessment of early AKI? - Additional benefit of serial microscopic evaluation? (7)

	- AUROC to predict AKI progression 0.75.	(although not properly investigated).		
Biomarkers (8)				
KIM-1 (9,10)	- Marker of renal cell damage. - Good prediction AKI and AKI severity. - Associated with long-term mortality in patients with and without AKI.	- Elevated in inflammatory diseases and chronic proteinuria.	- Not commercially available although a lateral flow dipstick that yields results within 15 minutes has been developed (11).	
Cystatin C (12)	- Stable plasma levels, almost fully filtered over the glomerular basal membrane and consequently a good marker of the glomerular filtration rate. - Good accuracy to diagnose and predict AKI.	- Different cut-offs used.	- Commercially available in most ICUs	- Define cut-off values for different clinical settings
NGAL (13)	- Marker of renal cell damage. - Diagnosis of AKI and AKI severity. - Studied in cardiac surgery patients, coronary angiography, ICU patients and emergency patients. - Can be measured on urine and plasma.	- Aspecific. - Lack of clear cut-off.	- Commercially available in Europe but not widely used in clinical practice.	- Ideal cut-off must be identified. - Cost-effectiveness needs to be further evaluated (14).
L-FABP (8,10)	- Marker of renal cell damage. - Accurate biomarker to diagnose AKI. - Associated with long-term mortality in patients with AKI (14).		- Not commercially available (except in Japan) (10).	

	- Can be measured on urine and plasma.			
IL18 (8,10)	- Marker of renal cell damage. - Good prediction of AKI and AKI severity. - Associated with long term mortality in patients with and without AKI (15).	- Elevated in inflammatory state.	- Not commercially available.	
TIMP-2xIGFBP7 (NephroCheck®) (16)	- Prediction of AKI development with very good accuracy when combined with clinical variables (AUROC 0.86) (17). - Improved outcome when applying KDIGO care bundle in patients with an elevated TIMP-2xIGFBP7 in a single and multicentre study of cardiac surgery patients and a single centre study in patients with major surgery patients (18-20).	- Diagnostic accuracy varies in different studies and might be affected by comorbidities (21).	- Commercially available in Europe and the USA.	- Confirmation of beneficial effect of KDIGO care bundle in patients with elevated TIMP-2xIGFBP7 and major surgery. - Ability to select patients for other interventional trials. - Cost-effectiveness to be further evaluated (14).
Urine angiotensinogen	- Predictive for AKI, especially in decompensated heart failure (AUROC for AKI prediction 0.84) (22). - Predictive for severe AKI and other adverse outcomes (23).	- Uncertainty about the predictive value for AKI in populations other than heart failure (e.g., after cardiopulmonary bypass (24)).	- Not commercially available.	- Validation in other ICU populations.
CCL14 (25)	- Predictive for persisting AKI in patients with AKI stage 2 or 3. - Validated in ICU population (26).		- Not commercially available.	- Ability to select patients in whom initiation of kidney replacement therapy is beneficial as compared to watchful waiting?

Syndecan 1 (27)	- Biomarker for endothelial cell dysfunction. - Association with fluid overload after cardiac surgery. - Association with progressive AKI in cardiac surgery.	- No data on accuracy to predict AKI progression. - No validation studies.	- Not commercially available.	- Can fluid management based on Syndecan 1 concentrations reduce AKI or AKI progression?
Contrast-enhanced ultrasonography (28)	- Non-invasive, non-nephrotoxic bedside test. - Quantification of renal cortical microcirculation. - The degree of cortical microcirculation is predictive for severe AKI in patients with septic shock (AUROC 0.82). - Useful to assess the effect of fluid resuscitation and vasopressors on cortical perfusion.	- Time-consuming. - Need for additional training.	- Currently not widely used in critically ill patients.	- Can renal cortical perfusion be used to individualize treatment?
Real-time GFR (29)	- Real time information on the glomerular function. - Information on the total plasma volume is also provided.	- Additional costs for percutaneous detection.	- Not available for clinical use.	- Phase 2 trials in non-critically ill are running. - If accurate in non-ICU patients, accuracy in critically ill patients needs to be further explored.
Artificial intelligence (30-33)	- Separate predictions for AKI, severe AKI and need for KRT are possible. - May be helpful to subphenotype AKI (34)	- Large databases needed. - May be less accurate in patients treated in other hospitals or other departments.	- Several machine-learning predictions available but only few are validated. - Not routinely incorporated in clinical practice.	- Effect of AKI prediction on the clinical outcome remains to be investigated.

	- All above diagnostic tests can be integrated in the models.			

Table: Overview of the diagnostic tools that are available or under investigation for AKI diagnosis. AKI: acute kidney injury, AUROC: area under the receiver-operating-curve, CCL14: C-C motif chemokine ligand 14, GFR: glomerular filtration rate, ICU: intensive care unit, IGFBP7: insulin-like growth factor-binding protein, IL18: interleukin 18, KIM-1: kidney injury molecule 1, KRT: kidney replacement therapy, L-FABP: liver-type fatty acid binding protein, NGAL: neutrophil gelatinase-associated lipocalin, TIMP-2: tissue inhibitor of metalloproteinase 2, UO: urinary output.

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