Title:

Prevalence and clinical significance of the medullary rim sign identified on ultrasound of feline kidneys

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Abstract

Objectives: The medullary rim sign (MRS) is an ultrasonographic (US) feature identified in normal and diseased feline kidneys. The prevalence and potential clinical significance of the MRS in a referral hospital cat population was investigated.

Methods: Retrospective case-control study. Ultrasonographic images from 661 cats were reviewed. Cats with a MRS were identified and compared with equal number of time-matched control cats. Medical data and MRS features: including thickness, intensity and symmetry, were collected. Associations between independent variables and the MRS were examined with conditional and unconditional logistic regression, with initial univariable, and subsequent multivariable analysis.

Results: Of the 611 reviewed cats, 243 (36.8%) showed a variation of the MRS. A thin MRS (133 cats) was not associated with azotaemic renal disease (P=0.87). A thick MRS (110 cats) was associated with azotaemic renal disease (P=0.001). There was an association between the presence of MRS and a final diagnosis of Feline Infectious Peritonitis (FIP) (P=0.028).

Conclusions and relevance: The MRS is a common finding in cats. In this cat population, a thick MRS was associated with azotaemic renal disease, while a thin MRS was not. In cases with a clinical suspicion of FIP, the MRS may be related to the underlying disease process and not be an incidental finding.

**INTRODUCTION**

The medullary rim sign (MRS) is sometimes seen on ultrasonographic (US) examination of kidneys. It is defined as a distinct, hyperechoic zone in the outer renal medulla, which forms a curvilinear band parallel to the corticomedullary junction and does not cast an acoustic shadow.[1-3] The MRS has been described in cats,[1,4-10] dogs,[2,4,5,11] and humans.[12] Published figures of the MRS describe and show it to be well defined,[1,5,13] isoechoic [5] to hyperechoic to the renal cortex,[1,5,13] and continuous.[1,5,11,13] Observations within clinical practice reveal that the rim sign can appear discontinuous, have variable echogenicity and variable thickness.

In Yeager (1989), histology performed on a sample of 11 cats with the MRS demonstrated it corresponded to a thin (1-3mm) rim of intraluminal mineral deposits without associated inflammation and the MRS was concluded to be an incidental finding.[1] Three recent publications, investigating other features of feline renal ultrasound and feline renal disease, have not found an association between the MRS and renal disease in cats.[7,9,10] However, other authors have considered the MRS an abnormal US feature of feline kidneys, although of unknown clinical significance.[6,8] Additionally, the MRS has been reported, with supportive histopathology, in cats with feline infectious peritonitis (FIP),[5] chronic interstitial nephritis,[5] and acute tubular necrosis secondary to ethylene glycol toxicity.[4]

In dogs, similar uncertainty concerning the clinical significance of the MRS can be found in published reports. The MRS and a hyperechoic outer medulla were shown to be present in dogs without clinical evidence of renal disease and concluded to be nonspecific US findings.[2, 13] However, changes compatible with, or similar to, the MRS (including a medullary band) have been reported in dogs in association with hypercalcaemic nephropathy,[5,11] ethylene glycol toxicity,[4,5] and leptospirosis[14]. In humans, the MRS is reported as a nonspecific US finding and considered to be poorly correlated to the severity of renal disease.[12]

Histopathology performed on a limited number of the reported cases in dogs and cats reveal a variety of possible aetiologies for the rim-like changes in medulla echogenicity including: intraluminal mineral deposits;[1,4] necrotizing pyogranulomatous vasculitis;[5] tubular necrosis and calcium oxalate crystal deposition;[4,5] metastatic calcification of the renal tubular epithelium and basement membrane;[5,11] and acute tubular necrosis with congestion, haemorrhage, necrosis and oedema.[14]

The MRS is thus currently considered to be a nonspecific US finding in cats and dogs, and when seen in isolation, to be clinically non-significant. Prior studies describing and mentioning the MRS in cats have low numbers of affected cats[1,4,5,7,9,10], and to the authors’ knowledge, the clinical significance of a MRS has not been investigated in a large population of cats as a primary objective. Additionally, specific features and variation in US appearance of the MRS are yet to be described and investigated for potential significance.

The objectives of this study were to 1) determine the prevalence of the MRS in a referral population of feline patients undergoing US examination, and 2) determine if the MRS or its specific features are associated with renal disease or a specific final diagnosis by comparing with a time matched control population. Our null hypothesis was that cats with a MRS have a similar frequency of renal disease compared to those without a MRS.

**MATERIALS AND METHODS**

For this retrospective case-control study, the electronic database of the Small Animal Teaching Hospital of the University of Liverpool was searched for cats that underwent an abdominal ultrasound examination between November 2010 and August 2016. Ethical approval was granted by the Committee on Research Ethics at the Institute of Veterinary Science of the University of Liverpool (VREC451). The US examinations were performed using several different ultrasound machines over the study time (Logiq 7, GE Medical Systems; Logiq LS7, GE Medical Systems; Zonare ZS3, Mindray). A multifrequency (8-11 MHz) microconvex or a multifrequency (10-14 MHz) linear transducer was used for ultrasound examination as per institutional protocol. All abdominal ultrasound examinations were completed by board-certified radiologists or radiology residents under direct supervision of a board-certified radiologist. Cats were excluded if there was history, US evidence or a final diagnosis of urinary tract obstruction, renoliths or ureteroliths at the time point of study inclusion, in an attempt to exclude cases with post renal azotaemia. A total of 661 cats with still US images of both kidneys and an ultrasound report available for review were included in the initial study group. The still images of the kidneys were retrospectively reviewed by one author (AF) and cats with a MRS were included in the MRS group. For each cat with a MRS, a time-matched control cat was assigned and included in the control group. This was done by selecting the next cat closest in time that received an abdominal ultrasound, met the inclusion criteria, and did not have a MRS. Each cat was included in the study only once. For cats which received multiple US studies during their hospital visit or during the study period, the first study where a MRS was identified and the temporally corresponding medical record was selected.

The subjectively assessed US features of MRS (presented in Table 1 with examples shown in Figure 1) were noted. When present bilaterally the MRS symmetry between the left and right kidney was assessed with respect to intensity, thickness and completeness. The MRS intensity was subjectively characterised relative to the echogenicity of the renal cortex as mild (hypoechoic), moderate (isoechoic) or marked (hyperechoic). The width of the MRS was categorised as thin if it measured < 2.5mm and thick if it measured ≥ 2.5mm. The MRS was categorised as complete if the rim-like changes were present in the entire medulla and as incomplete if the rim-like changes were discontinuous and not present in all areas of the medulla.

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| **Table 1: Ultrasonographic characteristics subjectively assessed in cats with a medullary rim sign including the number of cats identified with each characteristic** | | |
| **Ultrasonographic feature** | **Characteristics** | **Number of cats** |
| MRS Presence | Bilateral  Unilateral left  Unilateral right | 239  1  3 |
| Left and right symmetry | Symmetrical  Asymmetrical intensity  Asymmetrical thickness  Asymmetrical completeness | 239  3  0  1 |
| Echogenic intensity relative to the renal cortex | Mild  Moderate  Marked | 35  129  79 |
| Thickness \* | Thick  Thin | 110  133 |
| Completeness # | Complete  Incomplete | 180  63 |
| Repeat scan | Yes  No | 44  199 |
| MRS changes overtime | Intensity  Completeness  Thickness | 0  0  0 |
| **(\*)Thin MRS < 2.5mm, Thick MRS ≥ 2.5mm.**  **(#) Completeness was subjectively categorised as complete when rim-like changes were present in the entire medulla and as incomplete if the rim-like changes were discontinuous and not present in all areas of the medulla.** | | |

For all cats, additional renal US findings from the still images and the original US report were noted. These findings were divided into two categories: findings supportive of CKD and Other. Renal US findings reportedly associated with chronic kidney disease (CKD) included: mild pyelectasia, reduced corticomedullary definition, areas of parenchymal mineralisation, small size, irregular outline, infarction and polycystic kidney disease.[2,7,15] Other renal US findings noted include: nodules/masses, perinephric fluid, medullary speckles.

Data collected from the medical record when available included: age, sex, breed, body weight, serum urea and creatinine levels, urine specific gravity, urine protein:creatinine ratio, serum total calcium, serum ionised calcium, urinalysis abnormalities, presence of cardiac disease, presence of systemic hypertension, renal diagnosis (this included diagnoses of AKI, CKD, primary or secondary renal neoplasia, PKD, protein losing nephropathy, pyelonephritis, renal dysplasia), as well as final diagnosis (this included the following categories of final diagnosis: FIP, urinary, gastrointestinal, neoplasia, infectious, cardiovascular, endocrinopathy, hepatobiliary and miscellaneous) made by the attending clinician.

Azotaemia was defined as serum urea and serum creatinine above the normal laboratory reference interval. Azotaemia was classified as prerenal or renal in line with the medical records including USG values and individual case comments. Azotaemia was classified as unknown if medical records contained no confirmatory evidence. For this study renal disease was classified using the International Renal Interest Society (IRIS 2016) classification for CKD based on stable serum creatinine values in the presence of persistent structural or functional renal abnormalities. Cases with an IRIS Stage 2 CKD classification and above were considered representative of azotaemic renal disease for this study. Hypercalcemia was defined as a total serum calcium level above the laboratory normal reference interval.

All statistical analyses were conducted using commercial statistical software (SPSS 22.0, SPSS Inc, Chicago, Illinois, USA). Independent variables were derived from information obtained from the signalment data, patient records, ultrasound images and reports. Descriptive statistics were produced for all variables; continuous data were summarised as medians with interquartile ranges (IQR), and categorical data as frequencies with 95% confidence intervals (95% CI), with amalgamation of small-sized groups when considered necessary. For continuous variables (age and weight), normality was evaluated using graphical assessment and via the Kolmogorov-Smirnov test.

Differences in weight and age between MRS cats and controls were evaluated using the Mann-Whitney U Test, and differences in the proportions of breeds and sex between the MRS and control groups were assessed using the Chi-squared test. Exact conditional logistic regression was used to test for associations between the presence of a MRS (i.e. being a case or control) and all the collected independent variables.[16] Unconditional logistic regression was used to test for associations between the presence of azotaemic renal disease and renal US findings (including specific MRS findings and other abnormalities). For both analyses, any variables showing some association with their respective outcomes on initial univariable analysis (a *P*-value <0.25) were considered for incorporation into a multivariable model. For pairs of independent variables with a correlation coefficient of >0.70, the variable with the smallest *P*-value selected for analysis. The models were constructed by a manual backwards stepwise procedure with retention of variables with Wald *P*-values of less than 0.05. Potential confounders were identified by examining parameter estimates for substantial changes following their removal. *P*<0.05 was considered significant for all analyses.

**RESULTS**

In total, abdominal ultrasound images from 661 cats were reviewed with 243 cats demonstrating a MRS, giving an overall prevalence of 36.8% (95%CI 33.1-40.1%). Medical records were retrieved from all 243 cats with a MRS (MRS group) and from 243 time-matched control cats (Control group). There were 300 males (275 neutered) and 186 females (176 neutered). Median age was 8.1 years (range 0.25 – 20.1 years). Mean body weight was 3.9 kg (range 1.3- 7.9 kg). There were 304 (63%) domestic shorthair cats, 26 (5%) domestic longhairs, 24 (5%) British Shorthairs, 23 (5%) Siamese, 19 (4%) Bengals, 18 Ragdolls (4%), 13 (3%) Maine Coons, 13 (3%) Persians, 9 (2%) Burmese, 9 (2%) Orientals, 8 (2%) Birmans and 20 other cats representing 11 feline breeds with fewer than five individuals in each. Comparisons between the MRS and control cats revealed no differences between the breed, age and body weight. However, a statistically significant difference in sex distribution (P=0.003) between the two groups was found. Table 2 summarises the signalment data of the two groups.

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| **Table 2: Descriptive statistics detailing the signalment variables of cats with a medullary rim sign (MRS group) and time control cats (Control group). P values are calculated from the Chi-squared test (breed, sex) and the Mann-Whitney U Test (age, weight).** | | | |
|  | **MRS group**  **(n=243)** | **Control group**  **(n=243)** | **P value** |
| **Breed** |  |  | 0.402 |
| DSH | 167 | 166 |  |
| Oriental type | 40 | 30 |  |
| DLH | 17 | 17 |  |
| Maine Coon type | 13 | 22 |  |
| Persian type | 6 | 8 |  |
| **Sex** |  |  | 0.003\* |
| Male | 164 | 136 |  |
| Neutered | 148 | 127 |  |
| Intact | 16 | 9 |  |
| Female | 79 | 107 |  |
| Neutered | 71 | 105 |  |
| Intact | 8 | 2 |  |
|  |  |  |  |
| **Age (months)** |  |  | 0.859 |
| Median (range) | 98 (3-228) | 96 (3.6-241) |  |
| **Body weight (kg)** |  |  | 0.906 |
| Median (range) | 3.9 (1.3-7.2) | 3.86 (1.5-7.9) |  |
| **Numbers indicate number of patients unless otherwise indicated.**  **(\*) highlights features with statistical significance on analysis** | | | |

Results from univariable conditional logistical regression statistical analysis comparing medical data between the MRS and the control groups are summarised in Table 3 and Table 4.

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| **Table 3: Descriptive statistics of selected medical data comparing cats with a medullary rim sign (MRS group) and the time control cats (control group). P-values are from univariable conditional logistic regression.** | | | | | | | | | |
|  | MRS group  (n=243) | | | | Control group  (n=243) | | | | P-value |
|  | N | | Median range | | N | | Median range | |  |
| USG | 169 | | 1.029 (1.008-1.080) | | 158 | | 1.028 (1.004 -1.074) | | 0.93 |
| Serum creatinine  (μmol/l) | 232 | | 117 (28 -1819) | | 217 | | 116 (10 – 1348) | | 0.29 |
| Serum urea  (mmol/l) | 235 | | 9.5 (1.5 – 53) | | 218 | | 8.9 (2.6 – 57.1) | | 0.12 |
| Total calcium  (mmol/l) | 230 | | 2.36 (1.34 - 3.98) | | 216 | | 2.36 (1.01 – 3.71) | | 0.60 |
| Ionised calcium  (mmol/l) | 15 | | 1.6 (1.25-2.22) | | 8 | | 1.53 (0.61 – 2.02) | | 0.61 |
| **The number of cats for which the parameter was found in the medical record is noted (N)**  **(\*) highlights features with statistical significance on analysis**  **USG – urine specific gravity** | | | | | | | | | |
| **Table 4: Results of univariable conditional logistic regression showing association of categorical variables with the presence of a medullary rim sign in 486 cats**. | | | | | | | | | |
| Variable | | MRS group  n=243 | | Control Group  n=243 | | OR (95% CI) | | P-value | |
| Azotaemic renal disease  (CKD stage 2-4) | | 46 | | 24 | | 2.3 (1.3-4.3) | | 0.006\* | |
| Proteinuria | | 40 | | 48 | | 0.76 (0.37-1.6) | | 0.47 | |
| Hypercalcaemia | | 40 | | 36 | | 1.0 (0.62-1.7) | | 0.90 | |
| Azotaemia | | 172 | | 151 | | 1.1 (0.75-1.7) | | 0.52 | |
| Azotaemia class | |  | |  | | (Ref) | | - | |
| None | | 63 | | 67 | | (Ref) | | - | |
| Pre-renal | | 75 | | 71 | | 1.1 (0.66-1.8) | | 0.72 | |
| Renal | | 72 | | 54 | | 1.5 (0.89-2.4) | | 0.13 | |
| Unknown | | 25 | | 26 | | 1.1 (0.55-2.2) | | 0.80 | |
| Chronic kidney disease | |  | |  | | (Ref) | | - | |
| CKD not present | | 175 | | 173 | | (Ref) | | - | |
| IRIS Stage 1 | | 15 | | 21 | | 0.72 (0.36-1.5) | | 0.37 | |
| IRIS Stage 2 | | 35 | | 20 | | 2.0 (1.1-3.8) | | 0.024\* | |
| IRIS Stage 3 | | 6 | | 2 | | 6.4 (0.67-61) | | 0.11 | |
| IRIS Stage 4 | | 5 | | 2 | | 2.7 (0.51-14) | | 0.24 | |
| Renal diagnosis | |  | |  | | (Ref) | | - | |
| Normal kidneys | | 159 | | 182 | | (Ref) | | - | |
| AKI | | 7 | | 4 | | 2.0 (0.59-7.1) | | 0.26 | |
| CKD | | 61 | | 45 | | 1.6 (1.0-2.6) | | 0.049\* | |
| Neoplasia | | 3 | | 5 | | 0.67 (0.16-2.8) | | 0.59 | |
| Other | | 10 | | 6 | | 1.9 (0.69-5.3) | | 0.22 | |
| PKD | | 3 | | 1 | | 3.0 (0.31-29) | | 0.34 | |
| Final diagnosis | |  | |  | | (Ref) | | - | |
| Other | | 22 | | 30 | | (Ref) | | - | |
| Cardiovascular disease | | 28 | | 22 | | 1.7 (0.74-3.8) | | 0.21 | |
| Endocrinopathy | | 10 | | 12 | | 1.2 (0.42-3.5) | | 0.73 | |
| FIP | | 15 | | 8 | | 3.1 (1.0-9.5) | | 0.047\* | |
| Gastrointestinal disease | | 34 | | 39 | | 1.2 (0.58-2.4) | | 0.65 | |
| Hepatobiliary disease | | 33 | | 21 | | 2.1 (0.99-4.6) | | 0.054 | |
| Infectious disease | | 27 | | 13 | | 2.5 (0.79-8.0) | | 0.12 | |
| Neoplasia | | 64 | | 74 | | 1.2 (0.62-2.3) | | 0.60 | |
| Urinary tract disease | | 25 | | 32 | | 1.1 (0.52-2.4) | | 0.78 | |
| **(OR = odds ratio, 95%CI = 95% confidence intervals, Ref = reference category, FIP = feline infectious peritonitis, CKD = Chronic kidney disease, AKI = Acute kidney injury, PKD = polycystic kidney, Other = protein losing nephritis, pyelonephritis, renal dysplasia).**  **(\*) highlights features with statistical significance on analysis.** | | | | | | | | | |

There were no significant associations detected with regards to proteinuria (P=0.47), hypercalcaemia (P=0.90) or azotaemia (P=0.52) between the groups. Additionally, there was no association detected with regards to severity or classification of azotaemia between the groups. Significant associations were detected between the presence of a MRS and azotaemic renal disease (P=0.006), IRIS Stage 2 CKD (P= 0.024), a renal diagnosis of CKD stated in the medical records (P=0.049) and a final diagnosis of FIP (P=0.047).

On multivariable conditional logistic regression analysis only azotaemic renal disease (P=0.001) and a final diagnosis of FIP (P=0.028) remained statistically significant (Table 5) between the groups.

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| **Table 5: Results of multivariable conditional logistic regression showing association of categorical variables with the presence of a medullary rim sign in 486 cats.** | | | | |
| Variable | MRS group  n=243 | Control group  n=243 | OR (95% CI) | P-value |
| Azotaemic renal disease |  |  |  |  |
|  | 46  Thin MRS: 14  Thick MRS: 32 | 24 | 3.1 (1.6-6.2) | 0.001\* |
| Final diagnosis |  |  |  |  |
| Other | 22 | 30 | (Ref) | - |
| Cardiovascular disease | 28 | 22 | 1.7 (0.70-4.2) | 0.24 |
| Endocrinopathy | 10 | 12 | 1.1 (0.37-3.5) | 0.83 |
| Gastrointestinal disease | 34 | 39 | 1.1 (0.49-2.5) | 0.82 |
| Hepatobiliary disease | 33 | 21 | 2.2 (0.95-5.2) | 0.067 |
| Infectious disease  FIP | 27  15 | 13  8 | 2.7 (0.75-9.7)  4.2 (1.2-15) | 0.13  0.028\* |
| Neoplasia | 64 | 74 | 1.3 (0.61-2.7) | 0.52 |
| Urinary tract disease | 25 | 32 | 0.78 (0.32-1.9) | 0.58 |
| **(OR = odds ratio, 95%CI = 95% confidence intervals, Ref = reference category, FIP = feline infectious peritonitis).**  **(\*) highlights features with statistical significance on analysis** | | | | |

A final diagnosis of FIP was made in a total of 23 cats - fifteen cats within the MRS group and eight cats in the control group. In the FIP cats with a MRS, 12/15 (80%) of MRS were thin and 3/15 (20%) were thick, 8/15 (53%) MRS were marked in intensity, 5/15 (33%) were moderate and 2/15 (13%) were mild. The kidneys were otherwise judged to be ultrasonographically normal in sixteen cats but abnormal in seven: three cats with reduced corticomedullary definition and four cats with a hypoechoic subcapsular rim. None of these cats had azotaemic renal disease, as defined by this study, documented in the medical records.

Univariable unconditional logistic regression assessing US features showed MRS thickness (thick MRS P=0.001), MRS intensity (moderate P=0.015, severe P=0.02), MRS completeness (complete P=0.002) and additional renal US findings (signs consistent with CKD, see table 6 legend P=0.001) were associated with azotaemic renal disease. However, on multivariable analysis (Table 6), only a thick MRS (P=0.001) and US findings consistent with CKD (P=0.001) were significantly associated with azotaemic renal disease.

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| **Table 6: Results of multivariable unconditional logistic regression showing association of ultrasound identified variables with the presence of azotaemic renal disease in 486 cats** | | | | |
| Variable | MRS group  n=234 | Control group  n=243 | OR (95% CI) | P-value |
| MRS Thickness |  |  |  |  |
| None | 0 | 243 | (Ref) | - |
| Thick | 110 | 0 | 2.8 (1.5-5.1) | 0.001\* |
| Thin | 133 | 0 | 1.1 (0.51-2.2) | 0.87 |
| Additional ultrasound findings |  |  |  |  |
| Normal | 104  Thin MRS: 73  Thick MRS: 31 | 123 | (Ref) | - |
| CKD | 122  Thin MRS: 51  Thick MRS: 71 | 99 | 5.6 (2.8-11) | 0.001\* |
| Other | 17  Thin MRS: 9  Thick MRS: 8 | 21 | 0.92 (0.19-4.4) | 0.92 |
| **(OR = odds ratio, 95%CI = 95% confidence intervals, Ref = reference category, MRS = medullary rim sign, CKD = renal ultrasound features supportive of Chronic kidney disease, Other = abnormal renal ultrasound features not associated with CKD).**  **(\*) highlights features with statistical significance on analysis**  **Renal ultrasonographic features supportive of Chronic Kidney Disease include under the category of ‘CKD’ are: mild pyelectasia, reduced corticomedullary definition, areas of parenchymal mineralisation, small size, irregular outline, infarction and polycystic kidney disease.**  **Renal ultrasonographic abnormalities included under the category of ‘Other’ are: nodules/masses, perinephric fluid, medullary speckles**  **Thin MRS < 2.5mm, Thick MRS ≥ 2.5mm** | | | | |

The MRS was bilateral and symmetrical in all but four cats (Table 1). These four cats all had one grossly abnormal kidney secondary to unidentified causes although infarction, unilateral renal dysplasia and atrophy secondary to a chronic/previous upper urinary tract obstruction, were suspected in the medical records.

More than one US examination was performed in 44 cats with a MRS. The median number of scans was 2 with a range of 2 to 11 scans. The time interval between subsequent scans was highly variable with a median of 171 days and a range of 3 to 2152 days. The features of the MRS did not change in subjective assessment over time in any of these 44 cats. However, in 8 (18%) cats there were changes in other documented US renal findings. The changes included reduction in corticomedullary definition, mild renal pelvic dilation and development of non-obstructive urolithiasis.

**DISCUSSION**

The MRS was a common finding in our cat population, with a prevalence of 243/661 (36.8 %) (95% CI 33.1-40.1%) observed in this study population. Evaluation of specific features of the MRS revealed that it is often bilateral and symmetrical. The prevalence of 36.8% is similar to the prevalence of 30% previously reported by Yeager (1989). Interestingly, in more recent breed-specific studies, lower prevalence estimates have been reported: 14.2%,[9] 19.4%,[8] and 12.3%.[7] The current study population is limited to a single referral hospital population and similar to breed-specific studies, is highly selected and biased. The true prevalence of the MRS within the general feline population remains unknown. In the current study, no indication of a breed predilection was detected. The statistically significant sex difference detected (P =0.003) is unexpected and is most likely due to the very low number of intact females (10 cases) within the study population where there is a marked uneven distribution between MRS (8 cases) and control cases (2 cases) creating a statistical bias. There is a moderate overrepresentation of male cats present within the study population with a slight overrepresentation of male cats within the MRS group (see Table 2). However, this is not considered a large enough difference to create the statistical significance detected.

The presence of a MRS (not taking into account its specific features or other ultrasound findings) was associated with azotaemic renal disease (P = 0.006), leading us to reject our null hypothesis. Of the specific MRS features investigated in the present study, thickness was the only feature identified as a potentially significant US characteristic. A thin MRS (<2.5mm) was not associated with azotaemic renal disease (P = 0.87). This result was unsurprising, and although there is no supportive histopathology for any of these thin MRS cases in the present study, it is speculated that a thin MRS most likely represents the tubular intraluminal mineral deposits, described and observed by Yeager in 1989, in otherwise histologically normal feline kidneys. The presence of a thick MRS (≥ 2.5mm) was significantly associated with azotaemic renal disease (P = 0.001), suggesting that a thin and a thick MRS might represent different disease processes.

In a study by Mantis and Lamb (2000) investigating the association between a MRS and renal dysfunction in dogs, most dogs (72%) with a MRS as the only renal US abnormality did not have clinical renal dysfunction. However, the large majority of dogs (78%) that had a MRS combined with other renal abnormalities had biochemically confirmed renal disease. This study did not investigate different features of the MRS. Similarly, Lamb et. al. (2017) found no association between MRS and azotaemic cats.No details on the appearance of the MRS were included in that study. This is in contrast to the current study, which detected an association between the presence of a MRS and azotaemic renal disease. However, a large number of cats with azotaemic renal disease did not have a MRS and a large number of cats with MRS did not have azotaemic renal disease. The inconsistency of findings between these studies further supports the notion that changes in renal echogenicity are nonspecific and insensitive, and should be interpreted cautiously when found in isolation, and always within the context of additional clinical information. Future investigations into the MRS and its features would require a prospective study design that objectively measured the thickness of the MRS under standardized conditions, in addition to collection of specified clinical data and supportive histopathology.

Previous case reports and studies have related the presence of the MRS in cats with hypercalcaemic nephropathy,[5,11] and FIP.[5] In the present study, an association was detected between the presence of a MRS and a final diagnosis of FIP, where a thin, marked intensity MRS was frequently identified. Previous reports describing the US appearance of kidneys in cats with FIP document a thin MRS with a marked intensity visible on US images because of pyogranulomatous vasculitis identified on histopathology.[5] This is consistent with our findings, even though the MRS in the FIP cases in the current study had a variable subjective appearance, a thin and bright MRS was common. In clinical cases where there is a suspicion of FIP, the MRS may not be an incidental finding. Interestingly, there was no statistically significant association between the MRS and hypercalcaemia (P=0.90). However, the study design was not intended to assess hypercalcaemic syndromes in cats and the absence of documented total hypercalcaemia cannot exclude the possibility of previous hypercalcaemic episodes or ionised hypercalcaemia.

It is well established that changes in US echogenicity of the renal cortex and medulla are common and nonspecific.[6,8,15] Such US changes may result from a variety of underlying disease processes that alter either the number of acoustic interfaces e.g. cellular infiltration or proportion of vascular bundles;[5] or the acoustic impedance of the medullary tissue e.g. mineralisation, fibrosis, crystallisation.[1,17] It stands to reason that different US features including thickness, completeness and intensity may vary, and even progress over time, depending on the underlying histopathological changes. In the present study, a limited number (46/243 18.9%) of cases with a MRS had repeat US scans over a highly variable time period (3-2152 days) and the subjective appearance of the MRS did not change over time. This is consistent with what has been observed in dogs and humans.[5,12] However, no firm conclusions can be drawn regarding potential change in the MRS over time from the present study and further research is warranted to investigate this.

There are some notable limitations in the present study, mostly related to its retrospective nature and the method of data collection. A variety of machines, US probes and operators produced the reviewed US images, this would have introduced uncontrolled variability within the data set. However, the time-matched nature of the control cases will have countered this to some degree. When reviewing ultrasound images and reports, if an abnormality was not seen or reported, it was considered absent. This raises the potential for false negatives where the abnormality was present but not reported. None of the MRS cases had corroborating histopathology and so the underlying aetiology can only be speculated and not confirmed. Additionally, not all data points were obtained for every case because biochemical tests were performed at the discretion of the attending clinician, hence data extraction was limited by completeness of the medical records. Furthermore, the assumption of the presence or absence of renal disease was based on biochemical data, which has limited sensitivity and specificity in the diagnosis of renal disease.[6,18] Finally, the retrospective assessment and measurement of ultrasound images for the purpose of this study was performed by only one observer, which may have introduced some operator error.

A number of statistical tests were carried out; such multiple comparisons increase the risk of making a Type I statistical error. In an attempt to mitigate this, only variables where there was a reasonable prior expectation of a possible association were selected for testing. However, the possibility that some of the associations identified may be false positive findings should be considered.

**CONCLUSION**

This paper further supports the conclusion that a thin MRS is a nonspecific US finding in cats and is most likely incidental. A thick MRS is associated with azotaemic renal disease and may represent a different pathological process to that underlying the formation of a thin MRS. An association between the MRS and a final diagnosis of FIP was detected indicating it could be considered a supportive finding where there is a clinical suspicion of FIP.

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**Figure 1: Examples of the MRS categories including: thin (<2.5 mm in thickness), thick (≥ 2.5mm in thickness), mild intensity (hypoechoic to the renal cortex), moderate intensity (isoechoic to the renal cortex, marked intensity (hyperechoic to the renal cortex). A – Thin MRS with mild intensity, B – Thin MRS with moderate intensity, C – Thin MRS with marked intensity, D – thick MRS with mild intensity, E – thick MRS with moderate intensity, F – thick MRS with marked intensity**

**![A picture containing photo, showing, looking, man

Description automatically generated]()**