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RESEARCH ARTICLE

Comparative Study of the Clinical Utility of Measuring Free Light Chains in Urine Versus Urine Protein Electrophoresis in Monoclonal Gammopathies

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Abstract

Introduction: To date, UPE is the only recommended technique for measuring FLCs in 24-hour urine samples from monoclonal gammopathies, although it has low diagnostic sensitivity. The Freelite assay for FLCs is available as an alternative method, although very few studies in urine have been conducted on it.

Material and Methods: In this study, the clinical usefulness of the FLC assay was investigated respect to the UPE method in 24-hour urine samples (N = 180) from patients with different monoclonal gammopathies [multiple myeloma (MM), light chain (LC)-MM, monoclonal gammopathy of undetermined significance (MGUS), monoclonal gammopathy of renal significance (MGRS), and LC-MGUS] using the uIFE as the reference technique.

Results: FLCs, measured in mg/dL, showed for both urinary kappa and lambda FLCs, that the FLC assay has higher sensitivity compared to UPE (Kappa: 96.15% vs. 69.23%; Lambda: 94.12% vs. 78.43%; $p < 0.05$ in both cases), although it exhibits lower specificity for both types (Kappa: 77.77% vs. 93.90%; Lambda: 74.75% vs. 95.06%; $p < 0.05$). In the analysis in mg/24 hours, the mean values of both kappa and lambda FLCs showed higher levels compared to UPE ($p < 0.05$), and a positive correlation was also found between both techniques ($p < 0.05$). Conversely to analysis of FLCs measured in mg/dL, the study in mg/24 hours, showed that for both kappa and lambda FLCs, the urine FLC assay had greater diagnostic accuracy compared to UPE (Kappa: AUC = 0.919 vs. AUC = 0.819; Lambda: AUC = 0.970 vs. AUC = 0.869; respectively). Conclusion: The FLC assay is a useful method for determining monoclonal FLCs in urine, measured as urinary proteins in mg/24 hours, for both their detection and quantification.

Keywords: Free Light Chains, Kappa-free Light Chain, Lambda-Free light Chain, Monoclonal Gammopathy, Urine FLC Assay, Urine Protein Electrophoresis, Urine Immunofixation Electrophoresis.

1. Introduction

Immunoglobulin kappa and lambda free light chains (FLCs) can appear in blood as part of an overproduction mediated by plasma cells located at bone marrow and lymph nodes [1]. Plasma cells produce an excessive synthesis of FLCs of between 10% and 40% compared to heavy chains [2]. However, the biological significance of this excess is unknown [2].

Free light chains (FLCs), due to their lower molecular weight (22 kDa for the kappa chain as a monomeric and 45 kDa for the lambda chain as a dimeric linked by disulfide bonds), are filtered by the glomerular basement membrane in the nephrons and then reabsorbed and catabolized in the proximal tubules [1]. Therefore, under normal conditions no light chains passes beyond the proximal tubules. However,

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abnormal concentrations of kappa and lambda FLCs in urine can be due to different clinical conditions, such as decreased renal clearance in patients with chronic kidney disease (CKD) or monoclonal plasma cell disorders when overproduction exceeds reabsorption capacity [3,4].

Excess FLCs have toxic effects on glomerular membranes and/or renal tubules. They form aggregates and casts with Tamm-Horsfall protein in the distal tubules (cast nephropathy), leading to tubular obstruction and concomitant inflammation [5]. In addition, obstruction of urinary flow causes the death of the corresponding nephrons [5].

The detection of kappa and lambda FLCs in urine is routinely performed from 24-hour urine samples from patients with different monoclonal plasma cell disorders, including light chain amyloidosis (AL) [4], smoldering multiple myeloma (SMM) [6], light chain monoclonal gammopathy of undetermined significance (LC-MGUS) [6], and light chain multiple myeloma (LC-MM) [4], among other [6]. Similarly, the study of 24-hour urine is essential in renal pathologies involving nephrotoxic monoclonal FLCs, such as monoclonal gammopathy of renal significance (MGRS) [7].

To date, the technique recommended in clinical guidelines for performing a 24-hour urine analysis in both monoclonal plasma cell disorders [6] and MGRS [7] is urine protein electrophoresis (UPE) for detection and quantification, followed by urine immunofixation electrophoresis (uIFE), used only for detection, as it is the most sensitive [8].

However, the UPE has several technical problems that reduce its clinical utility. These include: a) a low sensitivity percentage due to the high detection limit for protein in urine (> 100 mg/L) [9,10], and b) analytical sensitivity varies between laboratories depending on the different systems used [11,12]. Therefore, it is essential to find an alternative technique to UPE for the detection and quantification of FLCs, which are found at low levels in urine, both for screening and for monitoring different monoclonal diseases that damage the kidney [4,6-7].

As an alternative method to UPE in 24-hour urine samples, the immunonephelometric FLC assay (Freelite), initially developed in serum samples in 2001 [13], has been performed in certain studies. Although the results obtained when comparing the UPE with the FLC assay in urine have been contradictory. Thus, different studies have shown a high rate of false positives using the urine FLC assay [9,12,14]. To this end, the detection and quantification capability of the FLC assay in urine (Freelite) has been evaluated in comparison with UPE in patients with various monoclonal plasma cell disorders.

2. Material and Methods

2.1 Patients and Urine Samples

One hundred and thirty-one adult patients (n = 131) (> 18 years old) treated between January 1, 2020 and September 30, 2026 at the Hematology Service of the University General Hospital of Ciudad Real (Spain) were enrolled for the study. The group of patients diagnosed in the Hematology Service (n= 131) presented different types of monoclonal gammopathies, including: multiple myeloma (MM), light chain (LC)-MM, monoclonal gammopathy of undetermined significance (MGUS), monoclonal gammopathy of renal significance (MGRS), and LC-MGUS (Table 1).

Table 1. *Clinical and laboratory characteristics of the enrolled patients with monoclonal gammopathies*

Characteristic	Clinical	Laboratory	
Nº of patients	N = 131	24-hour urine specimens	N = 180
Gender (sex ratio M/F)	79 M / 52 F (ratio: 1.52)	24-hour urine protein test (mg/24 h) (mean ± SD)	456.87 ± 1065 (mg/24 h)
Pathologies	MM, N = 25(IgG = 14; IgA = 9; and IgM = 2)	Positive uIFE	MM (N = 20)Kappa, N = 15 Lambda; N = 5
	LC-MM, N = 23		LC-MM (N = 40)Kappa, N = 11 Lambda; N = 29
	MGUS, N = 66 (IgG = 46; IgA = 16; and IgM = 4)		MGUS (N = 17)Kappa, N = 8 Lambda; N = 9
	MGRS, N = 14 (IgG = 12 and IgA = 2)		MGRS (N = 19)Kappa, N = 13 Lambda, N = 6
	LC-MGUS, N = 3		LC-MGUS (N = 3)Kappa, N = 2 Lambda; N = 1

Abbreviations: *F, female; h, hours; LC, light chain; M, male; MGRS, monoclonal gammopathy of renal significance; MGUS, monoclonal gammopathy of undetermined significance; MM, multiple myeloma; uIFE, urine immunofixation electrophoresis.*

The mean age at the time of diagnosis in the patient cohort was 68.51 ± 11.74 years (mean ± SD); gender, sex distribution, and the number of patients diagnosed with the various monoclonal gammopathies are summarized in Table 1.

Clinical data were collected from each patient by reviewing their medical records in accordance with the ethical standards of the institutional and/or national research committee, the 1964 Declaration of Helsinki, and its later amendments or comparable ethical standards; and all patients provided informed consent to participate in this study. The Ethics Committee of the Ciudad Real University General Hospital also approved the study.

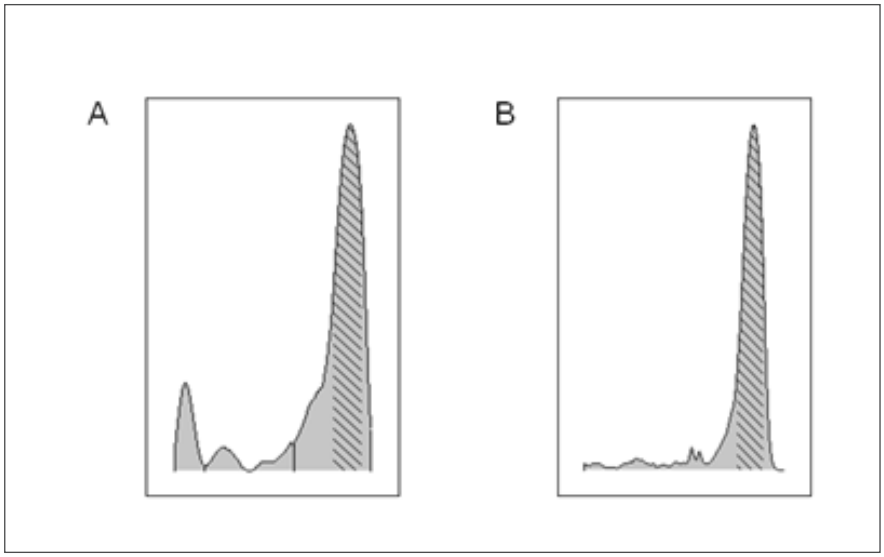
In all patients, 24-hour urine specimens were collected for parallel analysis of the following diagnostic assays: urine immunofixation electrophoresis (uIFE) as the reference technique [15], urine protein electrophoresis (UPE), and urine free light chain (uFLC) assay. Table 1 shows the number of 24-hour urine samples analyzed for each monoclonal gammopathy group that tested positive in the uIFE assay for kappa and lambda light chains.

2.2 Urine Immunofixation Electrophoresis (uIFE) and Urine Protein Electrophoresis (UPE) Assays

All determinations using uIFE and UPE were performed from 24-hour urine specimens, collected without any preservatives and refrigerated at 4°C until analysis in the laboratory according to published recommendations [15]. To carry out both techniques, non-concentrated urine samples from 24-hour urine specimens were used.

First, the uIFE reference method was performed using the SAS-MX urine IFE-1 Kit (Helena-Biosciences, Gateshead, UK) from 10 µL of un-concentrated urine samples. After electrophoretic separation at 100 V and 20ºC for 20 minutes in the SAS-1 automated electrophoresis analyzer (Helena), immunoprecipitation was performed using the uIFE antisera kit (anti-IgG, anti-IgA, anti-IgM, anti-free kappa and anti-free lambda antibodies) (Helena). The following steps were performed on the SAS-2 automated gel processing instrument (Helena), monoclonal bands of FLCs were detected by visual inspection of stained gels (data not shown).

For the UPE, urine samples of 20 µL were automatically prepared on gel plates (for a maximum of 24 urine samples) performed in the V8 capillary electrophoresis analyzer from Helena (Helena). Then, the gel plates with 24 urine samples were subjected to electrophoretic separation at 100 V and 20ºC for 20 minutes in the SAS-1 analyzer (Helena). After electrophoresis according to the manufacturer's recommendations (Helena), the gel plates were transferred to the SAS-2 system (Helena), which stains with acid violet, distains and dries the gel. Next, stained and dried gels were scanned by densitometry using the Platinum-5 analytical interpretation software (Helena) in the V8 analyzer (Helena); positive results were samples with proteinuria or abnormal protein bands observed as different patterns. Monoclonal pattern is presented as mainly a single band in the gammaglobulin region consisting of free light chains (Supplementary Fig. 1A and 1B).



Supplementary Figure 1. *The 24-hour urine samples were analyzed by agarose electrophoresis and scanning on the V8 system (Helena). Samples A and B showed a monoclonal pattern corresponding to free light chains (FLC); all these results were confirmed by uIFE (data not shown).*

2.3 Automated Immunoassay for the Measurement of Free Light Chains in Urine (uFLC)

Urinary FLCs (kappa and lambda) were quantified using the Optilite Freelite Mx Kappa Free kit (LK016.M.OPT.A) (Binding Site, Birmingham, United Kingdom) and the Optilite Freelite Mx Lambda Free kit (LK018.M.OPT.A) (Binding Site) from 24-hour urine samples using the Optilite analyzer (Binding Site). Quantification was carried out by a turbidimetric assay, using a latex reagent formed from sheep monospecific anti-human kappa and anti-human lambda [fragment F(ab')2] polyclonal antibodies (respectively) attached to 200 nm polystyrene latex particles (Binding Site).

The reference ranges in urine samples for free light chains were as follows: a) free kappa > 32.90 mg/L, and b) free lambda > 3.79 mg/L (above the 97.5th percentile, as mentioned in the Binding Site manufacturing brochure).

2.4 Quantification of Total Proteins in 24-hour Urine

The total protein level for the detection of proteinuria was determined from 24-hour urine samples using an immunoturbidimetric assay on a Roche/Hitachi Cobas c 303 system (Roche Diagnostic, USA) (values above 140 mg/24 hours were considered positive). The mean protein value in 24-hour urine samples (N = 180) from the patients evaluated is presented in Table 1.

The Roche Diagnostics urinary protein assay is based on the method described by Iwata and Nishikaze, later modified by Luxton et al., [16]. In this method, benzethonium chloride reacts with proteins in a basic medium to produce turbidity [16].

2.5 Statistical Analysis

The frequency of qualitative variables was expressed as a percentage, and comparisons of sensitivity and specificity between the UPE and uFLC assay were performed using Chi-square tests (2 x 2 contingency tables) and Yates' correction. Differences between means of quantitative variables were calculated by the T-test. Furthermore, associations were analyzed using Pearson's correlation coefficient, expressing the degree of association as the correlation coefficient (r).

Receiver operating characteristic (ROC) curves were constructed, using uIFE as the reference method, to detect the presence of FLCs in urine and to calculate the area under the curve (AUC), as well as the optimal cut-off points for analysis via UPE and the uFLC assay [17].

All statistical analyses were performed using IBM SPSS Statistics software (version 29). Differences were considered statistically significant with p-values less than 0.05.

3. Results

3.1 Assessment of the Sensitivity and Specificity of the UPE and uFLC Assays

The number of positive urine samples using uIFE in the different monoclonal gammopathies (MM, LC-MM, MGUS, MGRS, and LC-MGUS) is summarized in Table 1 (99 out of 180, 55%). Using uIFE as the reference method, a comparative analysis was performed between the UPE and uFLC methods from 24-hour urine samples (N = 180) (Table 2). For this purpose, free kappa and lambda light chains were analyzed separately using the cut-off points established by the Binding Site manufacturer: a) free kappa in urine > 32.9 mg/L and b) free lambda in urine > 3.79 mg/L. Thus, for both free kappa and lambda, the uFLC assay showed greater sensitivity with respect to UPE (96.15% *vs.* 69.23% for free kappa and 94.12% *vs.* 78.43% for free lambda; respectively, $p < 0.05$) (Table 2). In contrast, UPE showed greater specificity with respect to the uFLC assay for both free kappa and lambda (93.90% *vs.* 77.77% for free kappa and 95.06% *vs.* 74.75% for lambda; respectively, $p < 0.05$) (Table 2).

Using the uIFE method as a reference, the uFLC assay was able to identify N = 27 urine samples as true positives with respect to UPE in which the samples were negative (27 out of 103, 26.21%) (16 for free kappa and 11 for free lambda) (Table 2). However, the uFLC assay had a higher number of false positives N = 48 (48 out of 77, 62.33%) (22 for free kappa and 26 for free lambda) compared to UPE in which there were only N = 9 (9 out of 77, 11.68%) (5 for free kappa and 4 for free lambda) (Table 2).

3.2 Quantitative Analysis of Free Kappa and Lambda Light Chains in Urine using the UPE and uFLC Methods

To investigate the quantification capacity of both methods for free light chains in urine (kappa and lambda), urinary protein levels were determined in mg/24 hours.

The mean values (mg/24 hours) for free kappa determined by the uFLC assay showed significant differences with respect to UPE (2942.81 ± 6196.18 *vs*. 614.22 ± 932.29; respectively, $p = 0.009$) (mean ± SD) (Fig. 1, A1). Similarly, free lambda in urine

showed a higher protein level (mg/24 hours) by the uFLC assay compared to UPE (4107.78 ± 9015.06 *vs.* 941.41 ± 1613.71; respectively, $p = 0.015$) (mean ± SD) (Fig. 1, A2).

Despite the large differences in urine protein levels (mg/24 hours) of free kappa and lambda using the uFLC assay compared to UPE, the correlation study showed a significant positive association for both free kappa ($r = 0.289$, $p = 0.038$) (Fig. 1, B1) and lambda ($r = 0.921$, $p < 0.001$) (Fig. 1, B2) using both methods, although with a higher correlation with respect to free lambda.

Table 2. *Comparative analysis between the UPE and uFLCs assays in the detection of monoclonal FLCs in urine specimens (N = 180 specimens) from monoclonal gammopathies*

Isotype of free chain	**Positive-uIFE**	**Positive-UPE**	**Sensitivity of UPE**	**uFLC-Kappa > 32.9 (mg/L)**	**Sensitivity of uFLC-Kappa**	**UPE *vs.* uFLC-Kappa (p-value)**
Kappa	N = 52	N = 36	69.23%	N = 50	96.15%	$**p_c = 0.000753$
	Negative-uIFE	**False positive-UPE**	**Specificity of UPE**	**False positive-FLC-Kappa > 32.9 (mg/L)**	**Specificity of uFLC-Kappa**	**UPE *vs.* uFLC-Kappa (p-value)**
Kappa	N = 77	N = 5	93.90%	N = 22	77.77%	$**p_c = 0.000697$
Isotype of free chain	**Positive-uIFE**	**Positive-UPE**	**Sensitivity of UPE**	**uFLC-Lambda > 3.79 (mg/L)**	**Sensitivity of uFLC-Lambda**	**UPE *vs.* uFLC-Lambda (p-value)**
Lambda	N = 51	N = 40	78.43%	N = 48	94.12%	$*p_c = 0.017533$
	Negative-uIFE	**False positive-UPE**	**Specificity of UPE**	**False positive-uFLC-Lambda > 3.79 (mg/L)**	**Specificity of uFLC-Lambda**	**UPE *vs.* uFLC-Lambda (p-value)**
Lambda	N =77	N = 4	95.06%	N = 26	74.75%	$***p_c = 0.00001$

Abbreviations: *FLCs, free light chains; p_c, p-value corrected with Yates' correction; uIFE, urine immunofixation electrophoresis; UPE, urine protein electrophoresis *p < 0.05, **p < 0.001, ***p < 0.0001*

3.3 Optimal Cut-off Points for Free Kappa and Lambda Light Chains in Urine using UPE and uFLC Assays

ROC curves were calculated from data obtained with the uIFE from N = 180 urine samples, for both free kappa and lambda. For this purpose, the concentration of protein in urine was expressed in mg/24 hours.

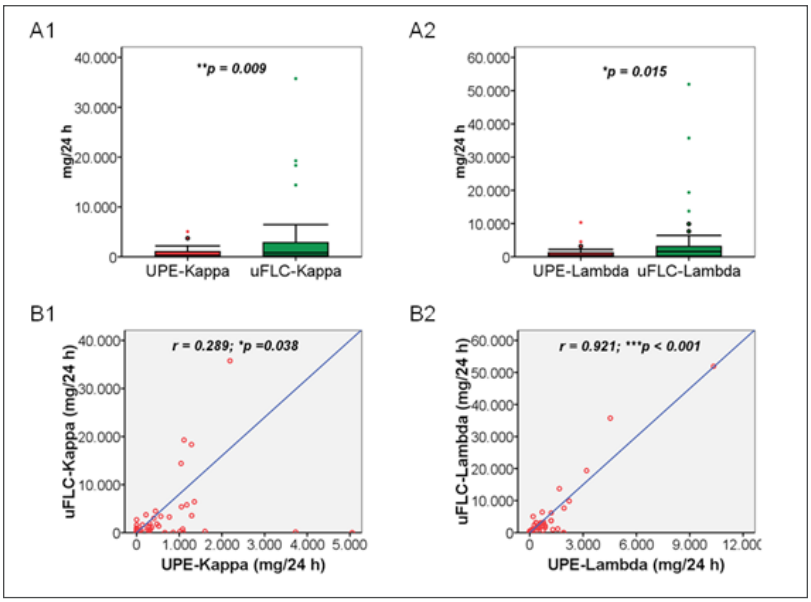


Figure 1. *A1 and A2 show comparisons between urinary kappa-free light chain protein levels (mg/24 hours) and lambda-free light chain protein levels (mg/24 hours) using the UPE and uFLC assays, respectively. B1 and B2 represent the linear correlations of urinary kappa-free light chain protein levels (mg/24 hours) and lambda-free light chain protein levels (mg/24 hours) measured with the UPE and uFLC assays. Abbreviations: h, hours; r, correlation-coefficient. *p < 0.05, ***p < 0.001*

In the analysis of free kappa in urine using the UPE and uFLC assays, the AUCs obtained were as follows: a) UPE, AUC = 0.819 (95% CI: 0.737-0.901; *p = 0.001*), and b) uFLC assay, AUC = 0.919 (95% CI: 0.867-0.970; *p = 0.001*) (Figure 2, A). For free lambda in urine, ROC curves showed similar AUC results: a) UPE, AUC = 0.869 (95% CI: 0.796-0.941; *p = 0.001*), and b) uFLC assay, AUC = 0.970 (95% CI: 0.945-0.996; *p = 0.001*) (Figure 2, B). Therefore, for both free kappa and lambda, measured as urine protein in mg/24 hours, the uFLC assay showed greater diagnostic accuracy compared to UPE.

Based on the ROC curves analysis, the optimal cut-off points obtained to detect free kappa and lambda in urine quantified as proteins in mg/24 hours using the uFLC assay were the following: a) free kappa: 108.75 mg/24 hours (Sensitivity = 94.23% and Specificity = 84.6%), and b) free lambda: 52.44 mg/24 hours (Sensitivity = 94.12% and Specificity = 89.53%). For the UPE assay, the cut-off point reached for free kappa was of 53.31 mg/24 hours (Sensitivity = 67.3% and Specificity = 93.5%), and for free lambda it was of 38.85 mg/24 hours (Sensitivity = 78.4% and Specificity = 93.5%).

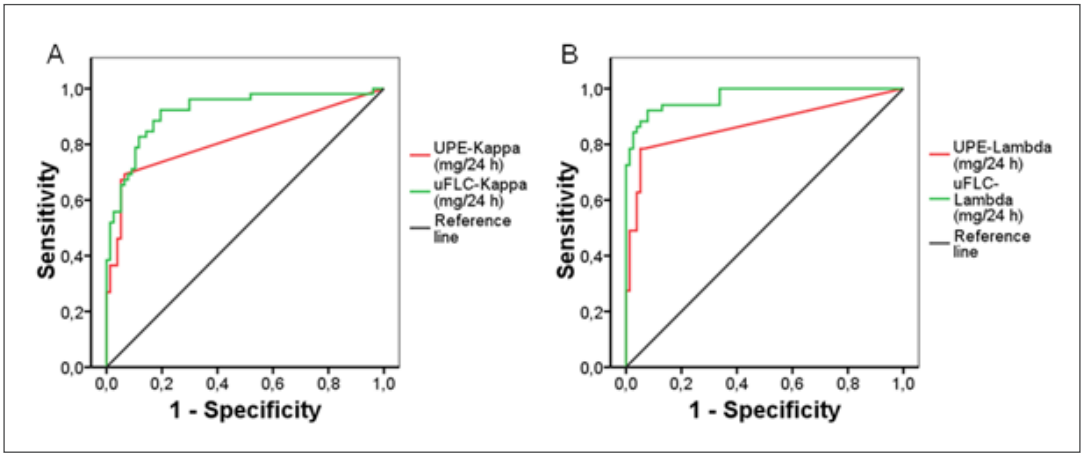


Figure 2. *Comparisons of ROC curves of urinary protein levels of kappa-free light chain (mg/24 hours) and lambda-free light chain (mg/24 hours) using the UPE and uFLC assay. Abbreviations: h, hours.*

4. Discussion

To date, the 24-hour urine study to detect and quantify kappa and lambda free light chains cannot be replaced by any other serum analysis both for the diagnosis and for the monitoring of different monoclonal plasma cell disorders and MGRS [18]. It is due to the nephrotoxic effect that FLCs have on renal structures, therefore acting as biomarkers of kidney injury [19]. For the detection of FLCs in urine samples, the uIFE represents the most sensitive test but is not able of quantification [8], with the UPE being the only recommended method to measure proteins in urine [6,7]. As an alternative method to UPE, the FLC assay has been scarcely investigated for this purpose. Therefore, the main objective of this study has been to investigate the clinical usefulness of the FLC assay (Freelite) in 24-hour urine samples with respect to UPE in different types of monoclonal gammopathies (Table 2).

In this study, uIFE, UPE and FLC assays were performed in parallel from 24-hour urine samples (N = 180). For this purpose, non-concentrated urine samples were used. The first study that applied the serum FLC assay to urine samples to quantify urinary kappa and lambda free light chains was published in 2002 by Le Bricon et al., [9]. Un-concentrated urine samples from 20 patients with MM were analyzed, and UPE and FLC (Freelite) techniques were performed, with both assays quantified proteins in mg/L [9]. They found, that the FLC assay overestimated the concentration in 75% of the samples, with a high false-positive rate [9]. In a second and more recent study of 658 samples of 24-hour urine, the authors compared both techniques for measuring FLCs in mg/L [12]. The urine FLC assay showed greater sensitivity than UPE (92% *vs.* 68.1%, respectively) [12]; conversely, it showed lower specificity compared to UPE (57.6% *vs.* 98.8%, respectively) [12]. Similarly, the results obtained in the present study showed, for both kappa and lambda free light chains in urine, measured in mg/L (Table 2), that the FLC (Freelite) assay is more sensitive than UPE, although it has lower specificity, consistent with previous studies published by Le Bricon et al. [9] and Delgado JC [12]. These differences observed between the two methods regarding specificity do not appear to be related to the use of concentrated or un-concentrated urine samples. Thus, Haran et al., [20] compared undiluted urine samples with concentrated samples, studying in parallel the UPE and urine FLC (Freelite) assay in samples from patients with different pathologies, including monoclonal gammopathies.

They found no differences between the use of concentrated and un-concentrated urine samples; moreover, concentrating the urine was a laborious and time-consuming process [20].

The quantification of monoclonal proteins in mg/24 hours is established in the diagnostic criteria of the International Myeloma Working Group (IMWG) for MM (≥ 500 mg/24 hours), as well as for SMM (≥ 500 mg/24 hours) and LC-MGUS (< 500 mg/24 hours) [6]. Furthermore, the decrease in urinary monoclonal protein levels, measured in mg/24 hours, is used to monitor treatment response in MM [21]. To this end, the study also measured urinary levels of free kappa and lambda light chains, expressed in mg/24 hours; a comparison of the UPE and FLC techniques yielded surprising results that, to date, have not been published.

The mean values of kappa and lambda free light chains, measured using the urine FLC (Freelite) assay, were higher than the levels detected with UPE (Fig. 1, A1 and A2). A significant correlation was also observed between the protein levels (mg/24 hours) quantified with both techniques, for both kappa and lambda free light chains (Fig. 1, B1 and B2). ROC curve analysis showed that the FLC assay in urine, compared to the UPE, had the best diagnostic accuracy for the levels of kappa and lambda free light chains measured in urine (Fig. 2, A and B), with greater sensitivity and specificity than the UPE. Therefore, when kappa and lambda FLCs are measured in mg/24 hours, FLC analysis in urine serves as a useful technique for detecting and quantifying levels of monoclonal protein, and can be used for both the diagnosis and monitoring of monoclonal gammopathies [6,21]. However, given that these are distinct techniques, the results obtained via UPE and urine FLC analysis (Freelite) are not interchangeable for patient monitoring.

To date, FLC analysis has not been incorporated into routine clinical practice due to the presumed variability in kappa and lambda FLC levels, attributable to changes in glomerular filtration and variability in tubular reabsorption, as well as a lack of data regarding its use [22]. Nevertheless, this study provided evidence regarding the clinical utility of this assay for monoclonal gammopathies, in comparison with UPE. Furthermore, previous studies involving random urine samples [22] and 24-hour urine samples [23] from patients with monoclonal gammopathies have documented a positive correlation between the quantitative levels of FLCs in serum and urine, both measured using the FLC (Freelite) assay. The FLC assay, which can serve as a complementary technique to UPE, increases both sensitivity and specificity, compared to using UPE alone, for the detection and quantification of kappa and lambda free light chains [24].

5. Conclusion

Among the monoclonal gammopathies included in this study (Table 1), the urine FLC assay (Freelite), expressing the levels of kappa and lambda free light chains in mg/24 hours, offers an alternative method to UPE with greater diagnostic accuracy (Fig. 3).

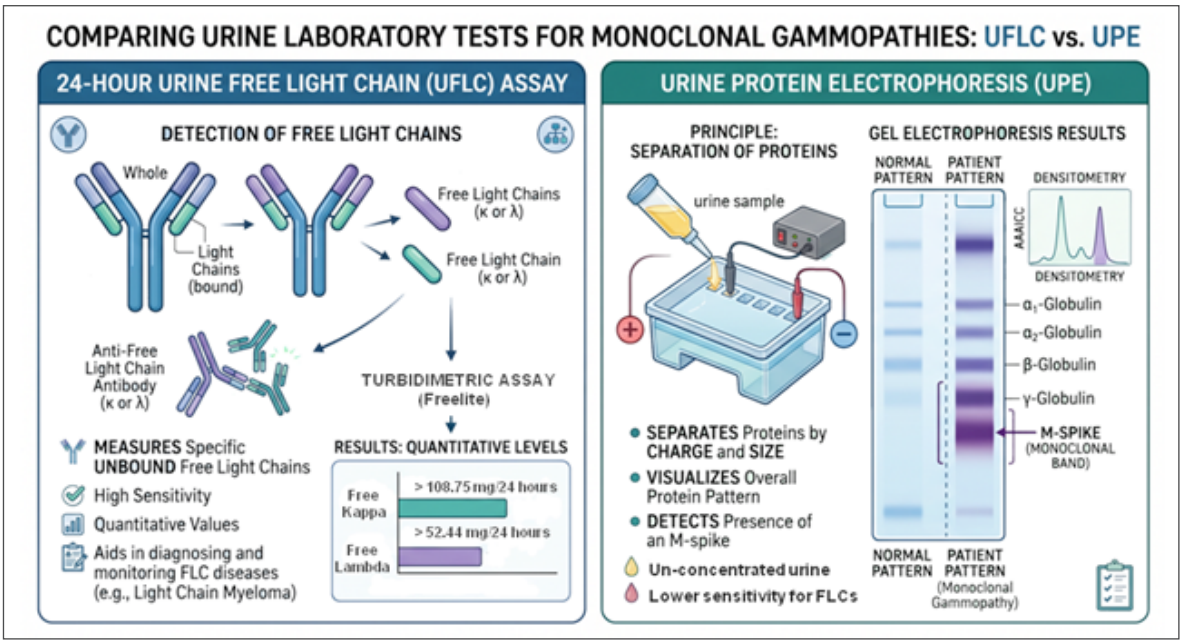


Figure 3. *Graphical representation of the clinical utility of the FLC (Freelite) assay versus UPE in urine samples from patients with monoclonal gammopathies.*

Furthermore, the urine FLC assay presents other advantages over the UPE, such as standardization between laboratories, which avoids differences in analytical sensitivity [11,12], as well as greater ease and immediacy in the analysis [13]. The combined use of this assay and UPE could improve detection and quantification capabilities in urine samples with free light chain levels below the detection limit of UPE. However, one limitation of the study that should be noted is that other monoclonal gammopathies, such as AL or SMM, were not included. Therefore, further research is needed, at least with regard to those monoclonal gammopathies not included in this study, to corroborate the clinical utility of measuring free light chains in urine using the Freelite assay.

Abbreviations: AL: Light Chain Amyloidosis, AUC: Area Under the Curve, CKD: Chronic Kidney Disease, FLCs: Free Light Chains, MGUS: Monoclonal Gammopathy of Undetermined Significance, MM: Multiple Myeloma, MGRS: Monoclonal Gammopathy of Renal Significance, SMM: Smoldering Multiple Myeloma, uFLC: Urine Free Light Chain Assay, uIFE: Urine Immunofixation Electrophoresis, UPE: Urine Protein Electrophoresis, ROC: Receiver Operating Characteristic Curve

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Disclosure of Potential Conflicts of Interest

The author declares that there is no conflict of interest.

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