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A URINARY PROTEOME-BASED CLASSIFIER FOR THE DIAGNOSIS OF CHRONIC KIDNEY DISEASE IN CHILDREN

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INTRODUCTION AND AIMS: Chronic kidney disease (CKD) is characterized by a gradual reduction in kidney function. The prevalence of CKD in the pediatric population is low but with such early CKD onset often results in devastating long-term consequences. A urinary proteome-based classifier, termed CKD273, has been validated in different studies, in the context of diagnosis and prognosis of CKD in adults. However, CKD273 was never evaluated in pediatric patients. Therefore, the aim of this study is to exploit and assess the diagnostic performance of CKD273 classifier in the pediatric population. Furthermore, we investigate whether an adjustment of CKD273 classifier according to a childhood population is necessary.

METHODS: In this retrospective study, we analyzed the low molecular weight urinary proteome (0.8-20 kDa) of 358 subjects aged 0 to 20 years. The cohort consisted of 86 patients with different CKD etiologies (*e.g.* focal segmental glomerulosclerosis, minimal change disease, IgA nephropathy, etc.) and all CKD stages and 272 controls. The receiver operating characteristic (ROC) curve analysis with calculation of areas under the curve (AUC), sensitivity and specificity, was performed using MedCalc software.

RESULTS: First, we evaluated the performance of CKD273 using the previously established CKD cut-off value of 0.343 for adults in this pediatric cohort, yielding an AUC of 0.931 and a specificity of 97.8% whereas sensitivity was only 65.1%. Therefore, we fitted a modified cut-off for children with CKD to 0.053. Applying this adapted cut-off, CKD273 predicted CKD with a sensitivity of 86.1% and a specificity of 88.6%.

Furthermore, evaluation of CKD273 with the pediatric cut-off across different age groups demonstrated high AUC, sensitivity and specificity for the prediction of CKD in children (Table).

CONCLUSIONS: This study demonstrates that CKD273, with the use of an adapted cut-off, can become an important tool for the diagnosis of CKD in childhood. Future work includes the analysis of an additional cohort of children with CKD with follow-up information about the progression to CKD to verify whether the classifier with the pediatric cut-off also identifies progressive CKD as it does in adults.

Table - Predictive values of CKD273 classifier in a cohort under 20 years and respective subgroups according to the age.

	Full cohort <20 years (n=358)	Subgroup: <5 years (n=115)	Subgroup: 6-10 years (n=76)	Subgroup: 11-15 years (n=58)	Subgroup: 16-20 years (n=109)
AUC	0.931	0.907	0.976	0.936	0.893
***Published Cut-off** > 0.343 (over 20 years)*					
Sensitivity	65.12%	50%	68.42%	68%	70.83%
Specificity	97.79 %	98.97%	98.25%	93.94%	97.65%
***New Cut-off** > 0.053 (under 20 years)*					
Sensitivity	86.05%	83.33%	89.47%	92%	79.17%
Specificity	88.60%	87.63%	89.47%	87.88%	89.41%