COMPARISON OF HOUNSFIELD UNITS OF THE RENAL PAPILLAE IN KIDNEY STONE FORMERS AND NON STONE FORMERS

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ABSTRACT

Objective: *To investigate whether renal papillae of patients with nephrolithiasis are more radiodense than that of control patients and to evaluate the predictibility of urolithiasis events using papillary density differences between stone and non stone formers.*

Material and Method: *Hounsfield unit (HU) values of the papillae of 212 patients with unilateral nephrolithiasis and 108 patients in the control group at the level of the upper pole, middle region and lower pole of both kidneys were evaluated.*

Results: *Mean HU density of all papillae of kidneys with stones was higher than that of stone free kidneys in nephrolithiasis patients (27.21±2.83 vs 25.66±2, p=0.000). Mean HU density of renal papillae of stone patients in calyces with stones was significantly higher than that of all papillae in control patients (25,82±1,97 vs 30,25±4,03, p<0,001). Mean HU density of all papillae in stone-free kidneys of nephrolithiasis patients was not significantly different from that of control patients (25.82±1.97 vs 25.66± 2.57, p=0.642). When the values for control and patient groups according to stone laterality was evaluated, the difference was significant only between right upper and right lower calyces for the right nephrolithiasis and the left middle region for the left nephrolithiasis. (26.32±3.30 vs. 27.90±3.92 and 25.10±3.34 vs. 26.95±4.73, p=0.003 and p=0.009 and 25.70±3.67 vs 27.15±3.77 p= 0.001, respectively).*

Conclusion: *Only the kidneys with stones and especially the patients with papillae facing the stones in nephrolithiasis have higher renal papillary HU. This fact implies the impossibility of HU per se in predicting future urolithiasis events and/or patients; opposing to the findings of a few previous studies.*

Keywords: *Computed tomography, Hounsfield unit, nephrolithiasis, renal papillae* ***Nobel Med 2014; 10(3): 63-68***

BÖBREK TAŞI OLAN VE OLMAYANLARDA RENAL PAPİLLALARDAKİ HOUNSFİELD BİRİMLERİNİN KIYASLANMASI

ÖZET

Amaç: Böbrek taşı olan hastalarda böbrek papilla yoğunluğunun taş olmayan bireylerdekine göre daha fazla olup olmadığını araştırarak ileride oluşabilecek ürolitiyazis olgularının öngörülebilirliğini değerlendirmek.

Materyal ve Metod: Tek taraflı böbrek taşı olan 212 hastanın ve hiç taşı olmayan 108 hastanın her iki böbreklerindeki üst pol, orta zon ve alt pol bölgelerinin Hounsfield (HU) değerleri incelendi.

Bulgular: Nefrolitiyazis hastalarında taşlı böbreklerin ortalama HU yoğunluğu, taş olmayan böbreklerinkinden yüksekti (27,21±2,83 vs 25,66±2, p=0,000). Taş hastalarının taşlı kalisteki ortalama renal papilla HU yoğunluğu, kontrol hastalarının tüm renal papilla ortalamasından yüksekti (25,82±1,97 vs 30,25±4,03, p<0,001). Nefrolitiyazis hastalarında taşı olmayan böbreklerin tüm papillalarının ortalama HU yoğunluğu, kontrol hastalarının papilla ortalamasından farklı değildi (25,82±1,97 vs 25,66± 2,57, p=0,642). Kontrol ve nefrolitiyazis hastalarında aynı taraf böbrekler değerlendirildiğinde, sağ taraf için sağ üst ve sağ alt kalisler arasında, sol taraf için, sadece sol orta zon arasında anlamlı fark vardı (sırasıyla, 26,32±3,30 27,90±3,92 ve 25,10±3,34 vs 26,95±4,73, p=0,003; p=0,009 ve 25,70±3,67 vs 27,15±3,77 p=0,001).

Sonuç: Sadece taşı olan hastalarda ve özellikle taş olan bölgedeki renal papillalarda daha yüksek HU yoğunluğu saptandı. Önceki birkaç çalışmanın aksine, bulgular tek başına böbrek papilla HU yoğunluğunun, hastalarda böbrek taş oluşabileceğini önceden belirlemede yetersiz bir etken olduğunu düşündürmektedir.

Anahtar Kelimeler: Bilgisayarlı tomografi, Hounsfield unitesi, nefolitiyazis, renal papilla **Nobel Med 2014; 10(3): 63-68**

INTRODUCTION

While the precise mechanisms for renal stone formation is not clearly elucidated, today extensive evidence supports the role of papillary interstitial deposits (Randall's plaques) at the formation of stones in the idiopathic, calcium oxalate stone formers.[1] Randall's plaque theory has been investigated extensively with biopsies during percutaneous or endoscopical interventions.

Histopathologic analysis of renal papilla biopsies in patients with nephrolithiasis has demonstrated their presence in a majority of stone formers.[2] However, these above mentioned methods are invasive. It is argued that recurrence can be determined by measuring the Hounsfield unit (HU) of the renal papillae by means of computed tomography (CT) which is a non-invasive method. Although CT imaging parameters of histopathologic alterations of renal parenchyma in stone forming patients have not been thoroughly studied, CT HU density has been used to differentiate renal calculi from blood clots, and to distinguish chemical composition of renal calculi.[3,4] With the hypothesis of that the renal papillae of patients with stones may appear more radiodense than those of control patients on CT, to date there have been few studies suggesting that HU density of the renal papilla or renal cortex is significantly increased in patients with nephrolithiasis when compared with controls.[5-7]

The purpose of this study is to confirm whether renal papillae of patients with nephrolithiasis are more radiodense than that of control patients as claimed in the previous studies and to evaluate the predictibility of urolithiasis events using papillary HU density differences between stone and non stone formers.

MATERIAL and METHOD

Subjects

Local Ethics Comittee approval was obtained prior to the study. The data base and evaluation of results were approved by the ethics committee of Maltepe University (MAL.UN.KAEK/MEG.27. 2011/22).

A total of 463 patients who were admitted to our hospital with renal colic complaints and underwent CT scanning were evaluated. Bilateral nephrolithiasis cases were excluded. CT scanning using contrast media orally or intravenously, creatinine values were above 1.6 mg/dl, a catheter in the urinary tract, calculi in the ureter, cysts in the kidneys, renal fusion anomaly, nephrectomy, solitary kidneys, calculi in the urinary bladder and renal hypoplasia, 212 patients with unilateral nephrolithiasis were included in the study. The control group covered 108 cases with normal renal function in which no calculus or anomaly was detected in the urinary system on CT.

A retrospective review was performed for 212 patients with a single renal calyceal calculus and 108 age-matched control patients without personal and family history of stone disease. →

CT scanning

All patients underwent CT using one of two machines. Either a Aquilion 64 64-detector row (Toshiba Medical Sysytem, Tokyo, Japan) with 0.5 mm section thickness or 3 mm reformat or a Philips Mx 8000 two-detector row (Philips Medical Systems, Eindhoven, The Netherlands) with 3 mm section thickness were used, depending on availability and departmental workload. CT was carried out through both kidneys to the bladder base in one breath-hold without the use of oral or intravenous contrast material. Patients were placed in supine position with full urinary bladder at the time of the CT.

Data Analysis

The CT images were retrospectively reviewed by two radiologist experienced in abdominal imaging. The reviewers were blinded to the patient's clinical data and analyzed the images independently. The analysis was done on Picture Archiving and Communication System (PACS version 4.0, Agfa, Richmond, VA). The HU densities of renal papilla were measured by placing ROIs (mean size 0.2 cm^2) in the region of renal papilla and the attenuation measurements were recorded (HU values) (Figure 1). The images were magnified to 5x to prevent contamination of the ROI with the fat in the renal sinus. The densities of the one upper, middle and lower pole renal papillae were measured separately in both the kidneys including the papillae in the region of calculi in patients with nephrolithiasis. The coronal reformatted images were used for better definition of the papillary anatomy and the density measurements were obtained on both axial and/or coronal images.

Statistical analysis

The density measurements of renal papillae of the control patients were separately compared with the density measurements of the renal papillae (with and without stones) in patients with nephrolithiasis. For analysis of the differences between the groups with regard to variables determined by measurement, the Mann-Whitney U-test and independent samples t-test were used. A p value of <0.05 was considered to be statistically significant. The reproducibility of results for density measurements was evaluated by analysing the interobserver variability for the density measurements.

RESULTS

Patient charactersitics are shown in Table 1. Patients with nephrolithiasis and control patients were similar with respect to mean age (40.1 years versus 38.7 years, p=0.77) and baseline serum creatinine (0.91 mg/dl versus 0.93 mg/dl, p=0.28). A minority

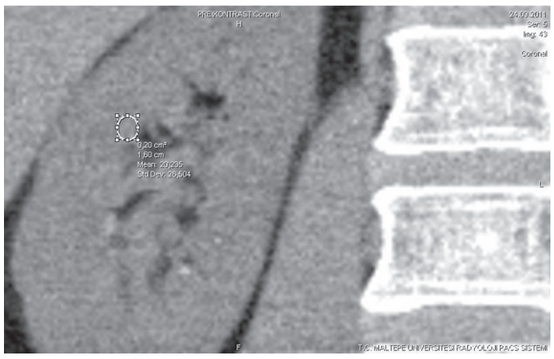

Figure 1: Measurement of the HU values of the papillae in kidneys

Table 1: Patients characteristics

	Controls	Nephrolithiasis
Age[1]	38.7 years (21–54)	40.1 years (23–58)
Sex (F:M)	52/56	88/124
Serum creatinine (range)[2]	0.91 mg/dL (0.8–1.1)	0.93 mg/dL (0.7–1.2)
Side calculus l:r	N/a	106:106
Location calculus		
lower:mid:upper pole	N/a	55/95/52
Stone size (range)	N/a	5 mm (3–9)
Medical history		
Hypertension	12	16
Coronary artery disease	6	9
Hypercholesterolemia	11	15
Diabetes mellitus	7	11

1: Not statistically significant; p=0.77, **2:** Not statistically significant; p=0.28, F:M: Female: Male

of patients (stone patients=controls) were affected by other associated systemic diseases (hypertension, coronary artery disease, hypercholestorelemia and diabetes). Mean stone axial diameter was 5 mm (range 3-9 mm). The density measurements were easily obtained on the CT images (average time taken 4-8 min).

Mean HU density of renal papillae of stone patients in calyces with stones was significantly greater than that of all papillae in control patients (30.25±4.03 vs.25.82±1.97, p=0.000). Mean HU density of all papillae of kidneys with stones in nephrolithiasis patients was greater than that of all papillae from control patients (27.21±2.83 vs 25.82±1.97, p<0.001). Mean HU density of all papillae in stone-free kidneys of nephrolithiasis patients was not significantly different from that of control patients (25.82±1.97 vs 25.66±2.57, p=0.642). Mean HU density of all papillae of kidneys with stones and was higher than that of stone free kidneys in nephrolithiasis patients (27.21±2.83 vs 25.66±2, p=0.000). When comparing mean HU density of both kidneys in nephrolithiasis patients with →

Table 2: The mean Hounsfield density in the affected vs unaffected kidney in urolithiasis patients, and in both kidneys vs control.

Papilla location	Hounsfield density (HU)	p value
Controls-all calyces (n=6) versus	25.82±1.97	<0.001
Stone patients-affected calyx (n=1)	30.25±4.03	
Controls-all calyces (n=6) versus	25.82±1.97	<0.001
Stone patients-all calyces from kidney with stone (n=3)	27.21 ±2.83	
Controls-all calyces (n=6) versus	25.82±1.97	0.642
Stone patients-all calyces from stone free kidney (n=3)	25.66± 2.57	
Stone patients - all calyces from kidney with stone (n=3) versus	27.21 ±2.83	<0.001
Stone patients- all calyces versus from stone-free kidney (n=3)	25.66 ± 2.57	
Controls all calyces (n=6) versus	25.82±1.97	0,049
Stone patients - all calyces from both kidneys (n=6)	26.43±2.35	

Table 3: Comparison of the HU values of the papillae of the right kidney and unaffected left kidney in the cases with right nephrolithiasis with the HU values in the control group.

Papilla location	Control	Patients	p value
Right Upper calyx	26.32±3.30	27.90±3.92	0.003
Right Mid calyx	26.00±3.45	27.65±5.49	0.058
Right Lower calyx	25.10±3.34	26.95±4.73	0.009
Left Upper calyx	25.88±3.95	25.71±3.42	0.611
Left Mid calyx	25.70±3.67	25.62±3.13	0.902
Left Lower calyx	25.93±4.00	25.52±3.84	0.483

Table 4: Comparison of the HU values of the papillae of the right kidney and unaffected left kidney in the cases with left nephrolithiasis with the HU values in the control group.

Papilla location		Control	Patients	p value
Left	Upper calyx	25.88±3.95	26.88±4.11	0.075
	Mid calyx	25.70±3.67	27.15±3.77	0.001
	Lower calyx	25.93±4.00	26.72±3.76	0.121
Right	Upper calyx	26.32±3.30	26.10±3.51	0.625
	Mid calyx	26.00±3.45	25.81±3.63	0.625
	Lower calyx	25.10±3.34	25.18±3.45	0.746

that of control, the difference was also statistically significant (25.82±1.97 vs 26.43±2.35, p=0.049). These results are summarized in Table 2. When the HU values for the papillae obtained from the upper pole, the middle region and lower pole of both the right kidney and for the unaffected left kidney in the cases with right nephrolithiasis were compared with those for the control group, the difference between two groups was significant only in upper and lower calyces for the kidneys on the right side (26.32±3.30 vs. 27.90±3.92 and 25.10±3.34 vs. 26.95±4.73, p=0.003 and p=0.009, respectively) (Table 3). A comparison of the HU values of the papillae obtained from the upper pole, middle region and the lower pole of the affected left kidney and right kidney free of calculi in the cases with left nephrolithiasis with those of the control group revealed that the difference was significant only for the left middle region between the affected kidneys and controls (25.70±3.67 vs 27.15±3.77, p=0.001) (Table 4).

DISCUSSION

Alexander Randall in the late 1930's proposed that stones grow on the renal papilla attached to underlying interstitial apatite deposits ('plaque').[8,9] The latest papillary biopsy and intraoperative visualisation data began to support this hypothesis in calcium oxalate (CaOx) stone formers. In a recent study authors demonstrated that in the common idiopathic CaOx stone former (ICSF) most stones grow attached to the papillary plaque.[10]

Furthermore, endoscopic mapping studies showed that the severity of calcium nephrolithiasis is associated with the extent of plaque coverage; an increase in plaque area results in a larger stone size and increased number of urolithiasis events.[5,11] However, the relationship among plaque density, renal parenchymal consistency and radiological findings in urolithiasis patients has not been the favourite subject of the studies.

To date, several studies have attempted to correlate the radiographic findings on CT with treatment success of stone disease, these studies concerning HU to predict success rate of stone treatment involved the stone size and location, body mass index (BMI) and skin to-stone distance.[12] Only three studies investigated radiographic difference between the renal papillae of patients with and without stones in which the authors suggested that the pronounced differences in the control and stone forming groups may enable HU density to be used as a screening tool for patients at risk for stone formation in the future.[5-7] The interesting results of these reports suggesting that HU differences in urolithiasis patients between stone free controls could predict urolithiasis events incited us not only to evaluate renal calyceal HU differences between urolithiasis patients and healthy controls in our department but to discuss the results of these previous studies as well. In the study of Eisner et al., mean HU of the renal papillae with stones of nephrolithiasis patients was significantly greater than that of papillae from the same location in controls (54.4 vs 36.6).[5] This significant difference was →

also confirmed in our study. In their pilot study, mean HU of both all papillae of kidneys with stone and all papillae of stone free kidney in urolithiasis patients were greater than that of all papilllae in controls (50.0 and 50.9 vs 36.1). Their findings suggested that the changes in renal papilla which resulted in elevated HU density measurements in nephrolithiasis patients occured in both kidneys, and not just in the calyx where the calculus had formed. In a similar study conducted by Bhuskute et al. with 90 patients and a control group, it was reported that both the affected and unaffected kidneys in the nephrolithiasis patients had a higher papillae density than those in the control group.

In a very recent report, Baran et al. obtained HU values for the papillae from the upper pole, the middle region and lower pole of both the right kidney and compared the unaffected left kidney in the cases with right nephrolithiasis with those for the control group, and reported that all the measurements revealed a significant difference.[6] They also evaluated the HU values of the papillae from the upper pole, middle region and the lower pole of the affected left kidney and right kidney free of calculi in cases with left nephrolithiasis and those of the control group and claimed that there existed a significant difference between the two groups on the basis of all the measurements. In consequence, the ability to identify precursor lesions in the kidney could provide to avoid future stone events in patients. However, our findings are in contrast with these previously reported results as we found that mean HU of all papillae in controls (25.82) was not significantly different from that of stone free kidney in urolithiasis patients (25.66); the significant difference was present between kidneys of controls (25.82) and kidneys with stones in urolithiasis patients (27.21), between kidneys with stones (27.21) and stone-free kidneys in urolithiasis patients (25.66). When the comparison for control and patient groups according to stone laterality was evaluated, the difference was significant only between right upper and lower calyces for the right nephrolithiasis and the left middle region for the left nephrolithiasis. These figures suggested that the elevated mean HU's of the kidneys with stone was due to increased density of the papillae facing the stone but not to increased HU's of all renal papillae in urolithiasis patients. Although the previous studies hypothesized the utility of this finding as a diagnostic and screening tool, our findings raised the doubt about the fact that the mean HU of all papillae in controls is lower than that of all papilla in nephrolithiasis patients from both kidneys making the previous hypothesis controversial. In accordance with these findings the recent study of Krambeck et al. assessed the ability of CT to detect interstitial calcium phosphate deposits (Randall's plaques) and duct of Bellini plugs, which are possible stone precursor lesions, the authors found out that current clinical CT scan technology appears inadequate for detecting Randall's plaques.[13]

The limitations of our study were also similar to the previous studies; it is a retrospective collection of data and imaging. The hydration status was not considered and chemical composition of stones was not known. While age-matched control patients who had been evaluated for renal donor nephrectomy were assigned as the control group in the pilot study, our control group was selected from people who denied stone disease in their individual and family history.[5] Both control and urolithiasis groups were quite healthy with minimal comorbidities.

CONCLUSION

The figures of the present study implied the impossibility of HU per se in predicting future urolithiasis events and/or patients. Larger series in prospective studies with refined methods are necessary to evaluate not only the relationship among stone formation, Randall plaques and renal paranchymal radiodensity but other co-factors as well.

* The authors declare that there are no conflicts of interest.

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