Decreased Renal Parenchymal Density on Unenhanced Helical Computed Tomography for Diagnosis of Ureteral Stone Disease in Emergent Patients with Acute Flank Pain

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Background: The purpose of this study was to determine the usefulness and optimal cutoff point of decreased renal parenchymal density (DRD) for diagnosis of ureteral stone disease (USD) in emergent patients with acute flank pain.

Methods: A total of 85 emergency patients with acute flank pain who underwent unenhanced helical computed tomography (UHCT) were prospectively included in this study as the study group. An additional 30 patients with no USD undergoing UHCT were retrospectively included as the control group. The mean parenchymal density difference between both kidneys of the control group was compared to that of the study group. Within the study group, the DRD of patients with USD and with no USD was compared. The sensitivities and specificities of DRD for diagnosis of USD in a range of possible optimal cutoff points were analyzed.

Results: There was a statistically significant difference in DRD between the study and control groups ($p < 0.0001$). In the study group, the DRD of patients with USD was significantly higher than that of patients with no USD [mean $\pm$ SD = 4.04 $\pm$ 3.4 Hounsfield units (HU) versus 0.08 $\pm$ 2.7 HU, $p = 0.0001$]. DRD using cutoff points of $\geq$ 8 HU, $\geq$ 5 HU and $\geq$ 2.06 HU had a sensitivity of 12.5%, 40.3% and 76.4%, and a specificity of 100%, 92.3% and 76.9%, respectively.

Conclusions: DRD may be helpful in the diagnosis of USD in emergent patients with acute flank pain. When a DRD of $\geq$ 2.06 HU is selected as a cutoff point, its sensitivity and specificity are both acceptable and higher than 75%.

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Key words: acute flank pain, ureteral stone, unenhanced helical computed tomography, decreased renal density

Patients with ureteral stones usually come to the emergency department presenting with acute flank pain. Several studies, including ours, have shown that unenhanced helical computed tomography (UHCT), using direct and indirect signs of ureteral stones, is a rapid and accurate method for

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diagnosis of ureteral stones, and UHCT can diagnose other causes of acute flank pain.(1-15) Recently, the difference in the renal parenchymal density of the acutely obstructed kidney and the non-obstructed kidney on UHCT has been suggested as an additional useful secondary sign.(16-18) As the parenchymal densities of both kidneys can be measured, the decreased renal parenchymal density (DRD) of the flank pain side is an objective and measurement-based indicator, unlike other subjective secondary signs of ureteral stones.(17) However, there have been discrepancies in the usefulness of DRD for diagnosis of ureteral stone disease as well as chosen cutoff points [DRD ≥ 5.00 Hounsfield units (HU) or ≥ 8.00 HU] and reported diagnostic values in the literature.(6,16-19) Thus, the purpose of our study is to analyze the usefulness of DRD using different cutoff points for diagnosis of ureteral stone disease (USD) in emergency patients with acute flank pain.

METHODS

During an 8-month period, emergency patients presenting with acute flank pain, except pregnant women and febrile patients, were prospectively enrolled in the study. After informed consent was obtained according to a protocol approved by the ethics committee at our institution, the patients underwent UHCT. Their final diagnoses were categorized as USD and diseases other than ureteral stones. The final diagnosis and the course of the therapy were documented by review of the patients' clinical medical records. Detection of a ureteral stone by ureteroscopy or lithotripsy, or documentation of a passed stone recovered in the patient's urine before or after the UHCT study were grouped as USD. Any disease other than ureteral stones documented by subsequent surgery, intervention or other examinations was also recorded. Patients who were lost to follow-up without documented final diagnosis, with bilateral flank pain or with final diagnosis of bilateral ureteral stones were excluded from the study group. An additional 30 patients who underwent UHCT but with no final diagnosis of USD were retrospectively included as a control group.

All UHCT studies were performed using a multidetector helical computed tomography (HCT) scanner (LightSpeed QX/i, GE Medical systems, Milwaukee, WI, USA) using 3.75 mm image thickness, image interval 200-280 mAs and 120 kV. There were two modes for HCT scanning: high quality mode with 3.0 helical pitch and high speed mode with 6.0 helical pitch. The high quality mode was used for its better imaging quality compared to the other mode. The images were acquired from the top of kidneys through the bladder base during breath holding of 15-22 seconds. Neither oral nor intravenous contrast medium was administrated. The mean density of each kidney's upper, middle and lower poles was recorded in HU by measurements of renal parenchymal densities using the same oval region of interest (0.5 cm^2) by a radiologist without knowledge of the final diagnosis (Fig. 1).(17,18) In the study group, if a ureteral stone was visualized on the symptomatic side, its largest diameter was measured and recorded as the stone size. The presence or absence of hydronephrosis on the symptomatic side was also noted.

In the control group, the renal parenchymal differences between both kidneys were calculated and compared with those of the study group. In the study group, when the mean renal parenchymal density of the kidney on the symptomatic (flank pain) side was less than that of the asymptomatic side, presence of DRD was considered. DRD difference was defined and calculated as the renal parenchymal density of the kidney on the asymptomatic side minus that of the symptomatic (flank pain) side. The DRD differences between groups of patients with USD and with no USD were compared using student *t* test. The *p* value was two-sided and the significance level was set at 0.05. In patients with USD, the correlation between stone size and DRD was analyzed using Pearson correlation coefficient. Receiver operating curve (ROC) of DRD with sensitivity and specificity of a range of potential cutoff points was calculated. The optimal cutoff point of DRD for diagnosis of USD was determined by the point of convergence, and minimum difference between sensitivity and specificity.(20)

RESULTS

Ninety-two emergency patients with acute flank pain underwent UHCT. Seven patients were excluded from the study group, including 3 patients with bilateral flank pain, 2 patients who were lost to follow-up and 2 patients with final diagnosis of bilateral

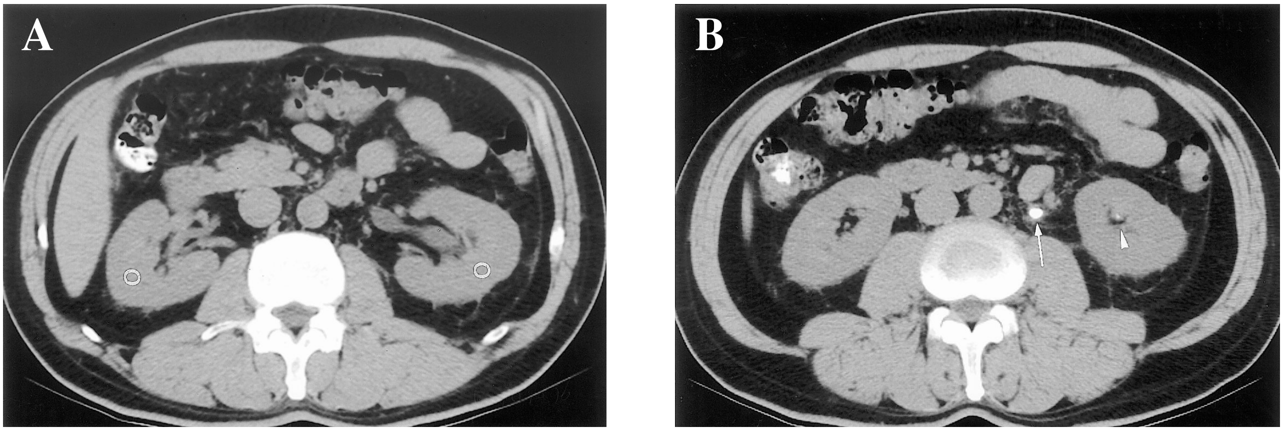

Fig. 1 A 49-year-old man visited our emergency department presenting with left acute flank pain. (A) Unenhanced helical computed tomography (UHCT) of both kidneys showing mild left hydronephrosis and left nephromegaly. By using oval regions of interest (oval shape areas), the mean density of the left renal parenchyma was measured and recorded as 32.75 Hounsfield units (HU) versus 35.64 HU in the right renal parenchyma. Thus, decreased left renal parenchymal density was present with a difference of 2.89 HU between each kidney. (B) UHCT 3 cm caudal to Fig. 1A showing a left proximal ureteral stone (arrow) and a left renal lower calyceal stone (arrowhead). This ureteral stone was subsequently disintegrated by ureteroscopic lithotripsy.

ureteral stones. The remaining 85 patients (78 men and 7 women) with a mean age of 40.52 years (range 22 to 67 years) constituted the study group. Of them, 48 patients had right flank pain, while 37 patients had left flank pain. Of these 85 patients, 72 had USD and 13 had diseases other than ureteral stones. The presence of USD in the 72 patients was confirmed by lithotripsy in 12, ureteroscopy in 18 and recovery of passed stones before or after HCT study in 42. Of the 13 patients without USD, 5 had urinary tract disease, including 2 ureteral or ureteropelvic junction (UPJ) stenosis and 3 bilateral renal stones, and 8 had non-urinary tract diseases, including 1 acute appendicitis, 1 intestinal obstruction, 3 acute pancreatitis, 1 gastritis, 1 enterocolitis and 1 sigmoid colon diverticulitis.

The DRD of all 85 patients in the study group ranged from –4.87 to 12.2 HU, with a mean of 3.44 HU [standard deviation (SD) = 3.6 HU], which was significantly different from the mean of 0.12 HU (SD = 0.6 HU) in the control group ($p < 0.0001$). In the study group, the mean DRD of 72 patients with a final diagnosis of USD was 4.04 HU (SD = 3.4 HU) (Fig. 2), while the mean DRD of 13 patients with diseases other than ureteral stones was 0.08 HU (SD = 2.7 HU). There was a statistically significant difference between these 2 groups ($p = 0.0001$). Five of 13 patients with bilateral renal stones, UPJ stenosis, enterocolitis, sigmoid colon diverticulitis or acute pancreatitis had DRD on the symptomatic side (Fig. 3). Of the patients with USD, there was no significant difference in DRD between patients with and without hydronephrosis (mean $\pm$ SD = 4.08 $\pm$ 3.41 versus 3.15 $\pm$ 1.86, respectively, $p = 0.6407$). The scatter plot of ureteral stone size and DRD is shown in Fig. 4. Their correlation coefficient was 0.03, which suggested nearly no linear correlation. The area under ROC of DRD for diagnosis of USD was 0.826 with 95% confidence interval of 0.716-0.935 (Fig. 5). The sensitivity and specificity of DRD in a range of potential optimal cutoff points for diagnosis of ureteral stones are illustrated in Fig. 6. The optimal point determined by the convergence of sensitivity and specificity was DRD $\geq$ 2.06 HU. Table 1 shows the sensitivity and specificity with 95% confidence intervals of different cutoff points (DRD $\geq$ 2.06 HU, DRD $\geq$ 5 HU, DRD $\geq$ 8 HU) used in our study and the literature. DRD $\geq$ 2.06 had a sensitivity of 76.4% and specificity of 76.9% for diagnosis of USD, which were significantly different from those of DRD $\geq$ 5 and DRD $\geq$ 8 (all $p < 0.0001$). Of 4 patients documented with USD but no direct sign on UHCT, 3 (75%) were correctly diagnosed as USD using DRD $\geq$ 2.06 HU versus 2 (50%) correctly diagnosis using DRD $\geq$ 5.00 HU or $\geq$ 8.00 HU.

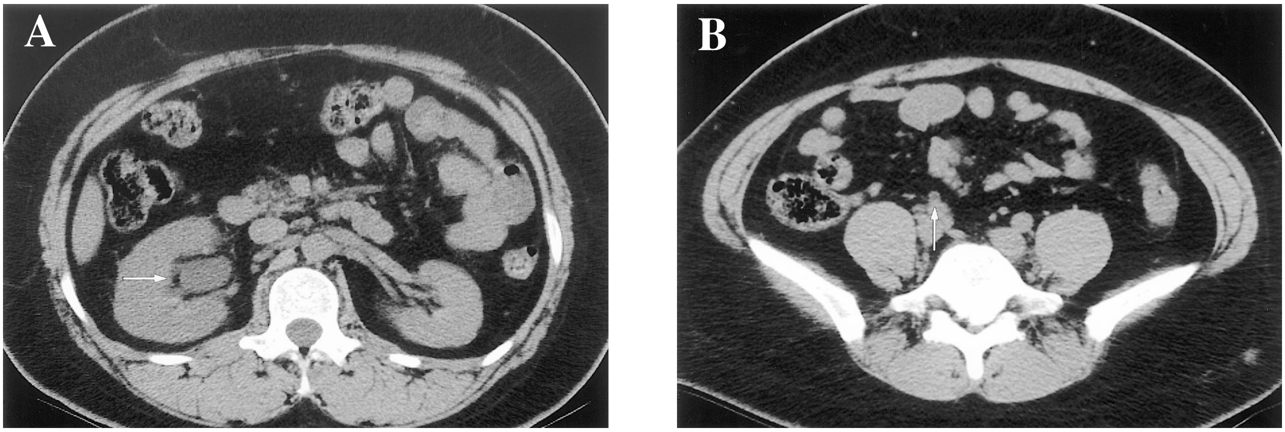

Fig. 2 A 29-year-old female patient came to our hospital as an emergency presenting with right acute flank pain. (A) Unenhanced helical computed tomography (UHCT) at the level of both kidneys showing right hydronephrosis (arrow) and right nephromegaly. Decreased right renal density with a difference of 11.58 Hounsfield units (HU) (right kidney: 25.87 HU versus left kidney: 37.45 HU) between each kidney was noted. (B) UHCT at the iliac crest level showing mild dilatation of the right ureter (arrow). No calculus in the right ureter was revealed on any UHCT images (not shown). The stone was passed and discovered by the patient herself before undergoing UHCT.

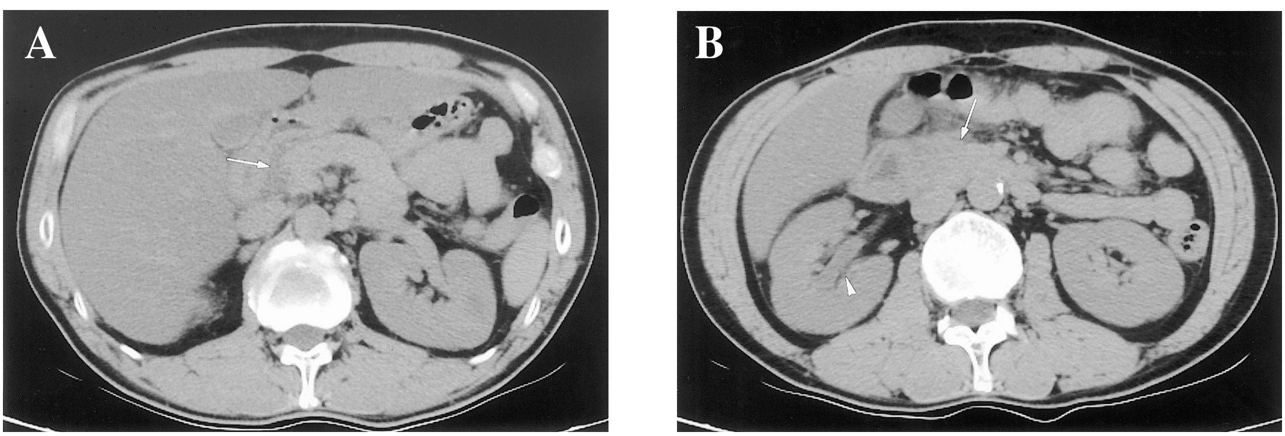

Fig. 3 A 42-year-old man complained of right acute flank pain and visited our emergency department. (A) Unenhanced helical computed tomography (UHCT) at the pancreas body level showing fatty liver and dirty peripancreatic fat (arrow) adjacent to the right half of the pancreas body. (B) UHCT at the pancreatic head level showing swelling of the whole pancreatic head (arrow) with obliterated fat plane between the pancreas head and duodenum. The right renal collecting system was mildly dilated (arrowhead). The renal parenchymal density of the right kidney was 3.14 Hounsfield units (HU) less than that of the left kidney (right kidney: 34.13 HU versus left kidney: 37.27 HU). Acute pancreatitis was impressed and confirmed by laboratory examinations.

DISCUSSION

When using UHCT to help diagnose acute flank pain, indirect (secondary) signs of obstruction are important for diagnosis if one does not see a ureteral stone or sees an indeterminate but suspicious calcification.[5] These indirect signs provide supportive evidence that an acute obstructive process is present either due to the most common cause, ureteral stones, or another obstructive cause.[4] There are a variety of responses of the kidney and ureter when a kidney is obstructed by a ureteral stone, including hydronephrosis, hydroureter, perinephric stranding, perinephric fluid and renal edema.[4,5,21] Hydronephrosis and hydroureter are phenomena that

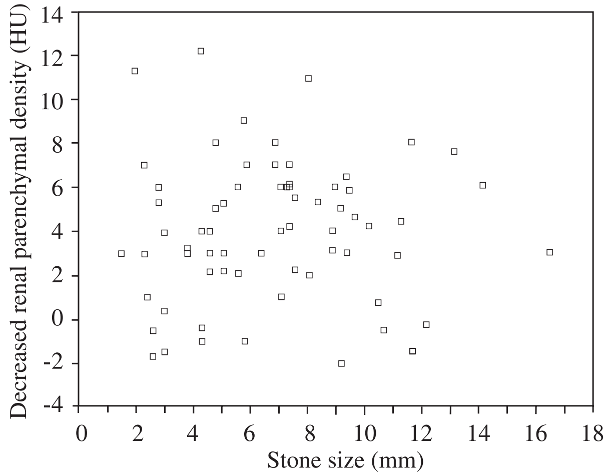

Fig. 4 Scatter plot of ureteral stone size and decreased renal parenchymal density in patients with ureteral stone disease. HU = Hounsfield units.

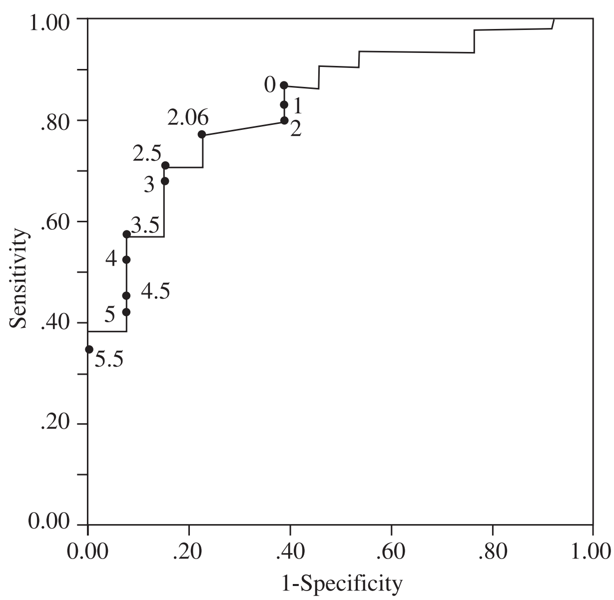

Fig. 5 The receiver operating curve of decreased renal parenchymal density (DRD) for the diagnosis of ureteral stone disease. The cutoff points of DRD ≥ 5.5 Hounsfield units (HU), ≥ 5 HU, ≥ 4 HU, ≥ 3.5 HU, ≥ 3 HU, ≥ 2.06 HU ≥ 2 HU, ≥ 1 HU and ≥ 0 HU are marked by small black oval circles.

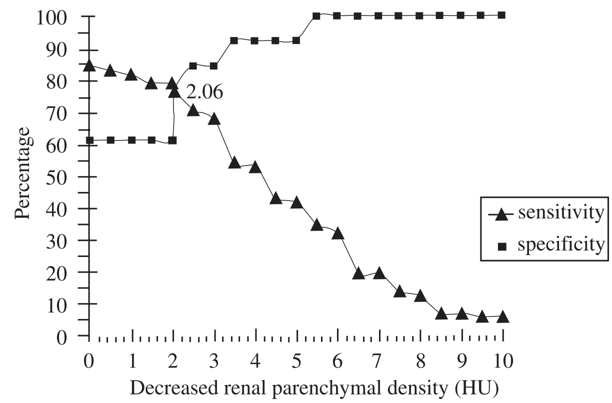

Fig. 6 The sensitivities and specificities of decreased renal parenchymal density of a range of cutoff points per 0.5 Hounsfield units (HU) from 0 HU to 10 HU. The convergence point of sensitivity and specificity was 2.06 HU.

Table 1. The Sensitivities and Specificities of Decreased Renal Parenchymal Density Using Several Potential Optimal Cutoff Points for Diagnosis of Ureteral Stone Disease

DRD cutoff points (HU)	US (+) (n = 72)	US (–) (n = 13)	SEN (95 % CI)	SPE (95 % CI)
DRD ≥ 8.00	9	0	0.125 (0.049-0.201)	1.000 (1.000-1.000)
DRD ≥ 5.00	29	1	0.403 (0.289-0.516)	0.923 (0.778-1.068)
DRD ≥ 2.06	55	3	0.764 (0.666-0.862)	0.769 (0.540-0.998)

Abbreviations: DRD: decreased renal parenchymal density; HU: Hounsfield units; US (+): presence of ureteral stones; US (–): diseases other than ureteral stones; SEN: sensitivity; SPE: specificity; CI: confidence interval.

depend on interaction of intra-luminal pressure and capacity of the collecting system or ureter.(16) In other words, mildly increased intraureteral pressure may cause marked dilatation of a flaccid ureter, whereas markedly increased intraureteral pressure could cause only mild dilation of a low capacity ureter.(16) Further, the increased renal collecting system or ureter pressure may induce hyperemia, and increased lymphatic pressure and flow, which then cause increased renal interstitial fluid.(16,21) The increased renal interstitial fluid results in renal edema, which appears on UHCT as two signs at the same time: (1) DRD and (2) nephromegaly.(16,21)

Although prior studies have proposed that DRD is a secondary sign in USD, the sensitivity of DRD ≥ 5 HU for USD varied from 61% to 89% in recent studies by Goldman et al. and Ó'zer et al. versus

41.7% in our study.[16,18] The discrepancies of reported sensitivities in our study and others actually reflect the time related nature of DRD presence and the differences in study designs. The presence of renal edema in patients with USD is related to their duration of flank pain.[22] In the study by Varanelli et al., nephromegaly increased from 40% at 1-2 hr to 54% at 7-8 hr and then decreased over time.[22] Thus, the differences in frequency of presence of DRD in these studies could contribute to the different distribution of flank pain duration in study groups, which were also affected by medical accessibility.

Study designs, especially selection of study groups, also had a large impact on the result of diagnostic tests. The study by Ó'zer et al. did not have a cohort of emergency patients with a similar presentation of acute flank pain as ours did.[18] Instead, their study was based on a selection of 55 emergency patients whose UHCT revealed ureteral stones as the study group and 22 emergency patients who were eventually diagnosed as acute appendicitis, acute pancreatitis or acute cholecystitis as the control group. Undoubtedly, patients presenting with acute flank pain but having negative ureteral stone findings on UHCT would be excluded by this selection criteria. Also, the arbitrary selection of emergency patients with the three diseases as the control group, regardless of their presentations, would also exaggerate the DRD differences between the study and control groups.

In our study, there were 11 out of 72 patients who had a higher renal parenchymal density on the ureteral stone side than on the normal side. This phenomenon has also been observed and reported by Goldman et al.[17] The renal parenchymal differences of the non-obstructed kidney minus that of the obstructed kidney in the same individual ureteral stones ranged from –3.3 to 13 HU in their report.[17] A possible explanation of this finding is that, when the renal edema of the obstructed kidney progressively decreased over time, it might attain a somewhat dehydrated status instead of going back to a normal renal water content status.

Another important issue is the selection of the optimal cutoff point in a diagnostic test. The use of DRD ≥ 5.00 HU or ≥ 8.00 HU in prior studies was basically arbitrarily determined.[6,16-18] Regarding a diagnostic test with the use of a continuous variable, a cutoff point selected with higher sensitivity inevitably has lower specificity, and visa versa. Thus, to balance compromises between sensitivity and specificity, an optimal cutoff point was determined as the point with convergence of sensitivity and specificity, as used by Dobbelsteyn et al.[20] In our study, the optimal cutoff point of DRD ≥ 2.06 HU had both sensitivity and specificity higher than 75%. In contrast, DRD ≥ 5.00 HU and DRD ≥ 8.00 HU had much poorer sensitivity of 41.7% and 12.5%, respectively, despite high specificity. Furthermore, more patients with USD but no direct sign on UHCT were correctly diagnosed using DRD ≥ 2.06 HU than DRD ≥ 5.00 HU and DRD ≥ 8.00 HU.

Our study also showed the presence of DRD in patients with diseases other than ureteral stones. Five out of 13 patients with no USD actually had DRD on the symptomatic side. The DRD in patients with right UPJ stenosis or bilateral renal stones was considered to be related to renal interstitial edema, as it has a similar mechanism as USD. In the patients with sigmoid colon diverticulitis, enterocolitis or acute pancreatitis, inflammatory processes that arose adjacent to the ipsilateral ureter or kidney might impair peristalsis of the ureter and renal collecting system. This then results in renal edema.[21] This phenomenon was neglected in prior studies because all urinary tract diseases other than ureteral stones were simply excluded or the control group was arbitrarily selected. This then failed to reflect the true distribution of diseases and their associated findings in emergency patients with acute flank pain.

There are several limitations in our study. First, the number of patients with a final diagnosis of no USD in the study group was small, which actually reflects the high occurrence rate of ureteral calculi in Taiwan. Second, we did not include the additional group of patients with no USD undergoing UHCT as the control group prospectively but retrospectively. Nonetheless, we believe that the measurement of renal parenchymal densities of patients in this control group would not be altered regardless of whether they were included in a prospective or retrospective way.

In conclusion, DRD for diagnosis of USD in emergent patients with acute flank pain has a large area under ROC of 0.826. With the use of a cutoff point of DRD ≥ 2.06 HU, a sensitivity of 76.4% and specificity of 76.9% (both higher than 75%) can be achieved. It also helps in the correct diagnosis of

75% of patients with USD who have no direct visualization of ureteral stone on UHCT.

Acknowledgments

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應用無顯影劑螺旋式電腦斷層檢查之腎臟實質密度的減少表徵，用以診斷急診腰痛病人之輸尿管結石

黃成之 黃耀祥 王俐人 邱德發[1] 黃集仁[1] 陳日昌[1]

背 景： 本研究的目的，是對急性腰痛的急診病人，以腎臟實質密度的減少來診斷輸尿管結石，並研究此徵象之實用性。

方 法： 本研究是以 85 位患有急性腰痛急診病人，接受無顯影劑螺旋式電腦斷層檢查爲研究組。另外 30 位非輸尿管結石患者，亦接受無顯影劑的螺旋式電腦斷層檢查作爲對照組。比較對照組和研究組病人兩側腎臟實質密度的差異，並在研究組中，比較有輸尿管結石和無輸尿管結石病患，其腎臟實質密度減少的差異，及不同程度的腎臟實質密度之減少，其用來診斷輸尿管結石之診斷敏感度及特異度。

結 果： 在研究組及對照組間，其減少的腎臟實質密度之差異有統計學上的意義 ($p <$ 0.0001)。在研究組中，輸尿管結石病人其減少的腎臟實質密度高於非輸尿管結石病人 (平均值 ± 標準差 = 4.04 ±3.4 HU 及 0.08 ±2.7 HU，$p = 0.0001$)。以腎臟實質密度減少達 8 HU 以上、5 HU 以上、及 2.06 HU 以上作爲診斷輸尿管結石標準時，其敏感度分別是 12.5%、40.3%、及 76.4%，其特異度分別是 100%、92.3%、及 76.9%。

結 論： 在急性腰痛的急診病人中，使用腎臟實質密度減少之徵象，可幫助輸尿管結石之診斷，以腎臟實質密度減少達 2.06 HU 以上爲診斷條件，其敏感度及特異度均高於 75%。

(長庚醫誌 2008;31:182-9)

關鍵詞： 急性腰痛，輸尿管結石，無顯影劑的螺旋式電腦斷層檢查，減少的腎臟實質密度

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