ORIGINAL RESEARCH

Diagnostic Performance of Renal Contrast Excretion on Early Phase CT Myelography in Spontaneous Intracranial Hypotension

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ABSTRACT

BACKGROUND AND PURPOSE: Early opacification of the renal collecting system during CT myelography (CTM) performed for the evaluation of Spontaneous Intracranial Hypotension (SIH) has been demonstrated in prior studies. However, these investigations often included CTMs scanned >30 minutes after intrathecal contrast injection, a longer delay than the myelographic techniques used in current practice. The purpose of this study was to determine whether renal contrast excretion (RCE) measured during this earlier time period (≤30 minutes) can discriminate patients with SIH from patients without SIH.

MATERIALS AND METHODS: Single-center, retrospective cohort of consecutive patients presenting for evaluation of possible SIH between July 2021-May 2022. RCE was measured in both renal hila using standardized (5-15mm^3) ROIs. ROC curves were constructed comparing RCE between patients with SIH to patients without SIH in the overall cohort, and within the subgroup of patients with negative myelograms.

RESULTS: The study cohort included 190 subjects. Both unadjusted and adjusted models demonstrated a statistically significant increase in renal contrast density among patients with SIH compared to those without SIH (p-values ≤ 0.001). The ROC curve showed moderate discrimination between these groups (AUC 0.76). However, using clinically meaningful test criteria of sensitivity >90% or specificity >90%, the two corresponding threshold HU values resulted in low specificity of 31.3% and sensitivity of 50.8%. Subgroup analysis of patients with negative myelograms showed poorer performance in discriminating SIH+ from SIH- (AUC 0.62). In this subgroup, using similar test criteria of sensitivity >90% or specificity >90 resulted in low specificities and sensitivities, at 26.0% and 37.5% respectively.

CONCLUSIONS: We found a statistically significant positive association between RCE and SIH diagnosis during early-phase CTM, however clinically useful thresholds based on cutoff values for renal HU resulted in poor sensitivities or specificities, with substantial false positives or false negatives, respectively. Thus, while we confirmed statistically significant differences in RCE in the ≤30 min time period, in keeping with prior investigations of more delayed time periods, overlap in renal attenuation values prevented the development of clinically useful threshold value for discriminating SIH+ from SIH- patients.

ABBREVIATIONS: SIH = spontaneous intracranial hypotension; RCE = renal contrast excretion; CTM = CT myelography; CVF = CSF-venous fistula; ICHD-3 = international classification of headache disorders third edition; CKD = chronic kidney disease

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SUMMARY SECTION

PREVIOUS LITERATURE:

Previous investigations have shown early renal contrast excretion (RCE) during myelography in patients with SIH. These studies predominantly evaluated CT myelography performed >30 minutes after intrathecal contrast injection. Current trends in advanced myelography for assessment of SIH are toward earlier scanning, however; the ability of RCE analysis to predict SIH status in this early time period is not known. Further, prior investigations have typically utilized subjective assessment of renal contrast excretion, and have not sought to determine objective thresholds for assessing the diagnostic performance of RCE analysis.

KEY FINDINGS:

While there is a statistically significant positive association with RCE and SIH diagnosis in the early time period (i.e.<30 minutes from time of intrathecal contrast injection), ROC analysis found no threshold value that could reliably discriminate SIH+ from SIH- patients with high sensitivity and specificity.

KNOWLEDGE ADVANCEMENT:

The clinical utility of RCE for discriminating patients with and without SIH <30 min after myelography is limited. RCE is even less reliable at differentiating SIH patients with a negative myelogram from patients without SIH, which would be the population most likely to benefit from an indirect indicator of SIH.

INTRODUCTION

When myelography is performed for Spontaneous Intracranial Hypotension (SIH), leakage of myelographic contrast either via dural tears or CSF-venous fistulas (CVFs) may lead to rapid intravascular reabsorption of contrast and subsequent early excretion by the kidneys. Previous investigations of patients with SIH have demonstrated statistically significant differences in the timing of renal contrast excretion (RCE) in patients with SIH compared to patients without CSF leak.[1-4] This observation parallels earlier observations of early radiotracer renal excretion during indium-111 DTPA cisternography in the setting of spinal CSF leak.[5]

Previous studies have examined RCE at delayed time points after intrathecal contrast injection, predominantly measuring renal collecting system density on scans obtained >30 min after contrast injection.[1-4] However, most advanced myelographic techniques in current use for epidural leak localization or CVF detection perform scanning earlier after contrast injection.[6] Since RCE is time-dependent, understanding the diagnostic performance of RCE for detecting SIH at this earlier time point would therefore be valuable when performing modern advanced myelography. In particular, the ability to use RCE to predict which patients have a CVF would be useful, since direct visualization of CVFs can be challenging, and indirect evidence of a CVF could assist with the decision of whether repeat myelography is needed.

The purpose of this investigation was to determine, in patients presenting for evaluation for possible SIH, whether RCE is capable of distinguishing patients with SIH due to any leak type from patients without SIH when scanning is performed ≤30 minutes following intrathecal contrast injection. A secondary aim was to assess whether RCE can discriminate the subgroup of patients with brain imaging changes of SIH but negative CTM (who presumptively harbor occult CVFs) from patients without SIH.

MATERIALS AND METHODS

This study was a single-center retrospective cohort of patients presenting for evaluation of possible SIH between July 2021 through May 2022. The study was approved by our local IRB and was compliant with HIPAA.

Subjects

Consecutive patients who underwent CT myelography for the evaluation of SIH were included. If subjects had >1 myelogram performed at our institution, the first myelogram performed at our institution was designated as the index scan for analysis, regardless of date. The time interval between intrathecal contrast injection and CTM scanning was determined using imaging time stamps in PACS. Exclusion criteria were subjects who were scanned >30 minutes from the time of intrathecal contrast injection, cases that did not include prone imaging, patients with IV contrast administration for an imaging exam <24 hours prior to the myelogram, or cases in which a reliable region of interest (ROI) was unable to be measured (e.g. renal collecting system excluded from the field-of-view, extensive streak artifact, or collecting system decompression).

Demographic information, CSF opening pressure at the time of the myelogram, creatinine values, and GFR were obtained from the electronic medical record. If multiple creatinine values were present in the chart, the value closest in time to the myelogram was used.

Imaging Analysis

Our institutional CTM protocol varies based on whether the patient has a known epidural fluid leak. Ultrafast CTM is typically performed for leak localization in patients with epidural fluid leaks seen on prior spinal imaging, while decubitus CTM using previously reported standardized technique is performed in patients with no epidural fluid leak.[6-9] However, in both protocols, a final prone scan of the total spine is typically performed for anatomic localization and to evaluate for subtle epidural leaks that may have been missed on prior MRI. All myelograms were performed using a standardized volume of 10 mL iopamidol contrast containing 300 mg/mL iodine (Isovue-M 300; Bracco, Princeton, New Jersey). Analysis of RCE was performed by placing standardized regions of interest (ROIs) measuring 5-15mm^3 over the bilateral renal hila on prone CTM images (Figure 1). All ROIs were measured on the thinnest available slices (0.625mm) using a standard soft tissue kernel. This ROI was preferentially placed over the renal pelvis unless decompression of the pelvis prevented ROI placement, in which case a renal calyx was selected, being careful to ensure that the ROI did not include any renal parenchyma. This analysis of the study cohort was performed by a senior radiology resident after undergoing a mentored training set of cases where measurements were validated against measurements obtained by a senior neuroradiologist with 15 years' experience interpreting myelograms for SIH.

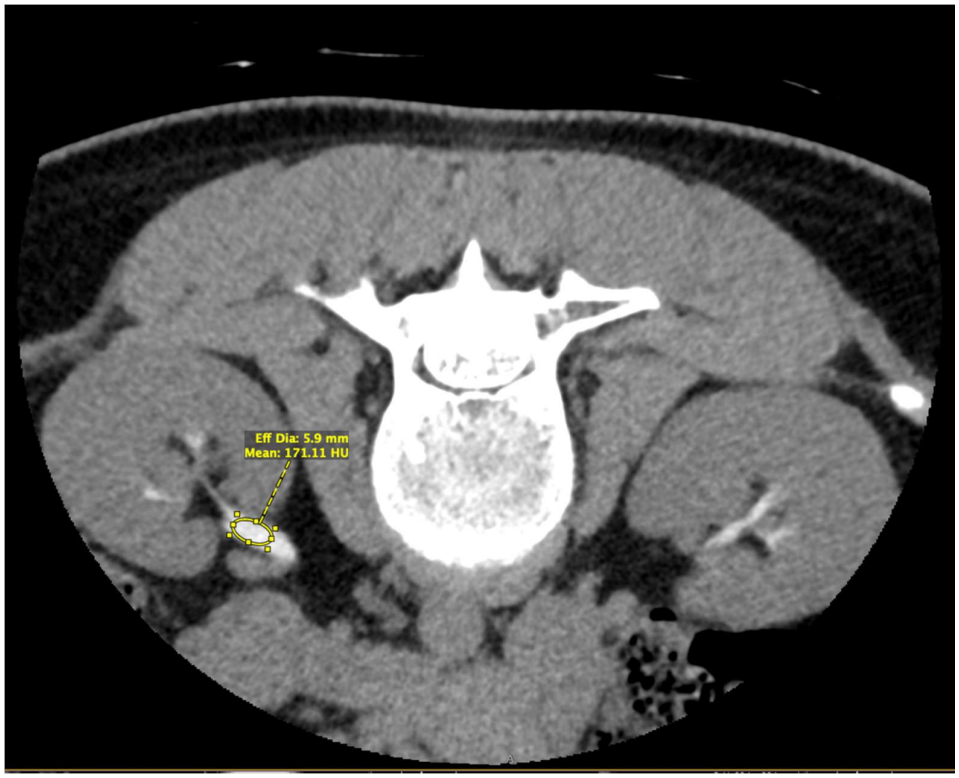

FIG 1. Axial CT image prone CTM for a SIH+ subject with example standardized ROI.

CT myelograms were reviewed by one of two study neuroradiologists with 12-15 years' experience evaluating CTM done for SIH to assess for the presence of a CVF. Assessment was based on the presence of a "hyperdense paraspinal vein" sign.[10] In equivocal cases, the imaging was jointly reviewed by both study neuroradiologists to reach consensus.

Brain MR imaging was reviewed for signs of SIH by one of 4 neuroradiologists and classified as positive or negative for signs of SIH. Positive MR brain findings included: diffuse dural enhancement, the venous distention sign or brain sagging, using previously described criteria.[11] The classification for each subject was documented in a structured clinical note in the electronic medical record at the time of initial patient assessment. Cases of missing data or ambiguous assessment or brain MR findings were re-reviewed by a senior neuroradiologist with 15 years of experience in evaluating patients with SIH.

Following imaging analysis, subjects were classified as having SIH (SIH+) or not having SIH (SIH-) based on whether they satisfied diagnostic criteria according to International Classification of Headache Disorders, 3rd edition (ICHD-3).[12]

Statistical Analysis

To determine if contrast density was associated with SIH diagnosis, both unadjusted and adjusted logistic regression models were fit separately to ROI measurements over the left renal hilum, the right renal hilum, and the minimum and maximum value of both measurements. For the adjusted models, the following potential confounders were accounted for: eGFR (categorical CKD stage), creatinine, time from injection to CTM, age, and sex. Complete case analyses were presented; however, since creatinine and eGFR were missing in 52 patients (27.4%) and 65 patients (34.2%) respectively, single imputation models were also reported as a sensitivity analysis (see Online Supplemental Data). For all models, linearity of continuous covariates was assessed via splines and collinearity was assessed using the variance inflation factor (VIF). To satisfy linearity assumptions, a linear spline with a knot at 15 was used for time from injection to CTM.

To assess the utility of renal contrast density in HU in discriminating between subjects who were SIH+ and SIH-, ROC curves were constructed for left, right, maximum, and minimum contrast density, and the area under the ROC curves (AUC) and 95% confidence intervals (CI) were generated. Potential thresholds were determined (in HU) based on clinically meaningful criteria defined by the investigators, including: sensitivity >90%, specificity >90%, and based on an 'optimal threshold' (Youden's index). Since the ideal use for RCE analysis would be a patient with a CVF that was not seen on initial myelogram, additional analyses using ROC curves were performed to determine the ability of renal contrast density to discriminate the subgroup of subjects who were SIH+ but with no leak seen on CTM (who presumably harbor occult CVFs) from SIH- subjects.

Time intervals after intrathecal contrast injection were compared using the Wilcoxon rank sum test. P-values <0.05 were considered statistically significant.

RESULTS

Subjects and Imaging

A total of 333 patients underwent CTM for the evaluation of SIH from July 2021 through May 2022. A total of 143 patients were excluded for the following reasons: 60 patients due to CTM scanned >30 minutes after contrast injection, 20 patients due to absence of prone imaging, 62 patients due to inability to place a reliable HU over the renal collecting system, and 1 patient who underwent a same day CT exam with IV contrast. The final study cohort thus consisted of 190 subjects.

Demographics and clinical characteristics for the patients and characteristics of their renal function are presented in Online Supplemental Data. Mean subject age (±SD) was 48.3±15.8 years (range 14.7-82.6). Subject sex was 66.3% female. Creatinine was missing in 27.4% of subjects (n=52, including 18 SIH+ and 34 SIH- subjects) and eGFR was missing in 34.2% of subjects (n=65, including 20 SIH+ and 45 SIH- subjects).

A total of 31.1% (n=59) of subjects met ICHD-3 criteria for SIH, including 38 female and 21 male subjects, with mean age 50.5±13.8 years. Of the SIH+ subjects, 89.8% (n=53) had positive findings on brain MRI. Direct evidence of CSF leak was seen on CTM in 72.9% (n=43) of SIH+ subjects, including 24 with epidural leak and 19 with a CVF. Of the subjects with epidural leak, 41.6% (n=10) were due to a ventral dural tear, 33.3% (n=8) were due to a lateral dural tear, and 25.0% (n=6) were due to a leak of undetermined source. The remaining 27.1% (n=16) SIH+ subjects had no leak seen on CTM.

Mean time interval between intrathecal contrast injection and prone imaging was 20.0±7.8 min for SIH+ subjects and 16.7± 5.9 minutes for SIH- subjects ($p<0.001$).

Statistical Analysis

We found similar results for analysis of the left renal collecting system, right renal collecting system, maximum density from either renal collecting system, and minimum density from either renal collecting system; therefore, only the models for maximum contrast density are presented (see Online Supplemental Data for all model results).

Both unadjusted and adjusted models testing the association between renal contrast density and SIH diagnosis demonstrated a statistically significant association between increased density and an SIH diagnosis (p-values ≤0.001), even after adjusting for age, sex, time interval to scanning, eGFR categories, and creatinine. After adjusting for confounders, the odds of SIH+ status increased by 64.2% (aOR: 1.642 (95%CI: 1.238-2.178)) per 10-unit increase in maximum contrast density (p-value 0.001). Sensitivity analyses using single imputation to account for missingness in eGFR and creatinine gave similar results (Online Supplemental Data).

ROC Analysis

The AUC for the maximum renal contrast density was 0.760 (95%CI: 0.682-0.838). To assess the potential clinical utility of using renal contrast density as a diagnostic test, we evaluated the test at clinically meaningful thresholds on the ROC curve (Figure 2). Specifically, we considered two potential clinical use cases for RCE analysis: use of the test to confidently rule out SIH (i.e. a high sensitivity test) or to confidently rule in SIH (i.e. a high specificity test). To obtain a desired sensitivity of >90%, we found that a threshold of 7.9 HU would result in sensitivity of 93.2%, but would only result in a specificity of 31.3%. To obtain a desired specificity of >90%, we found that a threshold of 31.5 HU would result in a specificity of 90.1%, but with a sensitivity of only 50.8%. The optimal threshold by Youden's index would be 28.0 HU, which would result in a sensitivity of 57.6% and specificity of 84.7% (Online Supplemental Data).

Subgroup Analysis: negative myelogram

We conducted a subgroup analysis to assess how contrast density discriminated between SIH+ and SIH- (i.e. patients who satisfied ICHD-3 criteria by other means, such as positive brain MRI) among patients with a negative myelogram. From our cohort, 147 subjects had no evidence of leak on myelogram. Of those, 16 were SIH+ and 131 were SIH-. The AUC for this subgroup was 0.618 (95%CI: 0.455-0.782), with poor discrimination between SIH+ and SIH- patients (Figure 2b). To obtain a test with a desired sensitivity >90%, we found that a threshold of 5.3 HU would result in a sensitivity of 93.8%, but a specificity of only 26.0%. To obtain a test with a desired specificity of >90%, we found that a threshold of 34.5 HU would result in a specificity of 93.1%, but with a sensitivity of only 37.5%.

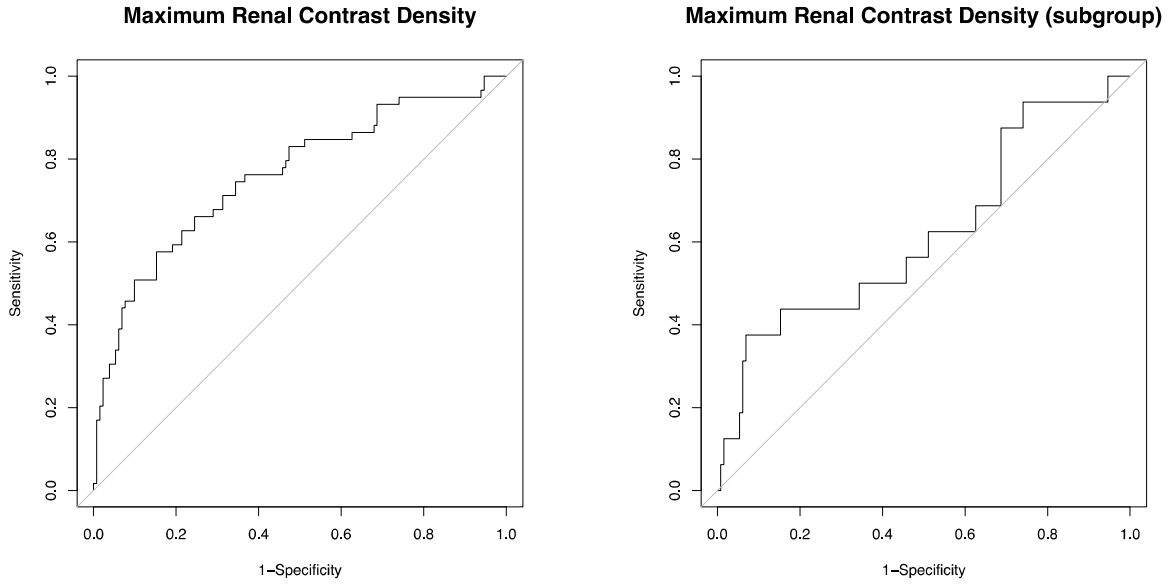

FIG 2. ROC curves for maximum contrast density overall and in the subgroup of patients with negative myelograms. Area under the curves are 0.760 (0.682-0.838) and 0.618 (0.455-0.782), respectively.

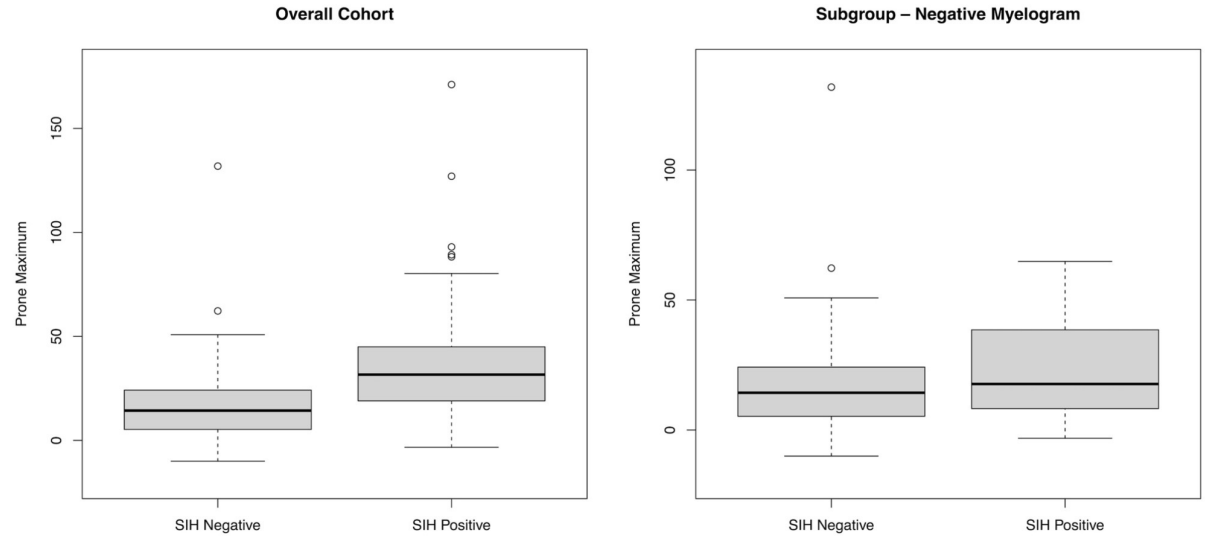

FIG 3. Box plots of maximum contrast density by SIH diagnosis overall and for the subgroup of patients with negative myelograms.

DISCUSSION

While our investigation of CTM performed in the early (i.e. ≤30 minute) time frame found a statistically significant higher level of RCE in subjects with SIH compared to subjects without SIH, similar to prior investigations of CTM in the >30 min time frame, the discriminatory ability of renal contrast density was insufficient to generate clinically useful thresholds predicting SIH+ versus SIH- without excessive false positives or false negatives. Subgroup analysis comparing SIH+ subjects with no leak seen on CTM to SIH- subjects performed even more poorly. For practitioners who are evaluating patients with possible SIH, this means that renal contrast density analysis based on CTM in the early time frame is not clinically useful to confidently differentiate individual patients with SIH from patients without SIH.

The ideal use of renal contrast density analysis would be to detect patients with a CVF that is occult on initial myelography, since patients with a CSF leak (i.e. either an epidural leak or CVF) confirmed on CTM will have already, by definition, met ICHD-3 criteria and had their leak localized, thus accomplishing the goals of myelography. Although a CVF is the presumptive diagnosis in patients with brain imaging evidence of intracranial hypotension and no leak seen on spinal imaging, a test capable of indirectly predicting the presence of a CVF with high accuracy might help patients and practitioners feel more confident in pursuing a repeat myelogram, which is sometimes required to visualize CVFs.[13] But more importantly, for patients with negative brain imaging and no CSF leak seen, a test that could help

with the critical decision of whether to stop a workup for spinal CSF leak altogether and consider alternative diagnoses would be highly clinically useful. Unfortunately, we found that, when CTMs are performed in the early time period, overlap in renal contrast excretion between SIH+ and SIH- patients precluded the use renal density analysis for confident categorization of SIH status in individual patients (Figure 3).

Previous investigations have found increased excretion of renal contrast among patients with SIH compared to patients without SIH. An initial study by Kinsman et al. investigating patients with SIH compared with control patients found renal contrast excretion was exclusively present in patients with SIH, as subjectively assessed in a non-quantitative fashion by neuroradiologists on initial CTM (2-113 minutes) and delayed CTM (79-386 minutes). Greatest excretion was found in patients with SIH due to CVF.[1] A subsequent investigation by Behbahani et al. quantitatively measured RCE on CTMs scanned between 45 and 74 minutes, and similarly found renal contrast excretion exclusively in patients with SIH.[2] Piechowiak et al. investigated CTMs scanned 37 to 61 minutes following intrathecal injection of contrast using a multivariable linear regression method to account for eGFR and time interval between contrast injection, and also found increased renal contrast excretion in patients with SIH, including those with negative CTM results.[3] More recent studies investigating the differential renal contrast excretion among patients with CVF undergoing decubitus CTM found an increase in RCE when patients were positioned in decubitus ipsilateral to the side of the CVF compared to those patients positioned in the contralateral decubitus, and speculated that this may be the result of preferential egress of contrast when intrathecal contrast dependently layers on the side of the CVF.[4, 14]

These earlier studies on scans performed predominantly in the late (>30 min) time frame consistently found statistical differences in RCE in patients with SIH compared to patients without SIH, similar to the findings of our study on CTMs performed in the early time frame. However, these prior studies did not assess whether a threshold for renal density could be defined that was clinically useful in characterizing individual patients. In this study, our analysis suggested that the corresponding specificity or sensitivity of a clinically useful test (>90% sensitivity or specificity) would result in large number of false-positive or false-negative results, and thus would be of limited clinical value. Specifically, selecting a highly sensitive (>90%) cutoff value for renal contrast density would result in a high number of false positive tests (on average, 68.7% of cases), leading to unnecessary repeat testing. On the other hand, selection of a highly specific (>90%) cutoff value would result in a high number of false negative tests (on average, 49.2%), leading to missed diagnoses of SIH. There are multiple possible explanations for the overlap in RCE between subjects with SIH and those without SIH. One possibility is that the RCE observed in the SIH- subjects represents normal physiologic excretion, and that normal excretion overlaps with the early excretion due to CSF leak seen in SIH. Although previous investigations reported that no RCE was seen in control subjects, some investigations used subjective (i.e qualitative) analysis, and it is possible that quantitative analysis might be more sensitive for measuring low-level normal physiologic excretion. A second possibility is that leakage of intrathecal contrast from the lumbar puncture site results in spurious CSF leak independent of SIH status, producing an overlap in RCE between SIH- and SIH+ subjects. Since there is no current method for preventing this leakage, it is not clear that this theoretical confounder could be avoided in future investigations.

Our study has several limitations. First, although based on a larger cohort size, the number of subjects with individual subtypes of myelographic findings (e.g. epidural leak, CVF, or positive brain imaging with negative myelogram) was relatively small. It is possible that larger subgroups might result in different threshold values. Although this might change the discriminatory characteristics of RCE, some overlap between SIH+ and SIH- patients would likely persist, based on the results of this investigation, which would decrease the utility of the sign as a diagnostic tool. Second, renal function data was missing in a substantial number of patients. To address this limitation, we presented both a complete case analysis and a sensitivity analysis with single imputation, both of which gave similar results. Third, we did not analyze CTM images done in the decubitus position, which are scanned before prone images in our institutional protocol due to the fact the renal collecting system was outside the field-of-view on many of these subjects. We cannot exclude the possibility that analysis of decubitus scans might have resulted in different ROC curves, although given the fact that contrast accumulation in the renal collecting system increases with time, it is far from certain that analysis of these scans at an earlier time point would produce better results. Given preliminary work showing some differences in RCE when CTMs are scanned decubitus ipsilateral versus contralateral to known CVFs, however, this topic merits further investigation.[14 4]

CONCLUSIONS

In conclusion, while we found a statistically significantly higher renal contrast excretion in patients with SIH compared to patients without SIH during early-phase CTM, no clinically useful threshold value could be established that could reliably distinguish these groups with both high sensitivity and high specificity. Renal contrast density performed even less effectively for differentiating patients without SIH from patients with SIH and negative myelograms, in whom an additional indirect indicator of SIH would be most beneficial to help practitioners determine which patients should undergo further imaging evaluation.

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SUPPLEMENTAL FILES

Online Supplemental Data: Demographics and clinical characteristics of subjects by SIH Diagnosis.

	SIH Negative (N=131)	SIH Positive (N=59)	Total (N=190)
Age at exam (y)			
Mean (SD)	47.3 (16.6)	50.5 (13.8)	48.3 (15.8)
Median (Q1, Q3)	49.4 (34.5, 58.6)	51.8 (39.8, 58.9)	50.1 (37.2, 58.9)
Range	(16.1-82.1)	(14.7-82.6)	(14.7-82.6)
Sex			
Female	88 (67.2%)	38 (64.4%)	126 (66.3%)
Male	43 (32.8%)	21 (35.6%)	64 (33.7%)
Creatinine (mg/dL)			
Missing	34	18	52
Mean (SD)	0.8 (0.2)	0.9 (0.2)	0.8 (0.2)
Median (Q1, Q3)	0.8 (0.7, 0.9)	0.8 (0.8, 1.0)	0.8 (0.7, 0.9)
Range	(0.5-1.9)	(0.5-1.3)	(0.5-1.9)
eGFR CKD Stage combined			
Missing	45	20	65
Stage 1/2	80 (93.0%)	35 (89.7%)	115 (92.0%)
Stage3	6 (7.0%)	4 (10.3%)	10 (8.0%)
Time between Injection and CTM (min)			
Mean (SD)	16.7 (5.9)	20.0 (7.8)	17.7 (6.7)
Median (Q1, Q3)	15.0 (12.0, 21.0)	23.0 (12.0, 27.0)	15.0 (12.0, 24.0)
Range	(8.0-30.0)	(5.0-30.0)	(5.0-30.0)
Density in left kidney (HU)			
Mean (SD)	13.8 (16.0)	34.5 (31.2)	20.3 (23.8)
Median (Q1, Q3)	10.4 (2.8, 22.5)	27.2 (13.8, 44.7)	15.2 (5.6, 27.0)
Range	(-10.8-117.1)	(-3.3-171.1)	(-10.8-171.1)
Density in right kidney (HU)			
Mean (SD)	14.0 (16.9)	33.7 (28.2)	20.1 (22.9)
Median (Q1, Q3)	12.5 (2.8, 22.7)	28.1 (15.7, 43.7)	16.2 (5.4, 28.2)
Range	(-14.6-131.9)	(-4.3-135.0)	(-14.6-135.0)
Maximum Density (HU)			
Mean (SD)	16.3 (16.4)	37.9 (31.4)	23.0 (24.3)
Median (Q1, Q3)	14.3 (5.3, 24.2)	31.6 (18.4, 45.3)	17.7 (8.3, 29.4)
Range	(-10.0-131.9)	(-3.3-171.1)	(-10.0-171.1)
Minimum Density (HU)			
Mean (SD)	11.6 (16.2)	30.3 (27.5)	17.4 (22.1)
Median (Q1, Q3)	7.7 (0.4, 19.1)	25.4 (12.3, 40.9)	13.7 (3.3, 26.1)
Range	(-14.6-117.1)	(-4.3-135.0)	(-14.6-135.0)

Single imputation method:

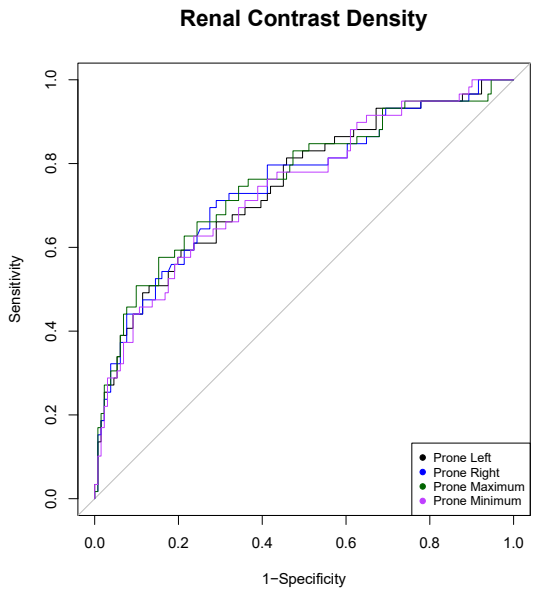
For the single imputation models, the R package *mice* was used to impute missing data via fully conditional specification. The imputation models included the covariates Age, Sex, time to prone (as a spline), eGFR categories, Creatinine, Prone left, Prone right, Maximum prone, and SIH status. The methods used to impute eGFR categories and creatinine were logistic regression and predictive mean matching, respectively, and m=1 imputed datasets were created.

Supplementary Table 1: Unadjusted and adjusted models testing for an association between contrast density and SIH diagnosis.

	Unadjusted models (N = 190)		Adjusted models: Complete case* (N = 125)		Sensitivity analysis Adjusted models: Single imputation** (N = 190)	
	OR (95% CI) per 10 unit increase	p-value	aOR (95% CI) per 10 unit increase	p-value	aOR (95% CI) per 10 unit increase	p-value

Left kidney density	1.619 (1.324, 1.978)	**<0.001**	1.655 (1.236, 2.217)	**0.001**	1.755 (1.383, 2.226)	**<0.001**
Right kidney density	1.598 (1.308, 1.952)	**<0.001**	1.634 (1.230, 2.170)	**0.001**	1.629 (1.308, 2.029)	**<0.001**
Maximum density	1.637 (1.335, 2.006)	**<0.001**	1.642 (1.238, 2.178)	**0.001**	1.700 (1.356, 2.131)	**<0.001**
Minimum density	1.612 (1.315, 1.975)	**<0.001**	1.682 (1.246, 2.269)	**0.001**	1.719 (1.355, 2.179)	**<0.001**

* Complete case analysis adjusting for Age, Sex, Time to scanning (spline), eGFR categories (Stage 1/2 vs Stage 3), and creatinine.
** Single imputation analysis adjusting for Age, Sex, Time to scanning (spline), eGFR categories (Stage 1/2 vs Stage 3), and creatinine.



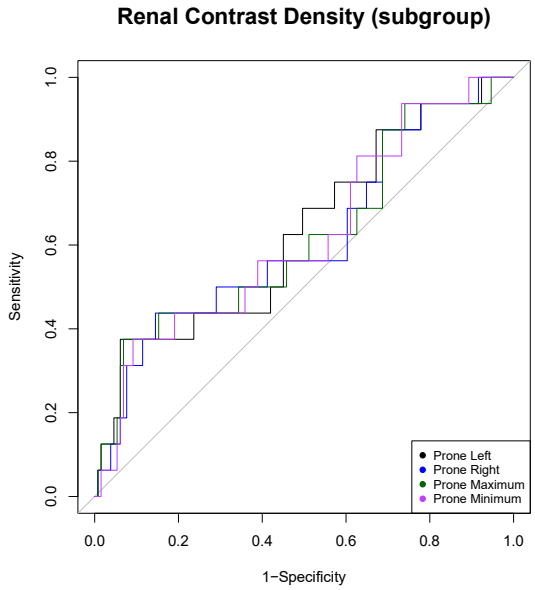
Supplementary Figure 1. ROC curves for left, right, maximum, and minimum contrast density. Area under the curves are as follows: 0.748 (0.670-0.825); 0.750 (0.672-0.829); 0.760 (0.682-0.838); 0.742 (0.664-0.820).

Supplementary Table 2. Sensitivity and specificities for the 3 thresholds on the ROC curves.

Contrast density	Threshold (HU)	Sensitivity*	Specificity*	Description
Left	5.565	0.932 (0.864, 0.983)	0.328 (0.252, 0.412)	Sensitivity > 90%
Left	31.47	0.441 (0.322, 0.576)	0.908 (0.855, 0.954)	Specificity > 90%
Left	24.755	0.593 (0.475, 0.729)	0.794 (0.718, 0.855)	Youden's Index
Right	5.035	0.915 (0.831, 0.983)	0.313 (0.237, 0.397)	Sensitivity > 90%
Right	30.805	0.441 (0.322, 0.576)	0.924 (0.878, 0.962)	Specificity > 90%
Right	19.34	0.712 (0.593, 0.831)	0.71 (0.633, 0.786)	Youden's Index
Max	7.87	0.932 (0.864, 0.983)	0.313 (0.237, 0.389)	Sensitivity > 90%
Max	31.471	0.508 (0.390, 0.627)	0.901 (0.847, 0.947)	Specificity > 90%
Max	27.98	0.576 (0.458, 0.695)	0.847 (0.779, 0.901)	Youden's Index
Min	4.36	0.915 (0.831, 0.983)	0.351 (0.275, 0.435)	Sensitivity > 90%

Min	28.7	0.441 (0.322, 0.559)	0.908 (0.855, 0.954)	Specificity > 90%
Min	19.78	0.627 (0.508, 0.746)	0.763 (0.687, 0.832)	Youden's Index

* 95% CI via 2000 stratified bootstrap replicates



Supplementary Figure 2. ROC curves for left, right, maximum, and minimum contrast density for the subgroup of patients with negative myelogram (N = 147). Area under the curves are as follows 0.630 (0.474, 0.786); 0.616 (0.456, 0.776); 0.618 (0.455, 0.782); 0.621 (0.466, 0.776).

Supplementary Table 3. Sensitivity and specificities for the 3 thresholds on the ROC curves for the subgroup of patients with negative myelogram (N = 147).

Contrast density	Threshold (HU)	Sensitivity*	Specificity*	Description
Left	1.795	0.938 (0.812, 1)	0.221 (0.153, 0.290)	Sensitivity > 90%
Left	34.525	0.375 (0.125, 0.625)	0.939 (0.901, 0.977)	Specificity > 90%
Left	34.525	0.375 (0.125, 0.625)	0.939 (0.901, 0.977)	Youden's Index
Right	1.995	0.938 (0.812, 1)	0.221 (0.153, 0.290)	Sensitivity > 90%
Right	30.805	0.312 (0.125, 0.562)	0.924 (0.878, 0.962)	Specificity > 90%
Right	27.995	0.438 (0.188, 0.688)	0.855 (0.786, 0.908)	Youden's Index
Max	5.315	0.938 (0.812, 1)	0.260 (0.183, 0.336)	Sensitivity > 90%
Max	34.525	0.375 (0.125, 0.625)	0.931 (0.885, 0.969)	Specificity > 90%
Max	34.525	0.375 (0.125, 0.625)	0.931 (0.885, 0.969)	Youden's Index
Min	1.795	0.938 (0.812, 1)	0.267 (0.191, 0.344)	Sensitivity > 90%
Min	28.955	0.375 (0.125, 0.625)	0.908 (0.855, 0.954)	Specificity > 90%
Min	28.955	0.375 (0.125, 0.625)	0.908 (0.855, 0.954)	Youden's Index

* 95% CI via 2000 stratified bootstrap replicates