Human Uromodulin: Unique serum biomarker for evaluation of kidney damage

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Introduction

Tamm-Horsfall protein or uromodulin is a valuable biomarker for evaluation of kidney damage level. Determination of uromodulin alongside estimated glomerular filtration rate (eGFR) can improve differential diagnostics through monitoring kidney function and diagnosing nephropathy, such as diabetic nephropathy, pyelonephritis, chronic renal failure or interstitial nephropathy. New IVD CLIA Uromodulin kit for automated, high-performance, quantitative measurements in clinical routine is available. The immunoassay uses specific antibody-coated magnetic particles to capture the biomarker, and acridinium ester antibody conjugate to detect the amount of captured biomarker in a sandwich format as depicted in **Figure 1**.

Materials and methods

CLIA Uromodulin kit (TestLine Clinical Diagnostics, Czech Republic) for KleeYa® automated analyzer was used. Serum samples from apparently healthy individuals (n = 127) and patients indicated for chronic kidney disease (CKD-EPI <90 ml/min/1,73m^2, increased albuminuremia and cystatin C, n = 133) were collected for the preliminary clinical trial. Concentration of uromodulin was determined using calibration curve with linear response from 10 to 640 ng/ml. Accuracy was continuously verified using CLIA Uromodulin Control set (TestLine Clinical Diagnostics, Czech Republic).
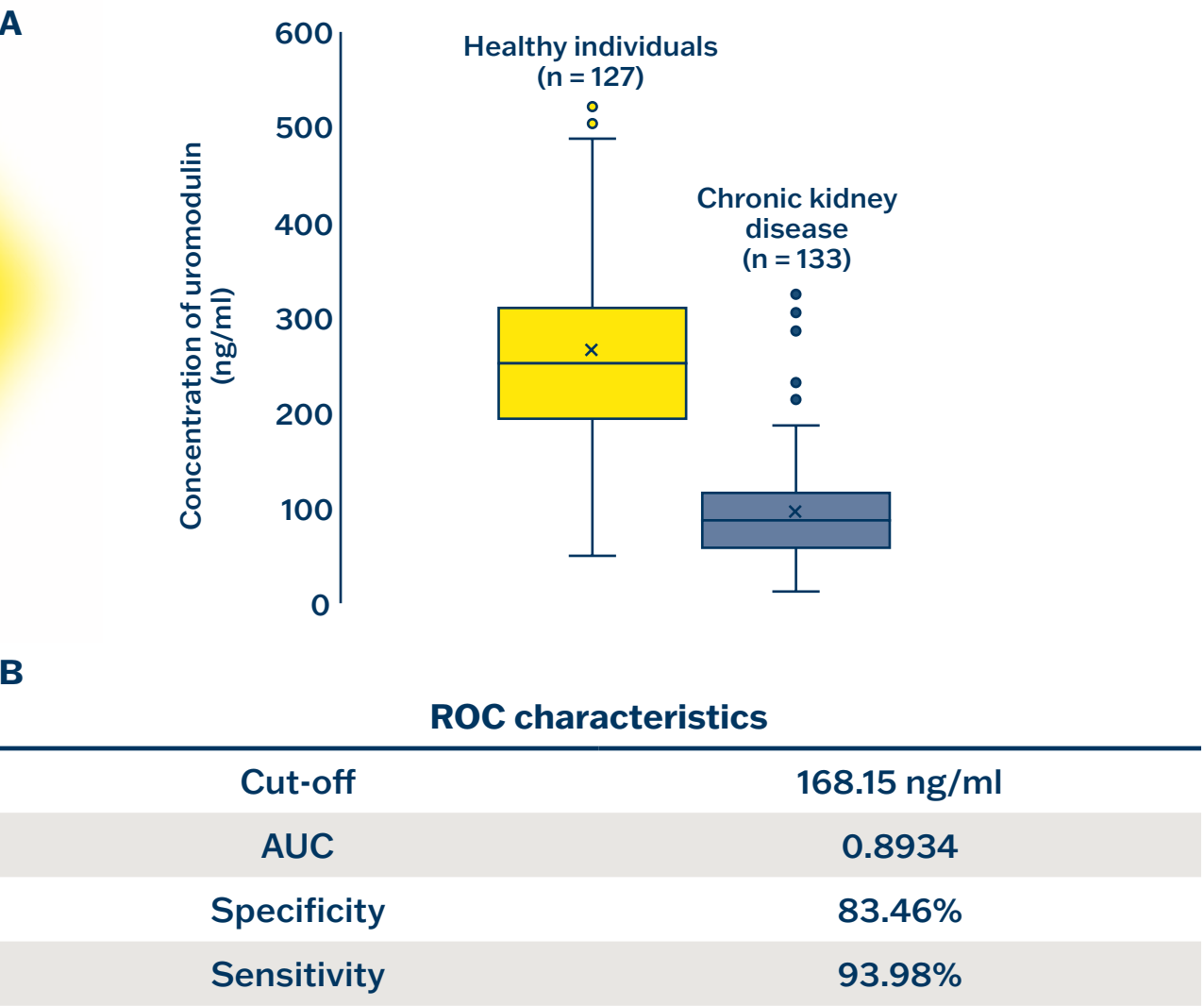
CLIA assay procedure

Measurement

Figure 1: *Description of CLIA assay procedure in automated random access analyzer KleeYa®. All reagents and samples or calibrators are mixed in a one-step procedure and resulting flash signal is evaluated in Relative light units (RLU). The intensity of signal is proportional to the amount of uromodulin captured in the immunocomplex.*

Results

Within two tested groups, the range of concentrations of uromodulin and its average on 95% confidence interval was evaluated as:

	range (ng/ml)	average (ng/ml)
Healthy individuals	109.9–482.0	265.1
CKD patients	14.4–172.0	86.8

According to **Figure 2A**, normal range of serum uromodulin is roughly from 200 to 300 ng/ml. Decrease of the concentration below certain cut-off point suggests insufficiency of kidney function.

Promising clinical performance of the measurement of uromodulin was observed (see **Figure 2B**). According to ROC curve, nearly 0.9 area under curve was obtained using cut-off 168.15 ng/ml.
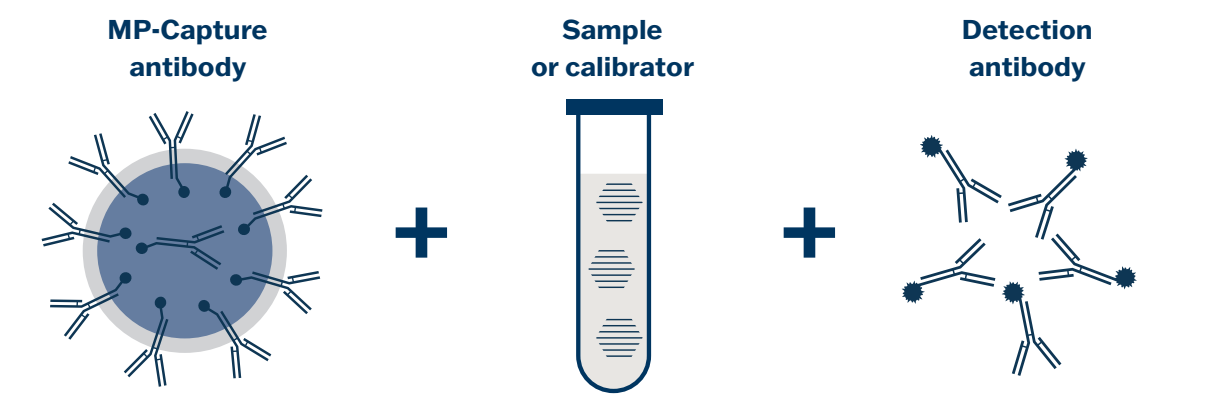
Levels of serum uromodulin are directly proportional with routinely estimated glomerular filtration rate (eGFR) based on creatinine clearance and CKD-EPI equation (**Figure 3**). CLIA Uromodulin kit provides first result in 15 minutes with the throughput of 120 tests per hour. Quick access to measured values significantly aids with the stratification and prediction of the severity of kidney damage.

A

B

ROC characteristics	
Cut-off	168.15 ng/ml
AUC	0.8934
Specificity	83.46%
Sensitivity	93.98%

Stage of CKD	eGFR result	Kidney damage
Stage 0–1	90 or higher	none to very mild
Stage 2	60–89	mild kidney damage
Stage 3a	45–59	mild to moderate
Stage 3b	30–44	moderate to severe
Stage 4	15–29	severe
Stage 5	less than 15	most severe

Figure 2: *Results from the preliminary clinical trial in the Faculty hospital of Olomouc. A: comparison of healthy individuals with the patients suffering chronic kidney disease of any stage. B: Receiver operating characteristic curve (ROC) main output from the clinical trial.*
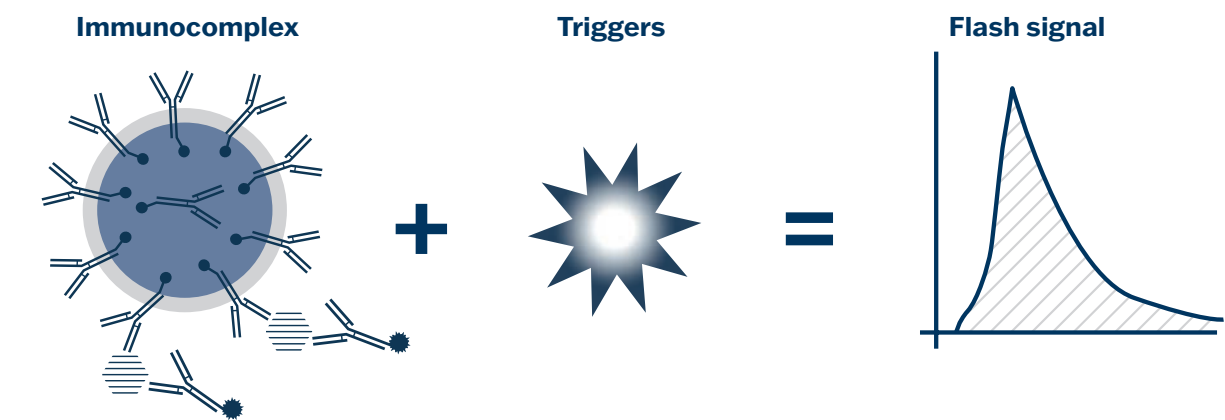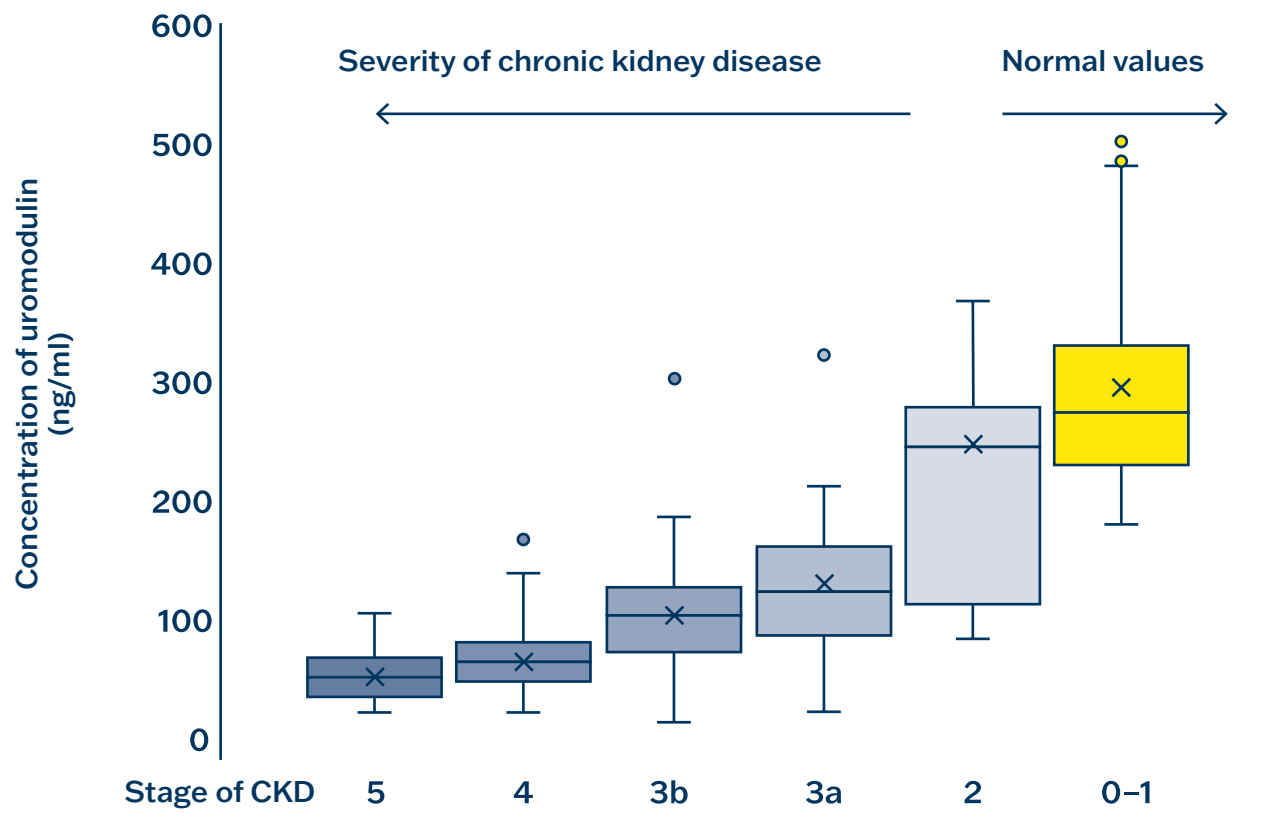
Figure 3: *Level of uromodulin correlates with the stage of the chronic kidney disease. Measured concentration can help with its stratification and prediction of kidney damage state.*

Conclusions

– Quantitative determination of serum human uromodulin shows great potential as a critical test for comprehensive evaluation of kidney damage.

– It allows quick identification of kidney function loss and early prediction of chronic kidney disease.

– Measurements of uromodulin can potentially enable direct evaluation of kidney state needless of equation-based estimations.

References

1.   Scherberich JE, Gruber R, Nockher WA, Christensen EI, Schmitt H, Herbst V, Block M, Kaden J, Schlumberger W. Serum uromodulin-a marker of kidney function and renal parenchymal integrity. Nephrol Dial Transplant. 2018 Feb 1;33(2):284-295.
2.   Leiherer A, Muendlein A, Saely CH, Brandtner EM, Geiger K, Fraunberger P, Drexel H. The value of uromodulin as a new serum marker to predict decline in renal function. J Hypertens. 201. 36 (1): 110-118.
3.   Risch L, Lhotta K, Meier D, Medina-Escobar P, Nydegger UE, Risch M. The serum uromodulin level is associated with kidney function. Clin Chem Lab Med. 2014 Dec;52(12):1755-61.

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