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Investigation of the computerized tomography histogram analysis in distinction of distal ureteral stone and pelvic phlebolith

Distal üreter taşı ile flebolit ayrımında bilgisayarlı tomografi histogram analizinin yerinin araştırılması

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ABSTRACT

Aim: The aim of our study is to investigate the efficacy of the region of interest (ROI) and histogram analysis method in cases where distal ureteral stone and phlebolith distinction cannot be made in abdominal computed tomography (CT) with the stone protocol.

Materials and Methods: A total of 100 adult patients (> 16 years old) with stones ≥3 seen in the distal third of the ureter on their tomography and 100 adult patients with pelvic phleboliths ≥3 were included in the study. For histogram analysis, the ROI measurement was conducted at the largest dimension with the most selectable edges using the hand-drawing tool.

Results: A total of 100 adult patients (> 16 years old) with stones ≥3 seen in the distal third of the ureter on their tomography and 100 adult patients with pelvic phleboliths ≥3 were included in the study. For histogram analysis, the ROI measurement was conducted at the largest dimension with the most selectable edges using the hand-drawing tool.

Conclusions: Histogram analysis can be used to differentiate between distal ureteral stone and pelvic phleboliths and may contribute to the diagnosis without additional examination.

Keywords: Distal ureteral stone, phleboliths, computed tomography, histogram analysis.

ÖZ

Amaç: *Çalışmamızın amacı; taş protokollü abdomen bilgisayarlı tomografi (BT)'de, distal üreter taşı ile flebolit ayrımının yapılamadığı durumlarda, ilgi alanı (İA) ile histogram analizi yönteminin bu iki durumu ayırt edebilmekteki yerinin araştırılmasıdır.*

Gereç ve Yöntem: *Tomografilerinde distal üreter taşı bulunan 100 erişkin hasta (>16 yaş) ile pelvik fleboliti bulunan 100 erişkin hasta seçildi. Üreter distal 1/3 kesimde görülen ≥3 mm taş ve ≥3 mm pelvik fleboliti olan hastalar çalışmaya dâhil edildi. Histogram analizi için İA ölçümü el çizim aracı kullanılarak, sınırları en net seçilebilen kenarlardan en geniş boyutta ölçülerek Hounsfield Unit (HU) değeri elde edildi. İlgi alanı içindeki her bir piksel için ölçülen X-ışını atenüasyon değerlerinin istatistiksel hesaplamaları yapıldı.*

Bulgular: *Histogram analizinde hesaplanan 13 farklı parametre iki grup arasında karşılaştırıldı. Standart deviyasyon (SD), minimum, maksimum, varyans ve kurtosis değerleri istatistiksel olarak anlamlı (p<0.05) bulundu.*

Sonuç: *Histogram analizi distal üreter taşı ile pelvik flebolit ayrımında kullanılabilecek ek incelemeye gerek kalmadan tanıya katkı sağlayabilecek bir metot olabilir.*

Anahtar Sözcükler: *Distal üreter taşı, flebolit, bilgisayarlı tomografi (BT), histogram analizi.*

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INTRODUCTION

Urinary system stone disease is the third most common urological disease after infection and prostate pathologies and is a common cause of acute lateral pain (1). In urinary system stone disease, non-contrast CT has high sensitivity and specificity in the diagnosis of ureter stones particularly (2, 3). However, in some conditions, it can be difficult to differentiate stones, especially in the distal ureter from pelvic phleboliths in this localization. Classic methods cannot always make this differentiation (3). As a result of two different studies investigating CT findings in the separation of pelvic phleboliths and distal ureter stones, they had contradictory results regarding the place of the radiolucent center in diagnosis. As a result of the study of Arac M et al. and Traubici J et al., a radiolucent center cannot be used to differentiate phleboliths from distal ureteral stones on unenhanced CT in patients with acute flank pain and suspected ureteral obstruction. Thin-slice CT revealed a round contour in 97% of phleboliths with 93% specificity. Central lucency is a characteristic finding of pelvic phleboliths on thin-slice CT. This finding can therefore be used in combination with roundness as a problem-solving tool in differentiating phleboliths from distal ureteral stones (4, 5).

In a study by Boridy I C et al. the tail sign has a sensitivity of 65% and a specificity of 100% in differentiating phleboliths from ureteral calculi. Although the tail finding is specific in distinguishing these two entities, it has been shown to have low sensitivity (6).

In another study by Heneghan J P et al., the rim sign was present in 105 of 136 ureteral calculi (77%) and 20 of 259 phleboliths (8%) and yielded a sensitivity of 77% and a specificity of 92% for distinguishing a ureteral calculus from a phlebolith (7).

The histogram is a series of numbers, often displayed as a bar graph, a distribution of numbers showing the specific grey value of the pixels within the structure. The distribution in an area or relationship involving grey-colored pixel levels allows objective evaluation and interpretation and can give an idea about the micro-environment of tissue. There are many studies regarding histogram analysis particularly in the diagnosis and follow-up of tumoral lesions, and other than in the field of oncology, especially of liver or lung fibrosis (8-11).

However, there are also limited studies in the literature that have used histogram analysis in the differentiation of stones and phleboliths. Lee et al achieved high diagnostic values in terms of shape and texture parameters with their artificial intelligence program with a limited number of patients. For the internal texture features, skewness and DHV (difference histogram variation) showed statistical differences between ureter stones and vascular calcifications ($p<0.05$). The performance of the ANN (Artificial Neural Network) was evaluated by examining the area under the ROC curves (AUC, Az). The Az value was 0.85 for the shape parameters and 0.88 for the texture parameters (12).

Mannil et al. analyzed the ESWL success status and the texture analysis properties of the stones in their phantom studies. This phantom study demonstrates the proof-of-principle of TA (texture analysis) for CT images of urinary calculi for identifying patients being suitable for successful ESWL. The information provided by TA has the potential of altering disease management by triaging patients suffering from the symptomatic urinary stone disease to either SWL or URS, which must be proven in future in vivo studies (13).

The aim of the current study was to investigate whether or not CT histogram analysis can contribute to the differentiation of stones and phleboliths in a large series, when a hyperdense structure is localized in the distal ureter tract. In this study, the diagnosis of ureteral stone and phleboliths is to compare CT histogram parameters retrospectively in the patient groups that were decided radiologically and clinically by consensus. From the data to be obtained, it was to reveal which parameter has the potential to work when these two distinctions cannot be made clear.

MATERIALS and METHODS

Patient population

The study was approved by the Clinical Research Local Ethics Committee, which waived the need for written informed consent.

Retrospective screening of consecutive samples of the abdominal CT images of adult patients applied with the stone protocol with an initial diagnosis of urolithiasis according to the clinical and laboratory test findings on presentation with the complaint of lateral pain at the Emergency Department and different clinics of a tertiary level hospital were made. A total of 100 adult patients (>16 years) were determined with distal ureter stone on tomography and 100 adult patients with pelvic phleboliths were selected. Patients with stones ≥3mm seen in the ureter distal third and those with pelvic phleboliths>3mm were included in the study. Patients were excluded if abdominal CT was taken with oral or IV contrast material, if tube voltage other than 120 kVP was used, if age was <16 years, or if stones or phleboliths were <3mm. Patients for whom stone and phlebolith differentiation could not be made radiologically were excluded from the study.

Image acquisition

The CT examination of the patients was applied with TOSHIBA Aquilion ONE (Toshiba Medical Systems, Nasu, Japan) and TOSHIBA Alexion (Toshiba Medical Systems, Nasu, Japan) devices. The tomography images were taken at a common voltage of 120 kVp in both devices. For both devices, window width was set at 400 and window level at 40. The examination was made with the patient positioned supine on the tomography table with the arms above the head. After adjusting the gantry angle to zero, starting by taking the anterior-posterior topogram, the acquisition plan was formed by setting the area to include the region between the kidney upper pole (approximately T12 vertebra) and the base of the bladder (symphysis pubis) and the pilot image was taken. The distance between the T12 vertebra and the symphysis pubis was scanned on the scanogram. Slices 3mm in thickness were obtained and reconstructed to 1.5 mm. In both devices, the automatic exposure control system was used.

Image analysis

The images of the patients determined with retrospective screening were evaluated on a workstation (27-inch iMac, Apple Inc, Cupertino, 88 CA, USA). The measurements of stone size, phlebolith size, and histogram analysis were all performed on the workstation by the same radiologist (we used Osirix MD as software in this workstation). When necessary, sagittal and coronal reformatted images were formed with the program and examined. The diagnosis of ureter stone was made from direct visualization of the stone within the ureter and with supporting secondary findings such as hydronephrosis, hydroureter, tissue rim signs around the ureter, or increased linear-circular density in the peripheral fatty tissue.

Phlebolith diagnosis was made from the presence of adjacent vascular structures and a comet- tail sign. The comet tail sign is helps distinguish a ureteric calculus from a phlebolith and strongly favors the latter. The size measurements of the stones and phleboliths were made on the largest axis (axial, sagittal, or coronal) compared to the longest axis. Placement of the region of interest (ROI) for the histogram analysis was made by magnifying the image as much as possible, then manually drawing from the borders which could be most clearly selected at the largest size. The HU value of each pixel within the ROI was transferred to an XML file (eXtensible Markum Language) (Figure-1). The histogram analysis was calculated on the XML files using MATLAB vn 2009b software (MATrix LABoratory, Mathworks Inc, Natick, USA).

In the histogram analysis, the following parameters were examined: mean, standard deviation (SD), minimum, maximum, median, variance, entropy, uniformity, size L% (mean low values from the area remaining below SD), size M% (mean area remaining below SD), size U%, skewness and kurtosis. The level of diagnostic effect of these parameters in the differentiation of stones and phleboliths was determined by calculating the threshold values with ROC analysis.

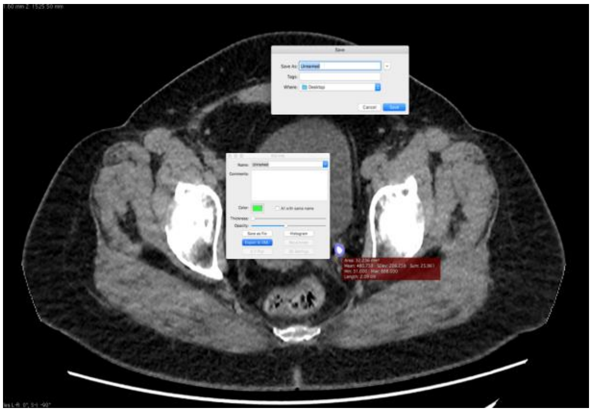

Figure-1. Insertion of ROI for histogram analysis on the workstation and then export to the XML file.

Statistical analysis

Data obtained in the study were analyzed statistically using SPSS vn. 22.0 software (Statistical Packages for the Social Sciences, SPSS version 22.0). Conformity of the data to normal distribution was assessed with the Kolmogorov-Smirnov test and variance homogeneity was tested with the Homogeneity of

Variance test- the Levene statistic. Normal distribution was seen with a value of $p>0.05$ in the normality test tables. In the comparisons between the groups, the Independent t-test was used as data were normally distributed. Categorical variables were stated as number (n) and percentage (%) and numerical variables as mean±standard deviation (SD). A value of $p<0.05$ was accepted as statistically significant. For the SD, minimum, maximum, variance, and kurtosis values in the histogram analysis, cutoff threshold values were estimated with the ROC curve (receiver operating characteristics) and the sensitivity and specificity values were determined. All the values were stated as mean±SD.

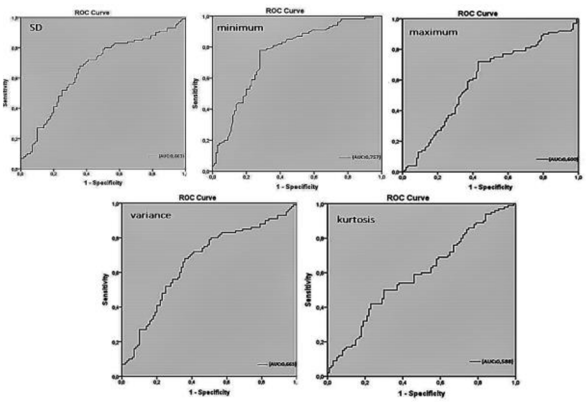

Figure-2. ROC curves of SD, minimum, maximum, variance, and kurtosis values.

RESULTS

The 200 patients included in the study comprised 72 (72%) males and 28 (28) females in the stone group and 58 (58%) males and 42 (42%) females in the phlebolith group. All patients were in the age range of 16-92 years. In the stone group, the mean age was 40.88 ± 17.83 years and in the phlebolith group, 49.58 ± 16.58 years. No statistically significant difference was determined between the groups in respect of age or gender ($p<0.01$).

The 13 parameters examined in the histogram analysis are shown in (Table-1).

The parameters of SD, minimum, maximum, variance, and kurtosis values were determined to be statistically significant between the stone and phlebolith groups (Figure-2).

Table-1. Parameters calculated with histogram analysis.

Mean
Minimum
Maximum
Median
Standard deviation (SD)
Entropy (irregularity)
Uniformity
Variance
Size L% (% of pixels below -1 of SD)
Size M% (% of pixels between -1 and +1 SD)
Size U% (% of pixels above +1 of SD)
Skewness
Kurtosis

The standard deviation mean values were determined to be statistically significantly higher in the stone group (238.64 ± 64) than in the phlebolith group (298.74 ± 110.53) ($p<0.001$). The minimum values in the histogram analysis were statistically significantly lower in the phlebolith group (-35.87 ± 88.14) than in the stone group (41.69 ± 71.35) ($p<0.001$). The mean maximum values were determined to be statistically significantly higher in the phlebolith group (950.33 ± 318.27) than in the stone group (851.72 ± 338.84) ($p<0.035$).

The variance mean values in the histogram analysis were statistically significantly higher in the phlebolith group (101343.60 ± 69182) than in the stone group (66372.59 ± 53613.35) ($p<0.001$). The mean kurtosis results were determined to be statistically significantly higher in the stone group (1.99 ± 0.4) than in the phlebolith group (1.88 ± 0.2) ($p<0.025$).

The area under the curve (AUC) of the SD value accepted as statistically significant ($p<0.05$) in the histogram analysis evaluation was 0.663 in the ROC analysis. When the cutoff value of 241.86 was selected for SD, sensitivity was calculated as 70% and specificity as 61% in stone-phlebolith differentiation. The AUC of the minimum value was 0.757 in the ROC analysis. When the cutoff value was selected as 1, the sensitivity was calculated as 76% and specificity as 72% in the differentiation of stone-phlebolith. The AUC of the maximum value was 0.600. When the cutoff value was selected as 800.50, the sensitivity was calculated as 72% and specificity as 57% in the differentiation of stone-phlebolith.

The AUC of the variance value was 0.663. When the cutoff value was selected as 58499.35, the sensitivity was calculated as 70% and specificity as 61% in the differentiation of stone-phlebolith. The AUC of the kurtosis value was 0.588. When the cutoff value was selected as 1.894, the sensitivity was calculated as 59% and specificity as 54% in the differentiation of stone-phlebolith.

DISCUSSION

Although non-contrast CT has extremely high sensitivity and specificity in the determination of ureter stones, it may be difficult to differentiate distal ureter stones in particular from pelvic phleboliths in this localization. The aim of this study was to evaluate the potential of histogram analysis to be able to make this differentiation in similar conditions. Of the 13 parameters examined, a statistically significant difference was determined between the two groups in respect of the SD, minimum, maximum, variance, and kurtosis values (Figure-2). In the ROC analysis, the minimum value was determined to have the highest level of diagnostic efficacy in the differentiation of stones and phleboliths.

In a 2007 study by Kılınc et al, CT was found to have a sensitivity of 96.4% and specificity of 100% in the diagnosis of ureter stones (2). In 1995, Smith et al. reported that non-contrast CT had a sensitivity of 97% and specificity of 96% in showing ureter stones. However, in the differentiation of urinary system stones from phleboliths, classic findings such as the tissue rim sign, linear-circular density in the perinephric fatty tissue, the comet-tail sign, and central lucency were shown not to make any contribution to the differentiation (3).

Histogram analysis is the examination with statistically-based programs of data expressing the appearance, structure, and organization of the parts of an object on an image. The histogram of a structure is the number of pixels in the structure showing a certain grey value. The distribution in an area or relationship involving grey-colored pixel levels allows objective evaluation and interpretation and can give an idea about the micro-environment of tissue. Parameters such as mean, variance, and standard deviation (SD) can be produced from the histogram formed from these obtained numbers (14). There are studies in current literature related to the place of histogram analysis in the diagnosis and follow-up of treatment of tumoral lesions in particular.

SD measures the extent of the data set. In other words, it states whether or not the data components are gathered close to the mean, or scattered everywhere. A large SD indicates that values are spread over a larger area. As one of the histogram analysis parameters, the SD shows the extent of the structured content measured with the IA value. In the current study, a statistically significant difference was determined between the SD values of the two groups in the examinations made for stones and phleboliths ($p<0.05$) (Figure-2).

Another parameter of the histogram analysis that emerged as statistically significant in this study was the minimum value. This expresses the smallest numerical value in the histogram distribution. The minimum value in the histogram analysis in this study was found to be statistically significant for stone-phlebolith differentiation ($p>0.05$). When these values are examined, it can be seen that the stone SD remains in a narrower range and phlebolith SD is in a wider range. This indicates that the internal structure of phleboliths is more heterogenous, which is explained by higher mean values. The stone structure can be said to be more homogenous than that of phleboliths.

Statistically, variance is the arithmetic mean of the square of the deviations from the means of all the data values in the data set. The variance used in the current study as one of the parameters of histogram analysis shows the distribution of the values in the stones and phleboliths measured with ROI. It was a significant parameter for the differences in the microstructures of the distal ureter stones and pelvic phleboliths ($p<0.05$). When these mean values were examined, the smaller values obtained for stones showed that the microstructures of the stones were more homogenous and the extent of distribution was narrower.

The maximum values in the current study were also a significant histogram analysis parameter ($p<0.035$). The maximum parameter expresses the highest value in the histogram distribution. In other words, it is the highest numerical value in the histogram analysis. It shows the peak point of the distribution. The maximum values in the phlebolith cases were statistically significantly higher than those of the stone cases ($p<0.035$).

The meaning of the word kurtosis can be expressed as lowness. Kurtosis is a concept related to the lowness or sharpness of the graphic distribution of the variable values observed in the data. The kurtosis value of variables with normal distribution is statistically zero. If the kurtosis value of a variable is positive, the distribution has a sharp appearance, and if it is negative, the distribution is flat/low in appearance. The X-ray attenuation values and HU values of the stones and phleboliths obtained in this study with ROI were examined and the kurtosis parameter was found to be statistically significant in the histogram analysis ($p<0.05$).

There were some limitations to this study, primarily that the numbers of patients in the stone and phlebolith groups were low. Second, the age ranges in the groups were different, which can be explained by the development of phleboliths being a process that increases with age. Thirdly, as this was a retrospective study, the diagnosis of the ureter stones could not be confirmed clinically in most. In some cases where the stone was removed in an out-of-hospital setting or was spontaneously expelled, this information was not in the hospital records system. Another limitation was that the measurements were taken manually. Marking with an automatic or semi-automatic segmentation method allows the process to be repeatable. As the measurements were taken by a single radiologist, inter-observer and intra-observer agreement were not evaluated. In the data collection process of our study, a sufficient number of cases with both stone and phleboliths could not be reached, so they were not included in the study. This creates a limitation for our study. Studies comparing visual CT findings and histogram analysis results can be performed.

CONCLUSION

When clinical and radiological differentiation is not possible in patients with distal ureter stone and pelvic phlebolith localized in this tract, it seems to be possible to make this differentiation with histogram analysis, with computer software on a workstation without the need for additional imaging or radiation. The use of SD, minimum, maximum, variance, and kurtosis parameters for this purpose facilitates diagnosis. Therefore, the standard addition of automatic histogram analysis software on workstations seems to be necessary for routine radiology practice.

Conflict of interest: The authors declare that they have no conflict of interest

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