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Optimization of screening strategy for chronic kidney disease by urine test strips using the albumin-creatinine read-out

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Abstract

Introduction Clinical laboratories play an important role in the diagnosis and monitoring of chronic kidney disease (CKD). Our aim was to evaluate the performance of qualitative and semi-quantitative albumin-to-creatinine ratio (ACR) and protein-to-creatinine ratio (PCR) test strip results as screening tools for albuminuria in multiple representative patient cohorts.

Materials and methods ACR and PCR were evaluated in both cross-sectional ($n=940$) and validation ($n=927$) patient cohorts. Semi-quantitative urinary ACR and PCR were performed using a UC-3500 instrument (Sysmex, Kobe, Japan). The diagnostic performance of semi-quantitative ACR and PCR was determined using quantitative ACR and PCR as reference method.

Results In the cross-sectional cohort, a sensitivity and specificity of 78.1% and 93.3%, respectively, were obtained for semi-quantitative ACR at a cut-off of 30 mg/g creatinine, with an overall agreement of > 90% between both methods. The sensitivity and specificity increased in the target population (validation cohort) to 89.9% and 92.1%, respectively. In contrast, the sensitivities of qualitative protein concentration (78.6%) and semi-quantitative PCR (69.8%) were lower.

Conclusion The results confirm that urine test strip readouts are a valuable screening tool for CKD in low-risk individuals. ACR should be the preferred criterion for reflex testing when using a urine test strip for screening CKD.

Keywords Albuminuria, Automated, Proteinuria, Urinalysis, Urinary test strip analysis

Introduction

Clinical laboratories play a crucial role in the diagnosis and monitoring of chronic kidney disease (CKD). The age-standardized global prevalence of CKD stages 1–5 in adults aged ≥ 20 years is 10.4% in men and 11.8% in women [1]. Early diagnosis and management may improve long-term outcomes [2].

Albuminuria, characterized by the presence of excessive albumin in urine, serves as a crucial indicator of kidney dysfunction and cardiovascular risk. Early detection of albuminuria is imperative for timely diagnosis, intervention, and management of patients predisposed to kidney damage. According to the Kidney Disease: Improving

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Global Outcomes (KDIGO) guidelines, albuminuria and estimated glomerular filtration rate (eGFR) are two laboratory-based criteria for the diagnosis of CKD [3]. In CKD populations, urinary albumin may be the first and only sign of kidney disease, making it a highly sensitive marker for the detection of CKD, particularly in its early stages [4, 5].

The measurement of albuminuria is important in screening for early CKD. Moreover, epidemiological studies have shown a graded relationship between increased albuminuria and mortality and kidney outcomes in diverse study populations, in addition to and independent of low eGFR and risk factors for cardiovascular disease [2]. The KDIGO guidelines, as well as the EFLM European urinalysis guideline 2023, primarily recommend screening using quantitative albumin tests [4–6]. However, the cost of laboratory-based quantitative methods and reimbursement restrictions (e.g. in Belgium) may hamper the routine use of quantitative urinary albumin by clinicians as a screening tool in the general population or even populations at risk, and thus, potentially leading to underdiagnosis of CKD. For example, in Spain, it was previously shown that urinary albumin is under requested to properly monitor patients with diabetes and arterial hypertension [7]. Screening by test strip analysis is suggested in the guidelines, albeit with lower priority and without further details on the type of reading to be used for screening or with the suggestion to use the total protein read-out [4–6].

In recent years, there has been growing interest in the use of test strip analysis as a cost-effective tool for screening albuminuria [7, 8]. Several studies have shown promising results in terms of the sensitivity and specificity for the detection of albuminuria. However, most of these studies were performed in cohorts in which known and unknown CKD patients were mixed or the CKD status was unknown. In the current study, we aimed to provide novel insights into the analytical performance of urine test strips as a screening tool for unknown CKD by comparing the performance of multiple test strip readouts in several patient cohorts, including a patient cohort not known to have CKD.

Materials and methods

Urine samples

Mid-stream urine specimens collected at the Ghent University Hospital were selected. Collection was performed in sterile containers (Container with screw cap™, Sarstedt AG & Co., Nümbrecht, Germany), aspirated in Monovette™ collection tubes without preservatives (Sarstedt AG&Co), and analyzed within 4 h after arrival in the laboratory. Exclusion criteria included slimy or viscous samples and the inability to collect a sufficient volume of urine. The study was approved by the Medical Ethics Committee of the Ghent University Hospital (project-ID: ONZ-2024-0113). After routine urine test strip analysis, urinary albumin (mg/L), urinary total protein (mg/L), and urinary creatinine (mg/dL) were determined. Albumin to creatinine ratio (ACR) and total protein to creatinine ratio (PCR) were calculated and expressed in mg/g creatinine.

Patient population

Cross-sectional cohort

The first group of urine samples ($n = 940$) was selected to evaluate the correlation between semi-quantitative and quantitative ACR results. Samples from patients who consulted the policlinic cardiology, nephrology, paediatric, urology and endocrinology departments, as well as the general internal clinic wards and on which a urinary test strip analysis was requested, were included. Other inclusion criteria were known serum creatinine concentration and concomitant eGFR [9] within 7 days before the test strip analysis.

Validation cohort

The validation cohort consisted of 927 patient samples for which a urinary test strip analysis was requested. Samples originated from outpatients not known to have CKD based on our laboratory records [i.e., no eGFR (CKD-EPI) < 60 mL/min/1.73 m^2 or positive albuminuria in current or previous samples] within a period of 5 years.

Laboratory methods

All analyses were performed in the clinical laboratory of the Ghent University Hospital. The UC-3500 (Sysmex, Kobe, Japan) is a fully automated urine test strip analyzer that was employed to semi-quantitatively measure the urinary protein, albumin, and creatinine levels. The measurement principle of the analyzer has been described previously [10]. The analyzer reports a semi-quantitative ACR result that is reported as normal (< 30 mg/g creatinine), moderately increased albuminuria (30–300 mg/g creatinine), and severely increased albuminuria (> 300 mg/g creatinine). Also, a semi-quantitative PCR result is reported as normal (< 150 mg/g creatine) or increased proteinuria (≥ 150 mg/g creatine). In addition, the analyzer reports semiquantitative results of albumin and protein (10, 30, 80, or 150 mg/L, and, 15, 30, 100, 300, 1000 mg/dL, respectively) and creatinine (10, 50, 100, 200, or 300 mg/dL). "Dilute" results indicate that the sample is too diluted to correctly calculate the ACR and PCR. These samples were excluded from analysis.

ACR and PCR were determined using Meditape UC-11 A test strips [lot # UCC02206 (cross-sectional cohort) and lot # AC2039, AC2043 and AC3047 (validation cohort)]. Urinary albumin was quantitatively

measured using an immunoturbidimetric assay (Cobas 8000; Roche Diagnostics, Mannheim, Germany). Sheep-derived polyclonal antibodies against human albumin interact with the antigen present in the sample, resulting in the formation of antigen-antibody complexes. These complexes undergo agglutination and are subsequently measured turbidimetrically. Urinary total protein and creatinine were measured using the enzymatic biuret kinetic colorimetric assay based on the Jaffé method (Architect c16000; Abbott Diagnostics, Wiesbaden, Germany).

Statistical analysis

The data were statistically processed and analyzed using the Medcalc software (version 15.6.1., Mariakerke, Belgium), SPSS and Microsoft Excel. To determine the correlation between the quantitative and semiquantitative ACR, ordinal scale categories were defined based on the KDIGO categories (low, moderate, high, and very high). The correlation was assessed using weighted Cohen's kappa coefficients. Descriptive statistics are presented as mean ± standard deviation (SD), and percentages for continuous and categorical data.

C-statistics were calculated using SPSS (Version 29.0.2.0, SPSS Inc., Chicago, IL, USA) by running a binary logistic regression model considering the strip read-out categories for semiquantitative ACR, PCR and the qualitative protein concentration as categorical variable. C-statistics were added to the table for both cohorts.

Results

Cross sectional cohort

In the cross-sectional cohort, 940 samples were analyzed. Four samples were excluded due to insufficient volume of urine and 2 patients were excluded due to slimy or viscous urine samples. At an ACR cut-off of 30 mg/g, the prevalence of albuminuria was 43.0% (404/940). In Table 1, the correlation between the semi-quantitative ACR, semi-quantitative PCR, qualitative protein concentration and the quantitative ACR is presented. An agreement of more than 90% was obtained between the semi-quantitative and quantitative ACR. At an ACR cut-off of 30 mg/g creatinine, a sensitivity of 78.1% (95%CI: 71.3–83.9%) and specificity of 93.3% (95%CI: 91.3–95.0%) were determined. An overall agreement of 0.70 was seen, using the weighted kappa coefficient. In contrast, agreements of 88.5% and 85.0% were determined between the semiquantitative PCR ratio (cut-off: 150 mg/g creatinine) and qualitative protein concentration towards the quantitative ACR with a sensitivity of 51.7% (95%CI: 44.1–59.2%) and 68.0% (95%CI: 60.6–74.8%), respectively. Specificities of 97.1% (95%CI: 95.7–98.2%) and 89.0% (95%CI: 86.5–91.1%) were determined for the semi-quantitative PCR and qualitative protein concentration towards the quantitative ACR, respectively. The semi-quantitative ACR showed the highest predictive probability for CKD, with an AUC of 0.873 (95%CI: 0.836–0.910), which was significantly higher than both the semi-quantitative PCR (AUC: 0.749, 95%CI: 0.700–0.797) and the qualitative protein (AUC: 0.785, 95%CI: 0.743–0.828).

Further, we determined the sensitivity and specificity in patients with moderate to high albuminuria (quantitative ACR > 300 mg/g creatinine) for semi-quantitative ACR (cut-off: 30 mg/g creatinine) and PCR (cut-off: 150 mg/g creatinine) results. For both ACR and PCR, a sensitivity and specificity of 100% was obtained. The correlation between the KDIGO CKD categories obtained with both ACR methods resulted in an agreement of 89.2% and 0.82, respectively, using the weighted kappa coefficient (Table 2).

Validation cohort

The primary aim of the validation cohort was to compare the performance of multiple readings on the test strip as a screening tool for albuminuria in an optimal target population, that is an outpatient population not known to have CKD. In the validation cohort, 927 samples were analyzed. Three samples were excluded due to insufficient volume of urine. Multiple readouts from the test pads (ACR, PCR, and quantitative protein concentration) were compared. At an ACR cut-off of 30 mg/g, the prevalence of albuminuria was 18.1% (168/928) in the validation cohort. The specificity of semiquantitative ACR [92.1% (95%CI: 89.9–93.9%)] and semi-quantitative PCR [93.8% (95%CI: 91.8–95.4%)] against quantitative ACR were similar, while the specificity of the qualitative protein concentration against the quantitative ACR was lower [76.1% (95% CI: 72.9-79.1%)] (Table 3). Optimal sensitivity was obtained for the semiquantitative ACR [89.9% (95%CI: 84.4–94.0%)], with lower values for qualitative protein concentration [78.6% (95%CI: 71.6-84.5%) and semi-quantitative PCR [69.8% (95%CI: 62.3–76.6%)]. This resulted in (almost) optimal positive and negative likelihood ratio (LR) for the semi-quantitative ACR [LR+:11.3 (95%CI: 8.8–14.5) and LR-: 0.11 (95%CI: 0.07–0.17)], while the likelihood ratios of semi-quantitative PCR [LR+:11.2 (95%CI: 8.4–15.1); LR-: 0.32 (95%CI: 0.26–0.41)] and qualitative protein concentration [LR+: 3.3 (95%CI: 2.8–3.8);LR-: 0.28 (95%CI: 0.21–0.38)] were less performant. In the validation cohort, the semi-quantitative ACR demonstrated the highest predictive probability for CKD, with an AUC of 0.933 (95% CI: 0.905–0.960), which was significantly higher than the AUC of 0.830 (95%CI: 0.787–0.873) for the semi-quantitative PCR and 0.774 (95%CI: 0.735–0.814) for the qualitative protein.

Of note, only in a minority of patient samples (3.3% of the cohort), quantitative albumin measurement was

Table 1 Summary of the agreement between the albumin to creatinine ratio (ACR) and protein to creatinine ratio (PCR) determined by test strip analysis as compared to the quantitative lab test in the cross-sectional cohort

	QUANTITATIVE ACR				**QUANTITATIVE ACR**				**QUANTITATIVE ACR**		
SEMI-QUANTITATIVE ACR	***Categories (mg albumin/g creatinine)***			**SEMI-QUANTITATIVE PCR**	***Categories (mg albumin/g creatinine)***			**Qualitative Protein Concentration**	***Categories (mg albumin/g creatinine)***		
Categories (mg albumin/g creatinine)	*< 30*	*≥ 30*	***Total***	*Categories (mg protein/g creatinine)*	*< 30*	*≥ 30*	***Total***	*Categories (mg protein/g creatinine)*	*< 30*	*≥ 30*	***Total***
< 30	711	39	*750*	*< 150*	*740*	*86*	*826*	*Negative*	*678*	*57*	*735*
≥ 30	51	139	*190*	≥ 150	*22*	*92*	*114*	Positive	*84*	*121*	*205*
Total	*762*	*178*	*940*	***Total***	*762*	*178*	*940*	***Total***	*762*	*178*	*940*
Agreement	90.4%			**Agreement**	88.5%			**Agreement**	85.0%		
Cohen's kappa (Weighted)	0.696			**Cohen's kappa (Weighted)**	0.566			**Cohen's kappa (Weighted)**	0.538		
Sensitivity	78.1% (95%CI: 71.3–83.9%)			Sensitivity	51.7% (95%CI: 44.1–59.2%)			Sensitivity	68.0% (95%CI: 60.6 – 74.8%		
Specificity	93.3% (95%CI: 91.3–95.0%)			Specificity	97.1% (95%CI: 95.7–98.2%)			Specificity	89.0% (95%CI: 86.5 – 91.1%)		
PPV	73.2% (95%CI: 66.3–79.3%)			PPV	80.7% (95%CI: 72.2–87.5%)			PPV	59.0% (95%CI: 52.0 – 65.8%)		
NPV	94.8% (95%CI: 93.0–96.3)			NPV	89.6% (95%CI: 87.3–91.6%)			NPV	92.2% (9%CI: 90.1 – 94.1%)		
LR+	11.7 (95%CI: 8.9–15.4)			LR+	17.9 (95%CI: 11.6–27.7)			LR+	6.2 (95%CI: 4.9–7.7)		
LR-	0.23 (95%CI: 0.18–0.31)			LR-	0.50 (95%CI: 0.43–0.58)			LR-	0.36 (95%CI: 0.29–0.45)		
Predictive probability	0.873 95%CI: 0.836–0.910			Predictive probability	0.749 (95%CI: 0.700–0.797)			Predictive probability	0.785 (95%CI: 0.743–0.828)		

Abbreviations: ACR: albumin-to-creatinine ratio; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio; PCR: protein-to-creatinine- ratio

Table 2 The kidney disease: improving global outcomes chronic kidney disease (KDIGO CKD)-risk score classification based on estimated glomerular filtration rate (eGFR) and albumin to creatinine ratio (ACR) determined by lab test vs. test strip in the cross-sectional cohort

	QUANTITATIVE ACR				
SEMI- QUANTITATIVE ACR	***Categories***				
Categories	***Low***	***Moderate***	***High***	***Very High***	***Total***
Low	674	37	0	0	*711*
Moderate	47	84	0	0	*131*
High	0	9	31	2	*42*
Very high	0	0	1	3	*4*
Total	*721*	*130*	*32*	*5*	*888*
Agreement	89.2%				
Cohen's kappa (Weighted)	0.819				

Abbreviations: ACR: albumin-to-creatinine ratio

initially requested by the physician, while 18.3% of the samples showed an ACR of > 30 mg/g creatinine. These data reflect a known underdiagnosis of albuminuria and CKD.

Discussion

Measurement of urinary albumin concentration is the cornerstone of CKD diagnosis and screening. The KDIGO guidelines recommend screening using quantitative albumin and creatinine assays [2]. However, the cost of the assay and the reimbursement conditions may hamper the general use of these assays in lower-risk populations. The KDIGO guidelines suggest using test strip readings to screen for proteinuria, although with lower priority and without specifying the type of readout [2]. Currently, automated strip readers offer multiple readings for protein concentration: semi-quantitative albumin, qualitative protein reading, ACR, and PCR. However, little is known regarding the diagnostic performance of these readings in patients with CKD.

In the first part of the study, we evaluated the general performance of the Meditape UC-11 A test strips on Sysmex UC-3500 by comparing the ACR and PCR readings to quantitative ACR and PCR, respectively. These results show good concordance between test-strip readings and the quantitative ACR and are in agreement with a previous study using the same methodology [7]. Previous studies evaluated the performance of test strip readers by using the output of reflectance data, thereby fully exploring the possibilities of reading [11–13]. However, the manufacturer only claims the use of the instrument based on reading the results on a semiquantitative scale. Moreover, the KDIGO guidelines also suggest the simultaneous determination of creatinine in spot urine samples, thereby eliminating the variable influence of diuresis [2]. These factors should be considered when implementing CKD screening strategies.

The primary aim of the validation cohort was to explore the performance of semi-quantitative readings for albuminuria and proteinuria and qualitative readings for protein concentration on the urine test strip as screening tools for albuminuria in an outpatient population not known to have CKD. First, we evaluated the agreement between the semi-quantitative and quantitative ACR and PCR ratios. These results confirm the good agreement between semi-quantitative and quantitative results, as shown in previous studies with varying screening populations [7, 14–18]. For example, Graziani et al. demonstrated a 90% sensitivity and 91% specificity in a general population, while Nah et al. demonstrated 92% sensitivity and 94% specificity in a (pre)-diabetes population [14, 16]. Interestingly, semi-quantitative ACR outperformed PCR, suggesting that it is a better decision maker for reflex testing. Also, we demonstrated that the predictive probability for CKD is higher for semi-quantitative ACR as compared to semiquantitative PCR and qualitative protein in this cohort. The difference in performance between the two test pads may be explained by the chemical properties of tetra bromophenol blue and the concentration of this indicator on the albumin and total protein test pads. The reaction on both test pads is based on the protein error of the pH indicator. The three dimensional structure of albumin and other proteins ensures ligand binding to bromophenol blue [13]. As albumin has more binding sites for interactions, less bromophenol is required for the reaction to occur, whereas non-albumin proteins (e.g. Bence Jones proteins) may have fewer binding sites and require higher bromophenol concentrations.

The cross-sectional sample's semiquantitative ACR was less sensitive than the validation cohort's. The higher prevalence of albuminuria in the cross-sectional population (43.1%) compared to the validation cohort (18.1%) could explain this disparity. This stresses the importance of considering patient demographics and medical histories when assessing diagnostic performance. In a more diseased population, test performance may be impacted by the presence of mixed proteinuria's and more advanced kidney dysfunction. Consequently, semi-quantitative PCR is less reliable in hospital settings where mixed proteinuria's are prevalent, as it has a reduced ability to distinguish albumin from other urinary proteins. This shows that more refining or additional testing is required for accurate CKD screening in such settings. Furthermore, our findings emphasize the importance of customized screening strategies that enhance test accuracy based on patient demographics and clinical contexts. Semi-quantitative ACR screening in an outpatient group without CKD revealed higher diagnostic performance, highlighting the importance of improving screening criteria to enhance effectiveness.

Table 3 Summary of the agreement between the albumin to creatinine ratio (ACR) and protein to creatinine ratio (PCR) determined by test strip analysis as compared to the quantitative lab test in the validation cohort

	QUANTITATIVE ACR				**QUANTITATIVE ACR**				**QUANTITATIVE ACR**		
SEMI-QUANTITATIVE ACR	***Categories (mg albumin/g creatinine)***			**SEMI-QUANTITATIVE PCR**	***Categories (mg albumin/g creatinine)***			**Qualitative Protein Concentration**	***Categories (mg albumin/g creatinine)***		
Categories (mg albumin/g creatinine)	*< 30*	*≥ 30*	***Total***	*Categories (mg protein/g creatinine)*	*< 30*	*≥ 30*	***Total***	*Categories (mg protein/g creatinine)*	*< 30*	*≥ 30*	***Total***
< 30	696	17	*713*	*< 150*	*709*	*51*	*760*	*Negative*	*576*	*36*	*612*
≥ 30	60	152	*212*	≥ 150	*47*	*118*	*165*	Positive	*181*	*132*	*313*
Total	*756*	*169*	*925*	***Total***	*756*	*169*	*925*	***Total***	*756*	*169*	*925*
Agreement	91.7%			**Agreement**	89.4%			**Agreement**	76.5%		
Cohen's kappa (Weighted)	0.746			**Cohen's kappa (Weighted)**	0.642			**Cohen's kappa (Weighted)**	0.409		
Sensitivity	89.9% (95%CI: 84.4–94.0%)			Sensitivity	69.8% (95%CI: 62.3–76.6%)			Sensitivity	78.6% (95%CI: 71.6 – 84.5%		
Specificity	92.1% (95%CI: 89.9–93.9%)			Specificity	93.8% (95%CI: 91.8–95.4%)			Specificity	76.1% (95%CI: 72.9 – 79.1%)		
PPV	71.7% (95%CI: 66.4–76.5%)			PPV	71.5% (95%CI: 65.2–77.1%)			PPV	42.2% (95%CI: 36.6 – 47.9%)		
NPV	97.6% (95%CI: 96.3–98.5)			NPV	93.3% (95%CI: 91.7–94.6%)			NPV	94.1% (9%CI: 92.0 – 95.9%)		
LR+	11.3 (95%CI: 8.8–14.5)			LR+	11.2 (95%CI: 8.4–15.1)			LR+	3.3 (95%CI: 2.8–3.8)		
LR-	0.11 (95%CI: 0.07–0.17)			LR-	0.32 (95%CI: 0.26–0.41)			LR-	0.28 (95%CI: 0.21 – 0.38)		
Predictive probability	0.933 (95% CI: 0.905–0.960)			Predictive probability	0.830 (95%CI: 0.787–0.873)			Predictive probability	0.774 (95%CI: 0.735–0.814)		

Abbreviations: ACR: albumin-to-creatinine ratio; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio; PCR: protein-to-creatinine- ratio

Expanding screening efforts to higher-risk individuals may still necessitate follow-up quantitative confirmation to ensure diagnostic precision. Based on these results, it is recommended that CKD screening via urine test strips be primarily directed towards lower-risk outpatient populations, where predictive accuracy is improved. This approach distinction is consistent with the overall goal of optimizing resource allocation while retaining diagnostic reliability [19]. However, the findings underline that test strip procedures should not be applied universally to all patient populations because their efficacy differs according on disease frequency and patient characteristics.

Given that the semi-quantitative ACR is the only readout demonstrating positive and negative likelihood ratios of 11.3 and 0.11, respectively, this readout should be preferred in CKD screening algorithms when urine test strips are used [20]. These results are confirmed by the high predictive probability of ACR for CKD as compared to semi-quantitative PCR and qualitative PCR [6]. Additionally, the agreement between the KDIGO CKD-risk score classification based on eGFR and semi-quantitative and quantitative ACR indicates that the semi-quantitative results obtained with the test strip are reliable. However, reporting the category in which the patient is classified has limited diagnostic value and should primarily serve as an indication for quantitative ACR determination. The CKD stage assigned based on semi-quantitative test strip results may necessitate confirmation by quantitative analysis.

Although it is clear that quantitative ACR is the best parameter for evaluating albuminuria in CKD, especially in high-risk patients, there is still debate on the appropriate screening technique in lower-risk patients. Lamb et al.. examined several algorithms for detecting proteinuria and concluded that urinary albumin measurement is analytically superior to total urinary protein measurement and should be prioritized as first-line test for detecting proteinuria due to its higher sensitivity, standardization, and ability to improve the consistency of early CKD detection [21]. Furthermore, they stated that semi-quantitative test strips have low sensitivity and clinical reliability, resulting in false-negative results and variation between laboratories. Recent evidence from Salinas et al. demonstrated that a semiquantitative ACR strip test can effectively identify pathological albuminuria values under certain conditions, with false negatives below 1% and significant cost savings by eliminating the need for unnecessary quantitative confirmation in up to 40% of cases [7]. However, in the current KDIGO and National Institute for Health and Care Excellence (NICE) guidelines, multiple options for the detection of proteinuria are presented without further defining whether quantitative or semi-quantitative test strip results should be used to screen for albuminuria or proteinuria in the general population [22, 23]. The recently updated EFLM European urinalysis guideline 2023 proposes using multi-property urine test strips as a screening tool for CKD in routine patient populations, followed by a quantitative test to confirm the diagnosis [8]. According to recent data, only a small percentage of clinical laboratories use test strips to screen for ACR in Belgium [24]. Total protein readout remains the standard screening read-out on test strips in the majority of clinical laboratories. However, our data demonstrate that protein readout may be suboptimal, and screening by the ACR pad on the urine test strip may be a more effective strategy.

In conclusion, our data further add to the evidence that urine test strips may be a valuable screening tool for CKD in low-risk individuals. Moreover, if urine test strips are used to screen for albuminuria and CKD, ACR-readout is preferred as a decision criterion for reflex testing.

Abbreviations

ACR	Albumin to creatinine ratio
CI	Confidence interval
CKD	Chronic kidney disease
eGFR	Estimated glomerular filtration rate
KDIGO	Kidney Disease: Improving Global Outcomes
LR	Likelihood ratio
NICE	National Institute for Health and Care Excellence
PCR	Protein to creatinine ratio
SD	Standard deviation

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Author contributions
SL (Stijn Lambrecht) and MO (Matthijs Oyaert) conceptualized the study and developed the methodology. SL and MO were responsible for data analysis. SL, MO and MS (Marijn Speeckaert) drafted the main manuscript text. All authors reviewed and approved the final manuscript.

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Data availability
The materials described in the manuscript, including all relevant raw data, will be available to any scientist wishing to use them for non-commercial purposes. The data that support the findings of this study are then available from the corresponding author (matthijs.oyaert@uzgent.be) upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Medical Ethics Committee of the Ghent University Hospital, project-ID ONZ-2024-0113. As this study was performed on left-over material, consent was waived.

Consent for publication
Consent to participate was waived due to the use of anonymized and de-identified data.

Competing interests
The authors declare no competing interests.

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