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Evaluation of a urine dipstick protein to urine specific gravity ratio for the detection of proteinuria in dogs and cats

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Abstract

Background: The utility of urine dipsticks for the quantification of proteinuria is limited because of the influence of urine specific gravity (USG). To circumvent the need for urine protein creatinine ratios (UPCR) some have proposed a calculated dipstick urine protein to USG ratio (DUR) for the detection of proteinuria. However, the performance of DUR has not been evaluated in veterinary patients.

Objectives: Evaluate the correlation between DUR and UPCR, while also assessing the effect of urine characteristics on this relationship and evaluating the performance of DUR in detecting proteinuria.

Animals: Urine samples from 308 dogs and 70 cats.

Methods: Retrospective cohort study of urinalyses and UPCRs from dogs and cats collected between 2016 and 2021.

Results: Both canine and feline urine samples showed a positive moderate correlation between the UPCR and DUR. The correlation was not influenced by the presence of active urine sediment, glucosuria, or urine pH. In detecting canine urine samples with a UPCR >0.5, an optimal DUR of 1.4 had sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 89%, 83%, 96%, and 63%, respectively. In detecting feline urine samples with a UPCR >0.4, an optimal DUR of 2.1 had sensitivity, specificity, PPV, and NPV of 70%, 100%, 100%, and 75%, respectively.

Conclusions and Clinical Importance: Use of the DUR can be a relatively reliable method for identification of proteinuria. However, given its poor NPV, the DUR cannot be recommended for exclusion of proteinuric patients.

KEYWORDS
albuminuria, glomerular, protein losing nephropathy, renal

1 | INTRODUCTION

In routine clinical settings, first line detection of proteinuria commonly is accomplished using urine dipsticks. These colorimetric reagent pads allow rapid semiquantitative measurement of proteinuria, detecting predominantly albumin.[1] Despite their ease of use and low cost,

Abbreviations: AUC, area under the curve; CI, confidence interval; DUR, dipstick protein to USG ratio; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic; UPCR, urine protein creatinine ratio; USG, urine specific gravity.

factors such as urine concentration, color, and pH have been reported to cause false positive or negative results.[2,3] In addition, dipsticks do not allow for quantification of daily urinary protein loss. In contrast, urine protein creatinine ratio (UPCR) measurement, which has been shown to accurately reflect urinary protein loss over 24 hours,[4] is recommended when persistent proteinuria is detected on dipsticks.[5,6]

Several studies have evaluated the effect of urine specific gravity (USG) on the performance of urine protein dipsticks for the detection of clinically relevant proteinuria in dogs and cats. A retrospective study of 394 dogs indicated that when urine samples were divided based on protein dipstick results, a significant inverse relationship between UPCR and USG was present. However, this correlation was relatively weak.[7] In another study, the sensitivities and specificities of the urine dipstick for the detection of protein varied substantially when samples were grouped based on their USG being above or below 1.012, further emphasizing the importance of USG in the interpretation of urine protein dipstick results.[2] Alternatively, some have investigated the use of higher dipstick protein thresholds for the detection of clinically relevant proteinuria. Although using higher urine dipstick thresholds has been shown to increase specificity of proteinuria detection in both cats and dogs, this approach predictably results in decreased sensitivity.[2,8] Because of the additional time and cost associated with performing UPCR, and the occasional need to collect additional urine samples, the use of a urine protein concentration to urine osmolality ratio has been proposed as a convenient means to estimate proteinuria, using a value ≥2.5 to identify people with renal protein loss in excess of 3 g per 24 hours.[9] Despite a lack of data evaluating its performance for proteinuria quantification in veterinary medicine, this ratio has been adapted for use in a study that employed a urine dipstick protein to USG ratio (DUR) to estimate urinary protein content.[10] In that study, a cutoff for detection of abnormal protein concentrations in urine was defined as a DUR of ≥1.5, which represents 1+ proteinuria (30 mg/mL) in urine with a USG of 1.020 as the upper limit of normal.[10]

Our aim was to evaluate the correlation between DUR and UPCR as well as to assess the influence of the physical, chemical and sediment properties of urine on this relationship. In addition, we assessed the performance of the DUR in detecting proteinuria based on the International Renal Interest Society (IRIS) guidelines. Lastly, we aimed to assess the performance of the previously reported DUR of 1.5 in its capacity to detect proteinuric samples.

2 | MATERIALS AND METHODS

2.1 | Case selection

The medical records of the Lloyd Veterinary Medical Center of Iowa State University were reviewed between August 2016 and August 2021 for dogs and cats that had complete medical records, including case history, physical examination findings, and case assessment, as well as urinalysis, urine culture, and UPCR performed within a 24-hour period. Cases were excluded from the study if medical records were incomplete or if >24 hours had elapsed between submission of urine for urinalysis and either urine culture or UPCR. Data collected included the patient's signalment, urine culture results, urine collection method, urine physical characteristics, urine dipstick data, UPCR and sediment examination results.

All urinalyses, UPCR, and urine cultures were performed by the same laboratory (Iowa State University Veterinary Diagnostic Laboratory, Ames, IA). Urine specific gravity was measured using a refractometer (Reichert Inc, Depew, NY). Dipstick urine analysis was performed according to the manufacturer's guidelines and was manually read (Siemens Multistix 10SG, Siemens Healthcare Diagnostics Inc, Tarrytown, NY). After physical and chemical analysis, approximately 5 mL of the urine sample was centrifuged for 5 minutes at 2000 rpm and the supernatant removed, leaving 0.5 mL in the centrifuge tube, and stored for UPCR analysis. For sediment examination, the sediment was resuspended in supernatant and underwent microscopic review. For UPCR analysis, urine protein concentration was measured by use of a pyrogallol red method (Randox Laboratories Ltd, Crumlin, UK) with a chemistry analyzer (Ortho Clinical Diagnostics, Raritan, NJ). Urine creatinine concentration was determined by the Jaffe method. A negative culture was defined as no bacterial growth after 72 hours.

For data analysis, a urine protein concentration was assigned to each dipstick protein color based on manufacturer data (Siemens Healthcare Diagnostics Inc, Tarrytown, NY): + = 30 mg/dL, ++ = 100 mg/dL, +++ = 300 mg/dL, and ++++ = 2000 mg/dL. Samples with trace protein detected were assigned a value of 15 mg/dL. Dipstick USG ratios were calculated using the following formula: dipstick protein result (mg/dL)/([Sample USG − 1] × 1000). For example, if a patient had 30 mg/dL protein detected with a USG of 1.015, the DUR would be 30/15 or equal to 2.

2.2 | Statistical analysis

All analysis was performed using R Version 4.1.1. Correlation between UPCR and DUR was assessed using Pearson's correlation coefficient. Correlations between UPCR and DUR also were computed based on different levels of grouping variables, and the correlation coefficients themselves were compared between groups using Fisher's r-to-z transformation. Area under the curve (AUC)-receiver operating characteristics (ROC) curves for analysis of performance of the DUR were created using the following UPCR cutoffs: 0.2, 0.4 (for cats), 0.5 (for dogs), and 2. The threshold, specificity, and sensitivity of the test are reported. Significance was set at $P < .05$.

For correlation analysis, urine samples were divided into subgroups based on active vs inactive sediment, positive vs negative urine culture, presence vs absence of glucosuria, urine pH groups, and USG groups. Urine samples were judged to have an active sediment if bacteriuria was detected on urinalysis, if there were >5 leukocytes/high powered field (hpf) or >10 erythrocytes/hpf for cystocentesis samples, and >10 leukocytes/hpf or >10 erythrocytes/hpf for samples collected by natural voiding or catheterization.[11] For the purpose of

sediment classification, samples for which the method of collection was not stated were assumed to be naturally voided. Urine samples were divided into 3 groups based on urine pH: <7, 7 to 8, and >8. Lastly, urine samples were divided into 4 groups based on USG: <1.008, 1.008 to 1.012, 1.013 to 1.030 (for dogs) or 1.035 (for cats), and >1.030 for dogs or >1.035 for cats. Samples with USG recorded as >1.060 had a value of 1.060 assigned to them.

3 | RESULTS

3.1 | Patient population

Three-hundred and eight canine and 70 feline urine samples were included in the study. Of the canine urine samples, 164 were from female spayed (53.2%), 123 from male neutered (40.0%), 8 from female intact (2.6%), and 13 from male intact (4.2%) dogs. Of the feline urine samples, 39 were from female spayed (55.7%) and 31 from male neutered (44.3%) cats.

3.2 | Urine characteristics

The method of urine collection was available for 272/308 (88.3%) dogs and 60/70 (84.2%) cats. Urine was collected by cystocentesis in 230 (74.7%) dogs and 58 (82.9%) cats. Nine (2.9%) canine urine samples were obtained by catheterization. Thirty-three canine urine samples (10.7%) and 2 feline urine samples (2.9%) were naturally voided. Twenty-seven (8.8%) dogs and 7 (10%) cats had glucosuria present on urinalysis. Of these, 12 dogs (44.4%) and 3 cats (42.9%) had urine glucose concentrations ≥2000 mg/dL. Sixty-one (19.8%) dogs and 20 (28.6%) cats had active urine sediments. Of these, 13 dogs (21.3%) and 8 cats (40%) had ≥30 erythrocytes or leukocytes/hpf or both. Urine pH was <7 in 153 dogs (49.7%) and 55 (78.6%) cats, between 7 and 8 in 100 (32.5%) dogs and 12 (17.1%) cats and >8 in 55 (17.9%) dogs and 3 (4.3%) cats. Trace or higher proteinuria was identified via dipstick in 300 (97.4%) dogs and 66 (94.3%) cats (Table 1). Eighty-one (26.3%) canine and 20 (28.6%) feline urine samples were isosthenuric or hyposthenuric (Table 2). Based on IRIS guidelines, 255 (82.8%) dogs and 37 (52.9%) cats were proteinuric (Table 3). Urine cultures yielded 42 (13.6%) and 5 (7.1%) positive results for canine and feline urine samples, respectively.

3.3 | Correlation of UPCR with DUR in dogs

For canine urine samples, a significant moderate positive correlation existed between UPCR and DUR (Figure 1, r = 0.51; $P < .01$). Correlation between UPCR and DUR did not differ based on the presence of an active sediment ($P = .06$) or the presence of glucosuria ($P = .31$). Correlations for samples with USG <1.008 did not differ from those with USG between 1.008 and 1.012 ($P = .81$), 1.013 and 1.030 ($P = .69$), or >1.030 ($P = .25$). In addition, samples with USG between 1.013 and 1.030 did not differ from samples with USG >1.030 ($P = .13$). Although isosthenuric samples did not differ in correlation with samples with USG between 1.013 and 1.030 ($P = .22$), their correlation did differ significantly from samples with USG >1.030 (r = .64 and r = 0.32, respectively, $P = .02$). When samples were grouped based on urinary pH, correlations did not differ between urine samples with pH <7 and those with urine pH between 7 and 8 ($P = .8$) or those with a urine pH >8 ($P = .54$). Correlations of samples with a urine pH between 7 and 8 did not differ from those with a urine pH >8 ($P = .70$).

TABLE 1 Urine protein dipstick results for 308 dogs and 70 cats.

Dipstick results	Dogs	Cats
Negative	8	4
Trace	48	29
1+	64	19
2+	74	10
3+	80	7
4+	34	1

TABLE 2 Distribution of urine specific gravities (USG) for 308 dogs and 70 cats. D, dogs; C, cats.

USG class	Dogs	Cats
<1.008	17	0
1.008-1.012	64	20
1.013-1.030 (D)/1.035 (C)	167	41
>1.030 (D)/>1.035 (C)	60	9

TABLE 3 Distribution of urine protein creatinine ratios for 308 dogs (D) and 70 cats (C).

UPCR class	Dogs	Cats
<0.2	22	21
0.2-0.5 (D)/0.2-0.4 (C)	31	12
>0.5 (D)/>0.4 (C)	255	37

3.4 | Correlation of UPCR with DUR in cats

For feline urine samples, a significant moderate positive correlation existed between UPCR and DUR (Figure 2, r = 0.47, $P < .01$). When comparing samples with or without an active sediment or samples with or without glucosuria, no significant differences in correlation were found ($P = .24$, $P = .78$, respectively). Correlation between UPCR and DUR did not differ between isosthenuric samples and samples with USG between 1.013 and 1.035 ($P = .78$) or USG >1.035 ($P = .39$), or between samples with USG between 1.013 and 1.035 and samples with USG >1.035 ($P = .45$). No feline urine samples had USG <1.008. When samples were grouped based on urine pH,

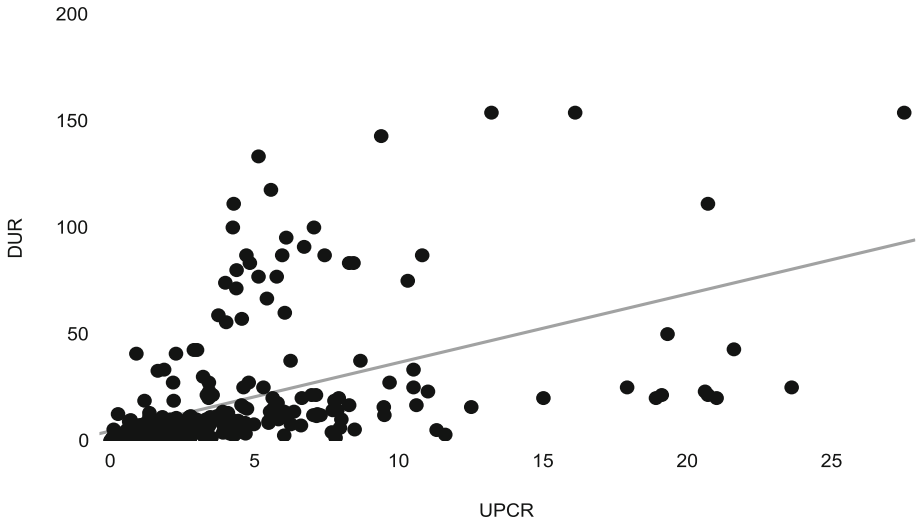

FIGURE 1 Scatterplot showing correlation between urine protein creatinine ratio (UPCR) and dipstick urine specific gravity ratio (DUR) in canine samples.

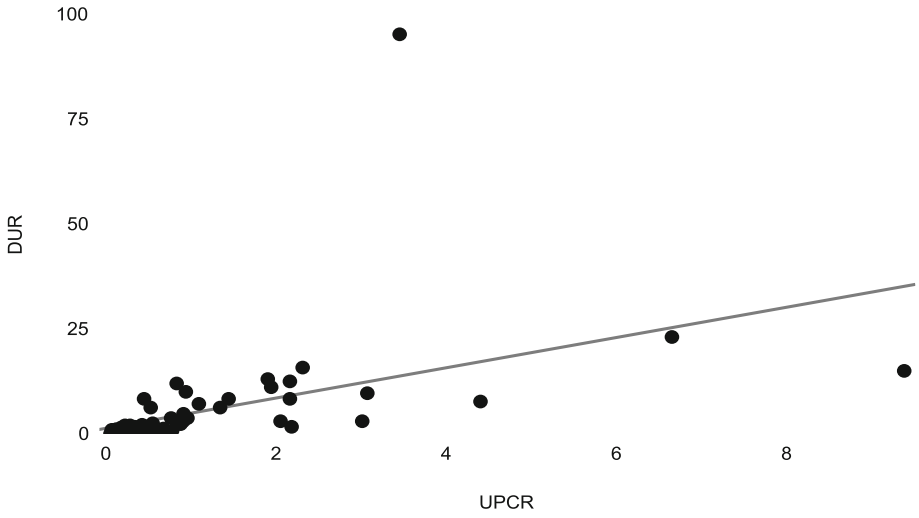

FIGURE 2 Scatterplot showing correlation between urine protein creatinine ratio (UPCR) and dipstick urine specific gravity ratio (DUR) in feline samples.

correlations did not differ between urine samples with a pH <7 and those with urine pH between 7 and 8 ($P = .46$) or those with urine pH >8 ($P = 1.00$). Correlations of samples with urine pH between 7 and 8 did not differ from those with a urine pH >8 ($P = 1.00$).

3.5 | Performance of DUR in detection of proteinuria in dogs

To assess the performance of DUR as a predictor of proteinuria in dogs, ROC analysis was used (Figure 3). For each optimal DUR cutoff, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were determined (Table 4). The performance of the previously reported DUR of 1.5 also was assessed for the detection of proteinuria. When this DUR was applied to the detection of a UPCR >0.2, the sensitivity and specificity were 82% (95% confidence interval [CI], 77%-86%) and 91% (95% CI, 71%-99%) with PPV and NPV of 99% and 27%, respectively. When the same DUR value was used to detect a UPCR >0.5, the sensitivity and specificity were 89% (95% CI, 85%-93%) and 83% (95% CI, 70%-92%) and the PPV and NPV were 96% and 62%, respectively. For the detection of a UPCR >2, the sensitivity and specificity of a DUR of 1.5 was 98% (95% CI, 95%-100%) and 45% (95% CI, 40%-53%), respectively, and the positive PPV and NPV were 65% and 96%, respectively.

3.6 | Performance of DUR in detection of proteinuria in cats

The ROC analysis also was applied to data from cats to assess the performance of DUR (Figure 4). For each optimal DUR cutoff, the sensitivity, specificity, PPV and NPV were determined (Table 5). The performance of the previously reported DUR of 1.5 also was assessed for the detection of proteinuria. When this DUR was applied to the detection of a UPCR >0.2 the sensitivity and specificity were 67% (95% CI, 52%-80%) and 90% (95% CI, 70%-99%) with PPV and NPV of 97% and 54%, respectively. For the detection of a UPCR >0.4, a DUR of 1.5 had sensitivity and specificity of 78% (95% CI, 62%-90%) and 82% (95% CI, 65%-93%) with PPV and NPV of 83% and 79%, respectively. For the detection of a UPCR >2, the sensitivity and

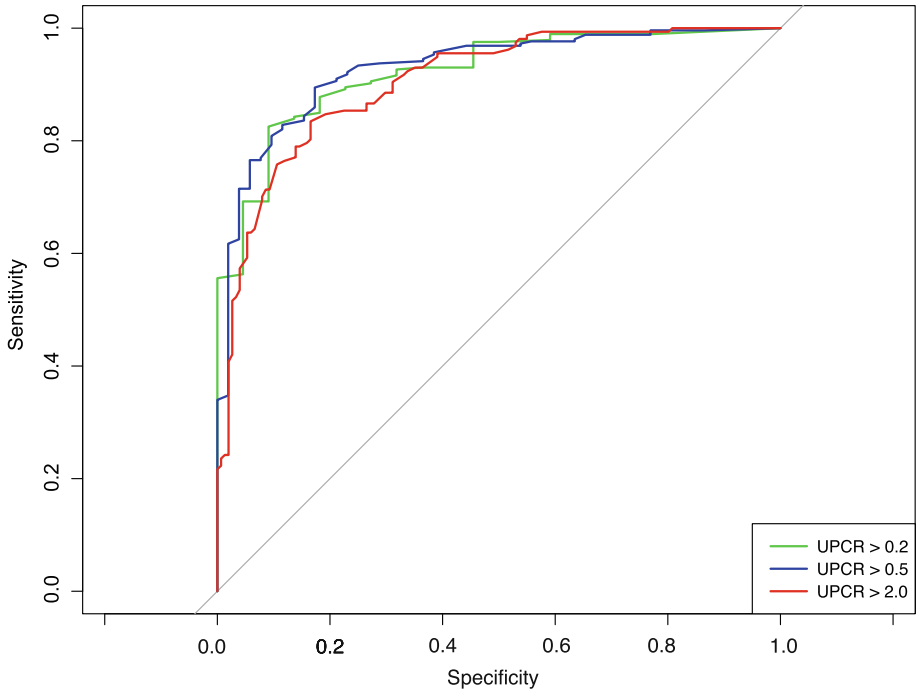

FIGURE 3 Receiver operator characteristic curve of DUR for detection of proteinuria based on data from 308 dogs. DUR, dipstick urine protein to urine specific gravity ratio; UPC, urine protein creatinine ratio.

UPCR	AUC (CI)	Optimal DUR	Sensitivity (CI)	Specificity (CI)	PPV	NPV
>0.2	0.92 (0.87-0.97)	1.4	83% (78-87)	91% (71-99)	99%	29%
>0.5	0.93 (0.89-0.96)	1.4	89% (85-93)	83% (70-92)	96%	63%
>2.0	0.90 (0.87-0.94)	5.7	83% (77-89)	83% (77-89)	84%	83%

Abbreviations: AUC, area under the curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; UPCR, urine protein creatinine ratio.

TABLE 4 Diagnostic accuracy of dipstick USG ratio (DUR) for the detection of proteinuria in dogs.

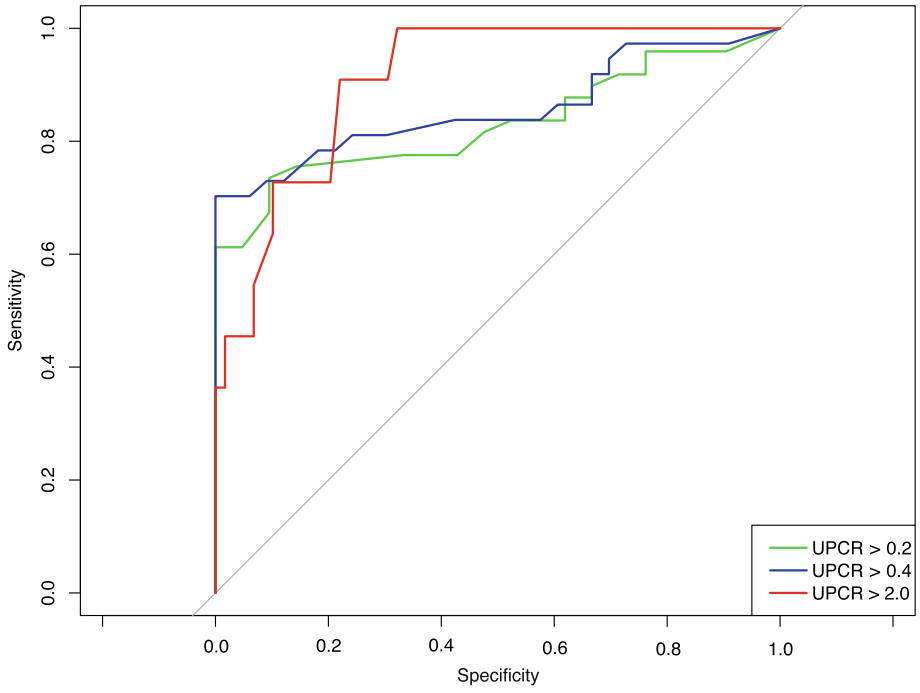

FIGURE 4 Receiver operator characteristic curve of DUR for detection of proteinuria based on data from 70 cats. DUR, dipstick urine protein to urine specific gravity ratio; UPC, urine protein creatinine ratio.

TABLE 5 Diagnostic accuracy of dipstick USG ratio (DUR) for the detection of proteinuria in cats.

UPCR	AUC (CI)	Optimal DUR	Sensitivity (CI)	Specificity (CI)	PPV	NPV
>0.2	0.83 (0.74-0.92)	1.20	73% (59-85)	90% (70-99)	95%	59%
>0.4	0.86 (0.77-0.95	2.1	70% (53-84)	100% (89-100)	100%	75%
>2.0	0.91 (0.83-0.99)	2.8	91% (59-100)	78% (65-88)	43%	98%

Abbreviations: AUC, area under the curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; UPCR, urine protein creatinine ratio.

specificity of the previously recommended DUR of 1.5 were 100% (95% CI, 72%-100%) and 59% (95% CI, 46%-72%) with PPV and NPV of 39% and 100%, respectively.

4 | DISCUSSION

Given the optimal DUR's very high PPV for detection of a UPCR >0.2, 0.4 (for cats), or 0.5 (for dogs), a positive result is strongly suggestive of urinary protein loss at or above the borderline range and supportive of further testing using UPCR. However, for detection of a UPCR >2, the low PPV of our optimal DUR suggests that this ratio cannot accurately identify patients with severe proteinuria. The DUR did not perform well with respect to its capacity to correctly identify patients that were not proteinuric. Indeed, except for the detection of feline and canine urine samples with a UPCR >2.0, the reported NPVs were too low to dependably allow exclusion of nonproteinuric patients. A secondary objective of our study was to evaluate the performance of a previously reported DUR value of 1.5 for the detection of abnormal urine protein concentrations. Similar to our optimal DUR of 1.4, a DUR >1.5 showed very high PPV for detecting borderline proteinuric and proteinuric urine samples in dogs. Furthermore, in both species, the very high NPV we obtained suggests that a DUR <1.5 can dependably be used to exclude patients with a UPCR >2.0.

The DUR and UPCR were only moderately correlated in our study. This finding is likely a result of urine dipstick interpretation being based on a colorimetric system identifying ranges of protein concentrations rather than specific values, as is obtained with UPCR. Therefore, this factor constitutes an inherent limitation in any use of the dipstick to estimate UPCR. Second, although automated systems available for urine dipstick reading have been shown to have less variation in results and be more precise than visual assessment, many institutions, including ours, still employ the visual technique of assessment.[12] This technique has been shown to introduce numerous preanalytical factors that can influence results such as improper contact times, not blotting urine strips, and incorrect orientation of the interpretation chart.[12,13] Moreover, color perception can be extremely subjective and has been shown to result in misclassifications of readings of 1 grade above or below the expected value in up to 18% of canine urine samples.[14] Duration and conditions of storage also could have impacted UPCR, but our study only included animals that had a urinalysis and UPCR performed within 24 hours of collection. Moreover, 2 recent studies in dogs suggested that storage conditions either did not or only minimally influenced UPCR results.[15,16]

One important difference between the dipstick method for protein detection and UPCR that could affect correlation is that the former technique principally detects albumin whereas the latter also can detect other proteins.[1,17] Consequently, the presence of lower urinary tract inflammation or blood could result in a disproportionate increase of UPCR in relation to urine dipstick results because of the increased presence of immunoglobulins and other inflammation-mediated proteins. However, a previous study of canine urine samples reported that samples with active sediments had significant increases in urinary albumin concentrations but not UPCR when compared to controls.[18] Moreover, the addition of blood to urine samples in that study had only a limited effect on UPCR, with the highest UPCR of 0.3 only being achieved when macroscopic hematuria was present. In contrast, when assessing the effect of blood contamination on urine dipstick and UPCR results, a previous study indicated that whereas UPCR significantly increased in samples that had no visible blood contamination, urine protein dipstick scores were significantly increased only when macroscopic hematuria was present.[19] Although we did not assess the relative effect of the severity or type of inflammation on sediment examination, the correlation between DUR and UPCR did not differ significantly when compared between samples with or without an active sediment.

When the correlation between UPCR and DUR was investigated by stratifying our data based on USG, a difference in correlation was only found in dogs when comparing isosthenuric samples to concentrated samples with USG >1.030. Moreover, this correlation was weakest in the samples with USG >1.030. This finding is in contrast with previously published data suggesting that detection of proteinuria can be improved when higher USG cut offs are applied. A previous study reported that when positive urine samples were defined by a dipstick result ≥2+, PPV and NPV varied by over 5% and 55%, respectively, between samples with a USG ≤1.012 and those with a USG ≥1.030.[2] Although we did not find any difference in correlation between UPCR and DUR in cats, no cats had hyposthenuric samples and a difference in correlation might still exist when comparing very dilute with very concentrated samples. However, when evaluating the use of urine dipsticks for protein detection in cats, a previous study found that the grouping of urine samples based on USG did not improve the accuracy of the dipstick result to predict UPCR.[20] Another study in dogs evaluating the relationship between USG and UPCR reported that although mild to moderate negative correlations existed between these 2 variables, the use of a predictive equation could not reliably predict the UPCR based on dipstick protein results.[7] Likewise, evaluating feline urine samples, another previous study reported that, for the detection of a UPCR >0.2, the application of a USG cutoff >1.035 moderately improved the accuracy of dipstick protein readings but did not improve agreement between dipstick and UPCR results.[20]

The 2004 American College of Veterinary Internal Medicine consensus statement on proteinuria suggested that urine alkalinity can result in false positive protein dipstick results.[21] In our study, urine pH did not have a significant impact on the correlation between the DUR and UPCR of either species when samples were divided between alkaline (pH >8) and nonalkaline samples. Despite alkaline urine often being mentioned as a cause of proteinuria overestimation when using the urine dipstick, little evidence supports this contention. A recent study in healthy cattle found that exclusion of urine samples with a pH >7.5 resulted in better correlation between urine dipstick protein results and UPCR, but this study did not specifically evaluate the relationship between urine pH and UPCR.[22] Using a rat model of urine pH modification, another study failed to show any difference in the agreement between urine dipstick protein and protein quantification results when alkaline and acidic samples were compared.[23] Furthermore, in a study using human urine samples, false positive urine dipstick results only occurred when urine pH surpassed 10.9, exceeding the physiologic range.[24] However, only a minority of samples in our study had urine pH >8, possibly undermining the detection of any influence of urine pH on protein dipstick performance.

Because of its ease of use, USG typically is used to estimate urine osmolality in a clinical setting. However, the presence of certain solutes can impact USG in a different way than osmolality, weakening the relationship between these 2 measurements of urine concentration.[25] Despite the fact that glucose is mentioned as increasing USG by 0.004 to 0.005 units for every 1000 mg/dL present,[26] little data supports this relationship in the veterinary literature and it is likely that glucose has a limited effect on USG. Although the addition of glucose to the urine of 102 dogs and 59 cats was shown to significantly affect USG measurements, this effect was considered clinically irrelevant, because the greatest increase in USG was only .008 with addition of 2400 mg/dL glucose.[27] Similar to a report in people, the presence of glucosuria failed to affect the correlation between USG and osmolality in a population of 60 dogs.[28,29] Consistent with these observations, the correlation of DUR and UPCR did not change significantly based on the presence or absence of glucosuria in our study. It must be noted that ≤10% of our samples were glucosuric and <50% had glucose concentrations ≥2000 mg/dL. Lastly, the specificity of detection of glucosuria, using an automated dipstick reader is extremely high (99% for dogs and 98% for cats). However, the reported sensitivity is quite variable, being as low as 23% for dogs and 68% for cats.[30] Thus, the absence of glucosuria's impact on the correlation between the UPCR and DUR also may be a result of the poor sensitivity of detection of glucosuria. Similarly, protein content in the urine is reported to influence USG measurements, possibly influencing the correlation between DUR and UPCR.[31,32] Consistent with a previous study in humans,[32] the only veterinary study evaluating the influence of protein on USG found protein content in feline urine samples did influence USG results, but only mildly and when in excess of 100 mg/dL or 2+ on a dipstick.[31] In our study, these values were found in 188/308 (61%) canine and 18/70 (26%) feline urine samples.

Because of its retrospective nature, our study had some limitations. First, although we limited inclusion of patients to those that had both a urinalysis and UPCR performed within 24 hours of each other, it is possible that a portion of cases had these tests performed on different samples. We did not review the medical histories of the included cases for factors that may have affected urine dipstick results or the relationship between UPCR and urine dipstick results. For example, the use of certain antibiotics, such as fluoroquinolones, has been associated with false positive dipstick protein results.[33,34] This phenomenon has not been reported in veterinary medicine but, if present, could have impacted our results. We did not identify the cause of proteinuria in our patients. Because we did not review cases to exclude those with a diagnosis of multiple myeloma, the possible presence of Bence-Jones proteinuria could have influenced the relationship between DUR and UPCR because dipsticks do not reliably detect Bence-Jones proteinuria.[35] Lastly, because an inclusion criterion for our study was that samples must have both a urinalysis and a UPCR, only a small number of dipstick negative samples were included. This bias leaves open the possibility that a number of false negative samples were excluded from our study, which could influence the diagnostic performance of the DUR in hyposthenuric and isosthenuric samples. However, the possible impact of this exclusion is likely limited because of the high sensitivity of urine dipsticks for the detection of protein.[2,7]

5 | CONCLUSION

Based on the high PPV obtained in our study, the DUR can be a dependable method for the identification of dogs and cats with clinically relevant proteinuria and can be used to determine if quantification, via UPCR, is indicated. However, given the variable NPV reported in our study, the DUR cannot reliably exclude cases with clinically relevant proteinuria and cannot replace the UPCR for the quantification of proteinuria.

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CONFLICT OF INTEREST DECLARATION

Jean-Sébastien Palerme is a consultant for Zoetis Animal Health and Antech Diagnostics. Dr. Palerme's consultation for Antech diagnostics and Zoetis animal health does not involve the promotion of their products and this article does not use any of their products or mention the companies. No other authors declare a conflict of interest.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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