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Do Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio Predict the Hardness of Kidney Stone

Onur Karslı[1], Murat Üstüner[2], Ahmed Ömer Halad[2], Levent Özcan[3], Fatih Gökalp[4], Ömer Koraş[4], Bekir Voyvoda[5], Ömür Memik[6]

[1] Asst.Prof., University of Health Sciences, Kocaeli Derince Training and Research Hospital, Kocaeli, Turkey
[2] M.D. Spec., University of Health Sciences,Kocaeli Derince Training and Research Hospital, Kocaeli, Turkey
[3] Assoc. Prof., University of Health Sciences, Kocaeli Derince Training and Research Hospital, Kocaeli
[4] Asst. Prof., Hatay Mustafa Kemal University, Department of Urology, Hatay, Turkey
[5] Asst. Prof., University of Health Sciences, Kocaeli Derince Training and Research Hospital, Kocaeli
[6] M.D. Spec., University of Health Sciences, Kocaeli Derince Training and Research Hospital, Kocaeli

Öz

Trombosit-Lenfosit Oranı ve Nötrofil-Lenfosit Oranı Böbrek Taşının Sertliğini Öngörür mü?

Amaç: Hounsfield ünitesi (HU), taş oluşumunu değerlendirmek için en yaygın değer ve aynı zamanda yönetim başarısı için öngörücü bir faktördür. Bu çalışmada, sistemik inflamatuar yanıt belirteçleri kullanarak taşın sertliğini tahmin etmeyi amaçladık.
Gereç ve Yöntem: 2015 ve 2020 yılları arasında konvansiyonel perkütan nefrolitotomi uygulanan 192 hastaya (61 kadın ve 131 erkek) ait veri retrospektif olarak gözden geçirildi. Malignite, preoperatif idrar kültürü pozitif olan hastalar çalışma dışı bırakıldı. Hastaların nötrofil lenfosit oranı (NLR), trombosit lenfosit oranı (PLR) ve NCCT'den elde edilen böbrek taşı Hounsfield Ünitesi (HU) verilere kaydedildi.
Bulgular: Ortalama yaş 47,2 ± 14,11 (11-82) yıldı. Hastaların taşlarının ortalama HU değeri 1135,47 ± 362,19 (348-2096) olarak bulundu. Taşların yeri pelvis (n: 64, %33,3), tek kaliks (n: 14, %7,2), iki kaliks (n: 93, %48,4) ve staghorn (n: 21, %10,9) olarak gruplandı. Alt grup analizinde taş lokalizasyonuna göre, pelvis ve staghorn taşlar için HU ve NLR arasında pozitif bir korelasyon bulundu. Bu korelasyonlar arasında sadece pelvis taş grubunda HU ve NLR arasındaki pozitif korelasyon istatistiksel olarak anlamlıydı (r=0.318, p=0.03). HU için 1000'in altında bir kesme değeri varsayıldığında ise, NLR ve HU arasında anlamlı bir korelasyon yoktu (r=0.266, p=0.171). Bununla birlikte, HU 1000'in üzerinde, NLR ve HU arasında anlamlı bir pozitif korelasyon vardır (r=0.145, p=0.045).
Sonuç: Bu çalışma, NLR'nin uygun tedaviyi seçmek için bir biyobelirteç olarak kullanabileceğini ve HU değerini tahmin ederek böbrek taşının sertliğini tahmin etmeye yardımcı olabileceğini gösterdi.
Anahtar Kelimeler: Böbrek Taşı, Hounsfield Ünitesi, Ürolitiyazis, Nötrofil

Abstract

Do Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio Predict the Hardness of Kidney Stone

Objective: The Hounsfield unit (HU) is the most common value to assess the stone formation and a predictive factor for the management success. In this study, it was aimed to investigate the prediction of the hardness of the stone using systemic inflammatory response markers.
Methods: 192 patients (61 female and 131 male) patients who underwent conventional percutaneous nephrolithotomy (PCNL) between 2015 and 2020 were reviewed retrospectively. Patients with malignancy and history of preoperative urinary tract infection were excluded from this study. Patients' neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) and HU of the kidney Stone, which was obtained from NCCT, were recorded to data.
Results: The mean age was 47.2 ± 14.11 (11-82) years. The average HU value of the patients' stones was 1135.47 ± 362.19 (348-2096). The location of the stones was grouped as pelvis (n:64, 33.3%), single calyx (n:14, 7.2%), two calyces (n:93, 48.4%) and staghorn (n:21, 10.9%). In subgroup analysis, when divided by stone location, a negative correlation was found between the HU and N/L ratio in the single calyceal stone group, and a positive correlation was found between the HU and N/L ratio for pelvis and staghorn stones. Among these correlations, only the positive correlation between the HU and N/L ratio in the pelvic stone group was statistically significant (r=0.318, p=0.03). Assuming an arbitrary cut-off value for HU below 1000, there was no significant correlation between NLR and HU (r=0.266, p=0.171). However, HU above 1000, there was a significant positive correlation between NLR and HU (r=0.145, p=0.045).
Conclusion: The findings suggest that NLR could be used as a biomarker to choose appropriate management and be helpful to anticipate the hardness of kidney stones by predicting the HU value.
Keywords: Kidney Calculi, Hounsfield Unit, Urolithiasis, Neutrophil

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Sorumlu Yazar/Corresponding Author: M.D. Fatih Gökalp
Email: fatihgokalp85@gmail.com
ORCID iD: 0000-0003-3099-3317

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INTRODUCTION

Kidney stones are among the most common urological diseases, with an incidence of 5% to 10% (1). The ideal treatment of renal stone must achieve stone-free status with lower morbidities (2). The success of treatments depends on operation type, operation time, the number of sessions, stone size and stone composition (3). The stones which are containing calcium are the hardest to fragment, and the Hounsfield unit (HU) value of stones obtained from non-contrast computed tomography (NCCT) can predict stone hardness and composition (4,5). The average HU was useful for predicting stone composition, but peak HU was not found convincing. Although some molecular markers have been investigated in urine and serum, an ideal feature to aid treatment selection has not been found (6).

As in many diseases, it is thought that there is a relationship between stone formation and the inflammatory process. An early study showed that Calcium oxalate induced IL1 secretion and activated NLRP3 (7). There is a change in the proportion of blood cells formed due to the systemic inflammatory response in some diseases and cancers. In the presence of systemic inflammatory response, blood cell markers whose distribution varies are neutrophil to lymphocyte ratio (NLR), derived neutrophil to lymphocyte ratio (dNL), platelet to lymphocyte ratio (PLR), and lymphocyte to monocyte ratio (LM) (8,9). Although these markers are used in the diagnosis and follow-up of many diseases and to predict their prognosis, to our knowledge, there is no study on these biomarkers' behavior in kidney stone patients (9).

In this study, we aimed to estimate the stone's hardness by comparing systemic inflammatory response markers with HU.

MATERIALS AND METHODS

In this retrospective study, the data of patients who underwent conventional percutaneous nephrolithotomy (PCNL) between 2015 and 2020 were reviewed retrospectively. In this study, 192 patients (61 female and 131 male) were included.

The inclusion criteria were determined as conventional PCNL made, no malignancy or chronic inflammatory disease history, no perioperative mortality, no preoperative and postoperative fever, no preoperative infection treatment, negative preoperative urine culture, no hydronephrosis, available preoperative blood parameters, available preoperative non-contrast computed tomography (NCCT).

Patients' neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and Hounsfield Unit (HU) of the kidney stone, which was obtained from NCCT, were recorded to data. The correlation between the HU and blood parameters was evaluated in all patients. Besides, the patients were divided into the single calyx, two calyces, pelvis, and staghorn groups according to the stone's location, and the correlation between the HU and blood parameters was examined in these groups. The arbitrary cut-off of HU was 1000, which was described in the literature (5). Data were split into two groups, group 1: HU of renal stone <1000 and group 2: HU of renal stone >1000.

The study protocol was implemented in accordance with the Declaration of Helsinki. Local ethics committee approved this study (2020-20). Written informed consent was obtained from all patients that patient data will be used for scientific purposes.

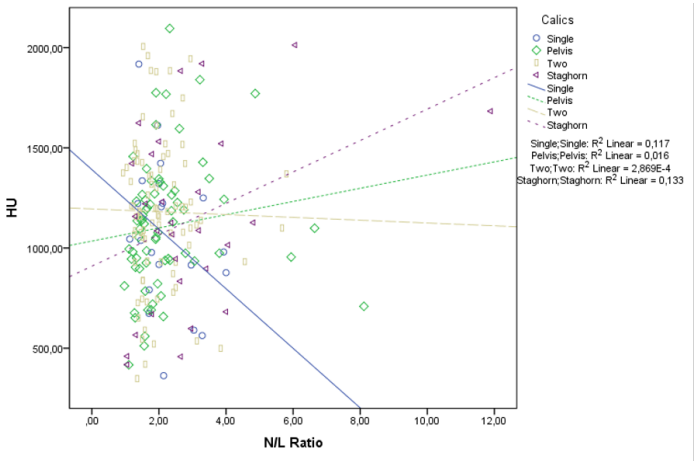

Figure 1. Positive correlation between HU and NLR for pelvis and staghorn stones

Statistical Analysis

Statistical Package 23.0 (Social SPSS Statistics; New York, USA) was used for statistical analysis. The distribution was examined by the Shapiro Wilk test and Q-Q plots. For continuous variables were expressed as mean and standard deviation. Data for categorical variables were expressed as percentage and frequency. The mean values were compared using an analysis of variance (ANOVA). In the case of categorical data, the comparison was made using the chi-squared test. Spearman test was used for correlation. Statistical significance level was accepted as $p < 0.05$.

RESULTS

The mean age of 192 patients participating in this study was 47.2 ± 14.11 years. The male patient number was 131 (68.2%), and the female patient number was 61 (31.8%). The locations of the stones were grouped as pelvis (n:64, 33.3%), single calyx (n:14, 7.2%), two calyces (n:93, 48.4%) and staghorn (n:21, 10.9%). The stone size was larger in two calyces and staghorn than the other ($p<0.001$). The average HU of the stones was similar in all calyx groups ($p=0.463$). The mean NLR of the patients was 2.25 ± 1.29 (0.93-11.89), and

Table 1. Comparison parameters of different calix stones

	Stone location				p-value
	Renal pelvis	Single calyx	Two calyces	Staghorn	
Operation time (min.)	51.99±18.54	61.90±24.26	70.06±30.12	117.24±36.78	**<0.001**
Fluoroscopy time (min.)	3.35±2.09	3.38±2.58	3.77±2.27	4.57±2.67	0.105
Stone size	401.62±389.74	322.74±181.92	639.56±352.54	1443.52±772.73	**<0.001**
HU	1107.10±327.45	1059.19±366.79	1180.70±365.55	1137.83±450.96	0.463
Neutrophil	5137.68±1861.14	4842.86±1709.26	4553.57±1505.85	5727.59±2260.04	**0.012**
Lymphocyte	2555.07±778.11	2304.76±790.24	2354.76±670.44	2227.59±682.90	0.145
Platelet	265275±70691	260381±67518	256405±100649	261414±69987	0.936
NLR	2.20±1.26	2.23±0.85	2.06±0.88	2.91±2.10	**0.015**
NLR	115.55±66.48	123.41±48.58	115.54±48.70	127.31±51.92	0.738

*All data were expressed as mean±SD.
HU: Hounsfield unit, NLR: Neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio

the mean PLR was 117.73 ± 56.33 (Table 1). The neutrophil and NLR was significantly higher in staghorn stones when compared to the other calyces (p=0.012, and p=0.015, respectively)

Table 2. Correlation between HU, N/L and P/L ratio in different calyx

Stone Location HU		r	p-value
Renal pelvis			
	NLR	0.318*	**0.08***
	PLR	-0.02	0.86
Single calyx			
	NLR	-0,363	0.10
	PLR	-0,455*	**0.03***
Two calyces			
	NLR	-0,012	0.91
	PLR	-0,186	0.09
Staghorn			
	NLR	0,266	0.16
	PLR	0,292	0.12

* Correlation is significant at the 0.05 level.
NLR: Neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio.

Spearman correlation test was used to investigate the relationship between HU and NLR, but there was no exact correlation between the two parameters. However, when the correlation was investigated in subgroups divided by stone location, a negative correlation was found between HU and NLR in the single calyceal stone group. A positive correlation was found between HU and NLR for pelvis and staghorn stones (r=0.318, p=0.008, and r=0.266, p=0.163, respectively) (Figure 1). There was a statistically significant correlation between NLR and pelvis stone. When the ratio of HU and PLR was examined, there was also a negative correlation in one calyx and was statistically significant (r =-0.455, p=0.038) (Table 2). Assuming an arbitrary cut-off value for HU below 1000, there was no significant correlation between NLR and HU (p=0.171). However, for HU above 1000, there was a significant positive correlation between NLR and HU (r=0.145, p=0.045) (Table 3).

DISCUSSION

Nephrolithiasis is a common disease that recurrence rates are up to 50% within the first five years (8). Stone clearance is the key factor for preventing recurrence. It is essential to determine the stone composition and the hardness of the stone before the management chooses an effective treatment method. This study demonstrated that inflammation parameters could be useful to predict the HU unit of the kidney stone. To our knowledge, this is the second study investigating the role of inflammation parameters to determine the HU unit in patients with a kidney stone.

Predicting stone parameters, including size, density and composition, is crucial to prevent inappropriate or excessive treatments and investigate the most effective treatment. This study showed that the elevation of the NLR ratio increases

the value of HU in staghorn and pelvis stones. In this case, a surgical treatment option instead of ESWL due to failure, will reduce cost. A novel study has investigated the association between NLR with infectious complications, such as sepsis and systemic inflammatory response syndrome (SIRS), after surgery (9). Additional, NLR and PLR are predictive factors to determine stone impaction and spontaneous stone passage for ureteral stone disease (10). All these results are thought to be related to hydronephrosis. Similar to these results, we think that our positive correlation is also related to the hydronephrosis that pelvis and staghorn stones commonly cause. Besides, the larger stones contain more bacteria. Staghorn stones are mostly struvite stones, i.e., infection stones. It has been found that more infection complications develop after PCNL after the infection stone (11). In the study conducted by Sen et al., infection complications developed more in patients with a stone composition of struvite and they found that the NLR cut-off value of 2.5 to be a statistically significant predictor for sepsis (12). Similar to the literature, in this study, it was found that NLR was higher in patients with staghorn stones than in patients with other calyceal stones. Published literature recommended that NLR be used as a marker of infection and predict disease severity in patients with sepsis (13). Additionally, pro-inflammatory cytokines, including IL1, IL 2, IL 6, IL 7, IL 8, IL 12, increased by NLR (14,15). Increased NLR seems to be a good indicator of immunity, and also, NLR is thought to represent the underlying inflammatory process accurately (16). We suggest that it is significant to suggest less invasive surgery in patients with high NLR due to reducing postoperative complications.

Table 3. Correlation between blood parameters and HU in different HU groups.

	HU <1000 p-value	HU >1000 p-value
Neutrophil	0.144	0.554
Lymphocyte	0.843	**0.045***
Platelet	0.343	0.097
NLR	0.171	**0.048***
PLR	0.871	0.872

* Correlation is significant at the 0.05 level.
HU: Hounsfield unit, NLR: Neutrophil lymphocyte ratio, PLR: platelet lymphocyte ratio

Some metabolic and radiographic tests are used to estimate chemical structure before the kidney stones' treatment selection. Thus, molecular concentration measurements, such as urinary sodium, calcium, oxalate and uric acid, may provide a suggestion for stone composition (6). With the help of non-contrast CT, the hardness of the stone can be calculated by measuring the HU value (17). Many researchers think that because of the widespread and effective use of CT, CT can be used to describe the contents of stones (18–21). In general, CT has been reported to consistently distinguish stones composed of uric acid (UA) from stones composed primarily of calcium. However, it is controversial whether CT imaging can distinguish stones composed of different calcium salts, such as calcium phosphate (CaP) stones from calcium oxalate (CaOx) stones. Matlaga et al. showed that better stone type determination could be made using dual-energy CT (DECT). In this study, Uric acid, calcium phosphate, and calcium oxalate stones used in DECT were distinguished (22). In another study supporting these findings, it has been shown that DECT is superior to conventional CT in determining stone composition, especially in distinguishing from non-uric acid uric acid stones (23). In this study, we used CT to measure the HU value and investigate the hardness of the stone. When an arbitrary cut-off of >1000, NLR is a positive correlation with HU. The hardness of the stone suggests to us the type of stone and treatment modality. In another study by Valente et al., it has been shown that stones with low HU value in patients with metabolic syndrome are more likely to be uric acid stones (24). Also, PLR is high in patients with metabolic syndrome (9). In this study, the increase of PLR in a single calyx correlates negatively with the HU value and indicates that the stone is not too hard. If the HU value of the stone is low in single calyx stones and the PLR is high, it may be considered as a possible uric acid stone, and oral chemolysis is treatment may be tried in such patients. Tang et al. showed that the high PLR was also associated with the development of post-PCNL SIRS (9). Oral chemolysis administration protects the patients from the high risk of post-PCNL SIRS and operation-related complications.

There are some limitations to this study. This study was performed retrospectively. A prospective study would have been more reasonable. Another important limitation is the absence of the stone analysis, metabolic analysis of patients and follow-up. The other limitation is the small number of patients.

CONCLUSIONS

The findings obtained in this study suggested that NLR could help anticipate the hardness of the kidney stone by assisting the HU to value. Therefore, NLR could be used as an objective biomarker to manage the disease and choose the appropriate treatment. Further large-scale studies are needed.

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Conflict of Interest

The authors declare that they have no conflict of interests regarding content of this article.

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Ethical Declaration

Ethical approval was obtained from University of Health Sciences, Kocaeli Derince Training and Research Hospital Clinical Research Ethical Committee with date 02.27.2020 and number 2020-20, and Helsinki Declaration rules were followed to conduct this study.

REFERENCES

1. Ziemba JB, Matlaga BR. Epidemiology and economics of nephrolithiasis. Investig Clin Urol. 2017 Sep;58(5):299-306. https://doi.org/10.4111/icu.2017.58.5.299
2. Zisman AL. Effectiveness of Treatment Modalities on Kidney Stone Recurrence. Clin J Am Soc Nephrol. 2017 Oct;12(10):1699-708. https://doi.org/10.2215/CJN.11201016
3. Mahalingam H, Lal A, Mandal AK, Singh SK, Bhattacharyya S, Khandelwal N. Evaluation of low-dose dual energy computed tomography for in vivo assessment of renal/ureteric calculus composition. Korean J Urol [Internet]. 2015/08/10. 2015 Aug;56(8):587-93. Available from: https://pubmed.ncbi.nlm.nih.gov/26279828 https://doi.org/10.4111/kju.2015.56.8.587
4. Joseph P, Mandal AK, Singh SK, Mandal P, Sankhwar SN, Sharma SK. Computerized tomography attenuation value of renal calculus: can it predict successful fragmentation of the calculus by extracorporeal shock wave lithotripsy? A preliminary study. J Urol. 2002 May;167(5):1968-71. https://doi.org/10.1016/S0022-5347(05)65064-1
5. Anastasiadis A, Onal B, Modi P, Turna B, Duvdevani M, Timoney A, et al. Impact of stone density on outcomes in percutaneous nephrolithotomy (PCNL): an analysis of the clinical research office of the endourological society (CROES) pcnl global study database. Scand J Urol. 2013 Dec;47(6):509-14. https://doi.org/10.3109/21681805.2013.803261
6. Torricelli FCM, De S, Liu X, Calle J, Gebreselassie S, Monga M. Can 24-Hour Urine Stone Risk Profiles Predict Urinary Stone Composition? J Endourol [Internet]. 2014 Jan 27;28(6):735-8. https://doi.org/10.1089/end.2013.0769
7. Mulay SR, Kulkarni OP, Rupanagudi K V, Migliorini A, Darisipudi MN, Vilaysane A, et al. Calcium oxalate crystals induce renal inflammation by NLRP3-mediated IL-1 secretion. J Clin Invest [Internet]. 2012/12/10. 2013 Jan;123(1):236-46. Available from: https://pubmed.ncbi.nlm.nih.gov/23221343 https://doi.org/10.1172/JCI63679
8. Proctor MJ, McMillan DC, Morrison DS, Fletcher CD, Horgan PG, Clarke SJ. A derived neutrophil to lymphocyte ratio predicts survival in patients with cancer. Br J Cancer. 2012 Aug;107(4):695-9. https://doi.org/10.1038/bjc.2012.292
9. Tang K, Liu H, Jiang K, Ye T, Yan L, Liu P, et al. Predictive value of preoperative inflammatory response biomarkers for metabolic syndrome and post-PCNL systemic inflammatory response syndrome in patients with nephrolithiasis. Oncotarget [Internet]. 2017 Aug 18;8(49):85612-27. Available from: https://pubmed.ncbi.nlm.nih.gov/29156745 https://doi.org/10.18632/oncotarget.20344
10. Abou Heidar N, Labban M, Bustros G, Nasr R. Inflammatory serum markers predicting spontaneous ureteral stone passage. Clin Exp Nephrol. 2020 Mar;24(3):277-83. https://doi.org/10.1007/s10157-019-01807-5
11. Koras O, Bozkurt IH, Yonguc T, Degirmenci T, Arslan B, Gunlusoy B, et al. Risk factors for postoperative infectious complications following percutaneous nephrolithotomy: a prospective clinical study. Urolithiasis. 2015 Feb;43(1):55-60. https://doi.org/10.1007/s00240-014-0730-8
12. Sen V, Bozkurt IH, Aydogdu O, Yonguc T, Yarimoglu S, Sen P, et al. Significance of preoperative neutrophil-lymphocyte count ratio on predicting postoperative sepsis after percutaneous nephrolithotomy. Kaohsiung J Med Sci. 2016 Oct;32(10):507-13. https://doi.org/10.1016/j.kjms.2016.08.008
13. Zahorec R. Ratio of neutrophil to lymphocyte counts--rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy. 2001;102(1):5-14.
14. Motomura T, Shirabe K, Mano Y, Muto J, Toshima T, Umemoto Y, et al. Neutrophil-lymphocyte ratio reflects hepatocellular carcinoma recurrence after liver transplantation via inflammatory microenvironment. J Hepatol. 2013 Jan;58(1):58-64. https://doi.org/10.1016/j.jhep.2012.08.017
15. Goodman DA, Goodman CB, Monk JS. Use of the neutrophil:lymphocyte ratio in the diagnosis of appendicitis. Am Surg. 1995 Mar;61(3):257-9.
16. Tamhane UU, Aneja S, Montgomery D, Rogers E-K, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol. 2008 Sep;102(6):653-7. https://doi.org/10.1016/j.amjcard.2008.05.006
17. Patel SR, Haleblian G, Zabbo A, Pareek G. Hounsfield units on computed tomography predict calcium stone subtype composition. Urol Int. 2009;83(2):175-80. https://doi.org/10.1159/000230020
18. Newhouse JH, Prien EL, Amis ESJ, Dretler SP, Pfister RC. Computed tomographic analysis of urinary calculi. AJR Am J Roentgenol. 1984 Mar;142(3):545-8. https://doi.org/10.2214/ajr.142.3.545
19. Mostafavi MR, Ernst RD, Saltzman B. Accurate determination of chemical composition of urinary calculi by spiral computerized tomography. J Urol. 1998 Mar;159(3):673-5. https://doi.org/10.1016/S0022-5347(01)63698-X

20. Saw KC, McAteer JA, Monga AG, Chua GT, Lingeman JE, Williams JCJ. Helical CT of urinary calculi: effect of stone composition, stone size, and scan collimation. AJR Am J Roentgenol. 2000 Aug;175(2):329-32. https://doi.org/10.2214/ajr.175.2.1750329

21. Matlaga BR, Kawamoto S, Fishman E. Dual source computed tomography: a novel technique to determine stone composition. Urology. 2008 Nov;72(5):1164-8. https://doi.org/10.1016/j.urology.2008.03.051

22. Wisenbaugh ES, Paden RG, Silva AC, Humphreys MR. Dual-energy vs conventional computed tomography in determining stone composition. Urology. 2014 Jun;83(6):1243-7. https://doi.org/10.1016/j.urology.2013.12.023

23. Valente P, Castro H, Pereira I, Vila F, Araújo PB, Vivas C, et al. Metabolic syndrome and the composition of urinary calculi: is there any relation? Cent Eur J Urol [Internet]. 2019/09/16. 2019;72(3):276-9. Available from: https://pubmed.ncbi.nlm.nih.gov/31720030