OPEN PEER REVIEW

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https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Iranian Journal of Radiology
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Peer Review Report for "Correlation Between CT-Based Bone Mineral Density and Kidney Stone Size and Their Association with 24-Hour Urinalysis Biometrics in Patients with Urinary Stones"

Author(s): Mohammad Ali Ganji Jameshouran, Amir Reza Abedi, Saeed Montazeri, Mohammad Ali Tasharrofi, Morteza Fallah Karkan, Mohammad Mersad Mansouri Tehrani

Review Timeline:

Submit Date: 27 Jul 2020
Revised Date: 12 Jun 2021
Accepted Date: 13 Jun 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 27 Aug 2020

Dear AE,
Although there are few similar articles about the relationship between BMD and hypercalciuria and renal stone, the correlation between these parameters and the size of the renal stone is new and interesting.
all keywords are according to the MESH database.
Thanks.

Madjid Shakiba: Reviewer | **Revision** (0) 28 Sep 2020

Dear AE,
Comments for the authors:
1- the conclusion of abstract is wrong. The authors mentioned: “Low BMD diagnosed through CT-scans is associated with abnormal 24-hours urine analysis biometrics and larger stones, and should be properly assessed.” They have implemented the study on patients with urinary stone while they are generalizing the study findings to all population and this

could be wrong. The data are not come from general population. Please correct.
2- what is the meaning of risk-assessment tool? [objective part?] risk of what?
3- as the patients are all candidate for PCNL, the data could be different in a considerable subgroup of stone patients that are not candidate for PCNL [for example in patients with small size stones that constitute majority of stone patients and are not candidate for PCNL]. If the authors add the data of all stone patients, the results could be different. Please explain in this regard and discuss.
4- the stones are different in their constituent regarding different pathophysiologic processes and mechanisms of formation [for example hypercalciuria]. Most of calcium stones are formed from calcium oxalate; however, some of them contains mainly calcium phosphate or are mix of phosphate and oxalate. This could remind in different pathologic baseline metabolic conditions. The authors mentioned they enrolled only the patients “having the predominant calcium component in the urinary calculi analysis,” Regarding the mentioned point, this sentence is vague and unclear. If the stones are composed from oxalate or phosphate or both? This could make a heterogeneity in the enrolled patients. Please explain.
5- some treatments could affect the urinary calcium such as VIT-D3 supplementation, PTH and the other agents affect the calcium and phosphorus metabolism. Did the authors consider these factors in exclusion criteria?
6- what was the time interval between [CT scan and PCNL] and between [PCNL and urine analysis]?
7- if the patient has more than one stones and the smaller is candidate for PCNL [for example, the larger is located in renal pelvis or in bladder], then what would be considered as the stone size? The size of stone candidate for PCNL or the largest stone?
8- how many radiologists did measure the imaging assessments? [size determination and drawing the ROI for BMD assessment]. did the authors determine the interrater and intrarater reliability between radiologists in these measurements?
9- is the cutoff point of 160 validate for Iranian population in differentiating low BMD? In addition, does this cutoff correspond with osteopenia or osteoporosis?
10- the size and location of ROI is important. [for example, lateral walls and two plated of vertebral body should not be included in the ROI]. Please complete the paper in this regard. In addition, what was the landmark for L1 vertebra?
11- The previous history of the stone in patients seems important. I mean a patient could have a previous history of stone fir example in ten years ago and a patient experiences the first stone episode. These two patients are different [regarding the paper goals. In addition, patients with previous history of stones could take a long-standing drug for the condition]. Please add the data of the history of the stone [presence and the time of the first stone up to now] and implement appropriate analyses and discuss [of course, if the data are available].
12- this part should be transferred to discussion: “While previous literature such as the Framingham cohort has established the protective effect of BMI on BMD(19); the effect of serum biochemistry on bone mineral content is a controversial issue, and is beyond the scope of this current study.”
13- the authors could implement the correlation coefficient and regression analyses [univariate and multivariate] between 24 h urine analysis biometrics and BMD values [as dependent variable in the regression model]. For this purpose, the authors could consider

the BMD value itself [not dichotomized BMD classification; low vs. high BMD]. It would be interesting for example if we can predict the BMD based on 24 h urine analysis biometrics. In addition, dichotomized BMD could be analyzed by logistic regression based on 24 h urine analysis biometrics [prediction of low BMD based on 24 h urine analysis biometrics] [even ROC analysis could be interesting if the study design permit such an analysis]. I recommend the authors add these adjunct analyses to the paper. [if the analyses are informative, significant and interesting].
14- please add p-values in table 1.
15- please add in statistical analysis if the normality of data is checked before the analyses.
16- tables 3 and 4 are based on ANOVA methods [parametric or non-parametric]. Please add in statistical analysis methods what are the tests used for these analyses? The ANOVA based methods need post hoc tests to determine if an ANOVA test is significant, which groups are statistically different. Please add post hoc tests results to the paper.
17- please add p-values to table 4.
18- is the HU of stone itself important to be considered in the statistical analyses?
19- an important confounding factor in the study could be age; as the age of the patients in the high BMD is lower significantly. This can affect the findings. Please discuss. In addition, the group of low BMD has higher percentage of females that are in the postmenopausal period and are at higher risk of low BMD. I think if the authors use multivariate regression models, they can adjust the effect of age and gender in their analyses and discuss better.
20- based on the design, it seems the study is not an analytical study and we can not make a causative inference. The study could find associations between variables. This point should be considered in writing of discussion.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 4 Oct 2020

Dear EIC,
The manuscript needs major revision considering a methodological review.
Thanks.

REFEREE: EIC | **Revision** (0) 4 Oct 2020

Dear authors,
Your article needs Major Revision.
Regards

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

To the editorial office of Iranian Journal of Radiology,

We would like to express our gratitude for the evaluation and suggestions made by reviewers about our manuscript **“The Correlation between CT-based bone mineral density and kidney stone size, and their association with 24-hours urinary analysis biometrics in urinary stone patients”.**

Revisions made are listed as follows which also marked using yellow color highlight in the text; on the basis of reviewer’s comments and suggestions.

We wish to resubmit the revised version of our manuscript to be evaluated for publication in the journal.

Sincerely yours

Mohammad Mersad Mansouri Tehrani

Corresponding author

Reviewer 1: Thank you for your kind consideration.

1: The conclusion of abstract is wrong. The authors mentioned: “Low BMD diagnosed through CT-scans is associated with abnormal 24-hours urine analysis biometrics and larger stones, and should be properly assessed.” They have implemented the study on patients with urinary stone while they are generalizing the study findings to all population and this could be wrong. The data are not come from general population. Please correct.

Answer1: Abstract conclusion changed as follows so that it would only include the stone former patients: Low BMD diagnosed through CT-scans "in patients with urinary stones" is associated with abnormal 24-hours urine analysis biometrics and larger stones, and should be properly assessed.

2: What is the meaning of risk-assessment tool? [objective part?] risk of what?

Answer 2: The aforementioned phrase was eliminated from the article.

3: As the patients are all candidate for PCNL, the data could be different in a considerable subgroup of stone patients that are not candidate for PCNL [for example in patients with small size stones that constitute majority of stone patients and are not candidate for PCNL]. If the authors add the data of all stone patients, the results could be different. Please explain in this regard and discuss.

Answer 3: All patients should undergo stone analysis and a basic evaluation after having passed a stone or undergoing treatment for a urinary stone. Stone patients with higher risk of recurrence should undergo specific metabolic evaluation with 24-h urine collection to identify altered urinary factors that could be corrected with specific treatment. Whether this correction can ultimately lead to an overall lower recurrence rates is unclear. But general consensus indicated that a more extensive metabolic evaluation is recommended for recurrent or high-risk stone formers. Patients with large stone is a subgroup of patients who need further

metabolic evaluation with 24-h urine collection. in this study, we enrolled patients who need PCNL due to large stones.

4: The stones are different in their constituent regarding different pathophysiologic processes and mechanisms of formation [for example hypercalciuria]. Most of calcium stones are formed from calcium oxalate; however, some of them contains mainly calcium phosphate or are mix of phosphate and oxalate. This could remind in different pathologic baseline metabolic conditions. The authors mentioned they enrolled only the patients “having the predominant calcium component in the urinary calculi analysis,” Regarding the mentioned point, this sentence is vague and unclear. If the stones are composed from oxalate or phosphate or both? This could make a heterogeneity in the enrolled patients. Please explain.

Answer 4: We only enrolled patients with predominantly calcium components stones including both calcium oxalate and calcium phosphate with the majority of these patients having calcium oxalate stones. Although there are some differences between the pathogenesis of these two types, but the basic pathogenesis mechanism remains the same and thus deduction based on these hypothesis is feasible.

5: Some treatments could affect the urinary calcium such as VIT-D3 supplementation, PTH and the other agents affect the calcium and phosphorus metabolism. Did the authors consider these factors in exclusion criteria?

Answer 5: One of our exclusion criteria was patients who received treatment or supplements of Calcium or Vitamin D3. These exclusion criteria added to the article.

6: What was the time interval between [CT scan and PCNL] and between [PCNL and urine analysis]?

Answer 6: Non contrast CT scan as the best diagnostic method scheduled one day prior to surgery and 24-hour urine collection was done one month after PCNL. These time intervals added to the study.

7: If the patient has more than one stones and the smaller is candidate for PCNL [for example, the larger is located in renal pelvis or in bladder], then what would be considered as the stone size? The size of stone candidate for PCNL or the largest stone?

Answer 7: As mentioned throughout the article, patients who were candidate for PCNL, entered the study and thus per your example, the size of kidney stone candidate for PCNL was considered in the analysis.

8: How many radiologists did measure the imaging assessments? [size determination and drawing the ROI for BMD assessment]. did the authors determine the interrarter and intrarater reliability between radiologists in these measurements?

Answer 8: Only one radiologist participated in the study and determined stone size and drew ROI for BMD assessment for all subjects. This point added to the article.

9: Is the cutoff point of 160 validate for Iranian population in differentiating low BMD? In addition, does this cutoff correspond with osteopenia or osteoporosis?

Answer 9: The cut- off point of 160 assessed by the same team and validate in Iranian people. The article was accepted recently in Iranian journal of radiology. This cut off point correspond with osteoporosis. Independent cut-offs for osteopenia have been described in the aforementioned article.

10: The size and location of ROI is important. [for example, lateral walls and two plated of vertebral body should not be included in the ROI]. Please complete the paper in this regard. In addition, what was the landmark for L1 vertebra?

Answer 10: As described in the article, the ROI was designated at the centermost of the vertebral body, following the methodology of the article published by Patel et. al. (doi: http://doi.org/10.1089/end.2018.0296). The requested point added to the article. In order to identify the L1 vertebrae, S1 vertebrae was used as a radiologic landmark.

11: Previous history of the stone in patients seems important. I mean a patient could have a previous history of stone for example in ten years ago and a patient experiences the first stone episode. These two patients are different [regarding the paper goals. In addition, the patients

with previous history of stone could take a long standing drugs for the condition]. Please add the data of the history of the stone [presence and the time of the first stone up to now] and implement appropriate analyses and discuss [of course, if the data are available].

Answer 11: First, thank you for the most astute comment. Unfortunately, these data are not available in our database and due to retrospective nature of our study, access to these data is not feasible.

12: This part should be transferred to discussion: “While previous literature such as the Framingham cohort have established protective effect of BMI on BMD (19); the effect of serum biochemistry on bone mineral content is a controversial issue, and is beyond the scope of this current study.”

Answer 12: The aforementioned part was moved to "Discussion" section.

13: The authors could implement the correlation coefficient and regression analyses [univariate and multivariate] between 24 h urine analysis biometrics and BMD values [as dependent variable in the regression model]. For this purpose, the authors could consider the BMD value itself [not dichotomized BMD classification; low vs. high BMD]. It would be interesting for example if we can predict the BMD based on 24 h urine analysis biometrics. In addition, dichotomized BMD could be analyzed by logistic regression based on 24 h urine analysis biometrics [prediction of low BMD based on 24 h urine analysis biometrics] [even ROC analysis could be interesting if the study design permits such an analysis]. I recommend the authors add these adjunct analyses to the paper. [if the analyses are informative, significant and interesting].

Answer 13: Linear regression analysis and correlation coefficient were utilized for analysis of the probable predictor role of urinary biometrics on BMD. However, no predictive effect was noted (*P- value* > 0.05). The requested findings were added to the article.

14: Please add p-values in table 1.

Answer 14: P-Values less than 0.05 considered to be significant. This was added to the Table 1.

15: Please add in statistical analysis if the normality if data checked before the analyses.

Answer 15: Normality, skewness and kurtosis of the data was checked and added in the manuscript.

16: The tables 3 and 4 are based on ANOVA methods [parametric or non-parametric]. Please add in statistical analysis methods what are the tests used for these analyses? The ANOVA based methods need post hoc tests to determine if an ANOVA test is significant, which groups are statistically different. Please add post hoc tests results to the paper.

Answer 16: Scheffe post-hoc test was used to evaluate the significance of the variables in Tables 3 and 4. We noted meaningful relation between the assessed parameters in both of the tables ($P < 0.05$). However, no causative inference can be definitely outlined, due to the non-analytical nature of the study. The results were added to the study.

17: Please add p-values to table 4.

Answer 17: P-Values less than 0.05 considered to be significant. This was added to the Table 4.

18: Is the HU of stone itself important to be considered in the statistical analyses?

Answer 18: Clinically, attenuation of the urinary stones is considered an important entity in evaluating the patients and planning appropriate interventions; smaller stones (between 1-

2cm) with an attenuation less than 900 HU can be treated through extracorporeal shockwave lithotomy (ESWL), whereas stones with an attenuation greater than 1000 HU are candidates for PCNL. However, since all the subjects for the current study had undergone PCNL, stone attenuation was not statistically important in our analyses.

19: An important confounding factor in the study could be age; as the age of the patients in the high BMD is lower significantly. This can affect the findings. Please discuss. In addition, the group of low BMD has higher percentage of females that are in the postmenopausal period and are at higher risk of low BMD. I think if the authors use multivariate regression models, they can adjust the effect of age and gender in their analyses and discuss better.

Answer 19: We performed linear regression to assess the possible confounding effects of gender and age on our analysis. Both of the variables showed no confounding effects on the study (*P*-value for gender > 0.05) (*P*-value for age > 0.05). Furthermore, discussing the probable effects of gender and age on BMD is beyond the scope of this retrospective analysis.

20: Based on the design, it seems the study is not an analytical study and we cannot make a causative inference. The study could find associations between variables. This point should be considered in writing of discussion.

Answer 20: The discussion section changed per your instructions and any phrase indicating causative inference were eliminated.

Reviewer 2: Thank you for your kind consideration.

Although there are few similar articles about relationship between BMD and hypercalciuria and renal stone, but correlation between these parameters and size of renal stone is new and interesting. All key words are according to the MESH database.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Madjid Shakiba: Reviewer | **Revision (1)** 16 Nov 2020

Dear AE,
The authors have responded many questions and points. there are some points to be corrected or added in paper:
The authors corrected many points. Some are left to be furtherly corrected.
1- I asked in question 3, “As the patients are all candidate for PCNL, the data could be different ……..” The answer I think did not address the question; however, it contains good points. I recommend two points to the authors in this regard: I-it is better the authors add useful points of the response to this question to the paper. II-as the patients' candidates for PCNL has larger stones and thus, the metabolic profile of these patients could be different with other patients with stones [for example patients with smaller stones], it is better they add a small part in the discussion and point out this matter and mention this as a potential limitation. [in fact they could mention the results could not be generalized to all patients with urinary stone]
2- the authors have added some points to question 4 [The stones are different in their constituent regarding different pathophysiologic ……]. Important points in the response are useful to be mentioned in the discussion and paper.
3- in the response to question 9, the authors mentioned: “The cut-off point of 160 assessed by the same team and validate in Iranian people. The article was accepted recently in Iranian journal of radiology. This cut off point correspond with osteoporosis. Independent cut-offs for osteopenia have been described in the aforementioned article.” It is better they add this point to the paper.
4- in response to question 11, the authors added: “Unfortunately, these data are not available in our database and due to retrospective nature of our study, access to these data is not feasible.” I recommend the authors add this point in paper and make a brief discussion and mention this as a limitation.
5- I asked the authors to add p-values for comparison between low and normal BMD subgroups in table 1. But they added a phrase to legend as: “P-Values less than 0.05 considered to be significant.” There is no p-value for comparison in the table. We know that the p-value lower than 0.05 is significant. Please add p values for comparison in table1. In addition, it is better the authors add exact p value in all table. $P<0.05$ is not precise data. Please delete “P-Values less than 0.05 considered to be significant” from the tables. It has been mentioned in stat methods of paper.
6- Regression analysis was requested for prediction of BMD based on 24 h urine analysis biometrics, stone size, time of stone history and age and sex. But the authors added only

this sentence in the paper: “Additionally, linear regression assessment established that both gender and age have no confounding effect on the findings (P > 0.05).” This sentence is not enough. If there is no considerable correlation between BMD with other variables, and they can not make a good prediction for BMD based on mentioned variables, they should mention clearly this point in the paper and the sentence about age and sex is not enough in this regard. The authors mentioned this sentence in response: “Linear regression analysis and correlation coefficient were utilized for analysis of the probable predictor role of urinary biometrics on BMD. However, no predictive effect was noted (P- value > 0.05).” this sentence should be mentioned in the paper.
7- I asked: “The ANOVA based methods need post hoc tests to determine if an ANOVA test is significant, which groups are statistically different. Please add post hoc tests results to the paper.” but the authors only reported using scheffe test and mentioned P value of ANOVA. They should report post hoc result. If ANOVA is meaningful, we should know which groups are statistically different.
Thanks.

REFEREE: Associate Editor | **Revision (1)** 17 Nov 2020

Dear EIC,
The manuscript needs minor revision considering the methodological review.
Thanks.

REFEREE: EIC | **Revision (1)** 17 Nov 2020

Dear authors,
Your article needs Minor Revision.
Regards

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

To the editorial office of Iranian Journal of Radiology,

We would like to express our gratitude for the evaluation and suggestions made by reviewers about our manuscript **“The Correlation between CT-based bone mineral density and kidney stone size, and their association with 24-hours urinary analysis biometrics in urinary stone patients”.**

Revisions made are listed as follows which also marked using yellow color highlight in the text; on the basis of reviewer’s comments and suggestions.

We wish to resubmit the revised version of our manuscript to be evaluated for publication in the journal.

Sincerely yours

Mohammad Mersad Mansouri Tehrani

Corresponding author

Reviewer 1: Thank you for your kind consideration.

1-I asked in question 3, “As the patients are all candidate for PCNL, the data could be different ……..” The answer I think did not address the question; however, it contains good points. I recommend two points to the authors in this regard: I-it is better the authors add useful points of the response to this question to the paper. II-as the patients candidate for PCNL have larger stones and thus, the metabolic profile of these patients could be different with other patients with stones [for example patents with smaller stones], it is better they add a small part in discussion and point out this matter and mention this as a potential limitation. [in fact they could mention the results could not be generalized to all patients with urinary stone]

Requested points from the answer such as the necessity of biochemical assessment in urinary stone patients were emphasized upon through the paper. The second requested point was added to the article as a limitation in the Discussion segment.

2-the authors have added some points to the question 4 [The stones are different in their constituent regarding different pathophysiologic ……]. Important points in the response are useful to be mentioned in the discussion and paper.

Requested parts of the response were added in the Discussion segment.

3-in the response to question 9, the authors mentioned: “The cut- off point of 160 assessed by the same team and validate in Iranian people. The article was accepted recently in Iranian journal of radiology. This cut off point correspond with osteoporosis. Independent cut-offs for osteopenia have been described in the aforementioned article.” It is better they add this point to the paper.

The matter of radiologic thresholds was discussed further in the Discussion chapter, with regards to the recently published article among the Iranian population.

4-in response to question 11, the authors added: “Unfortunately, these data are not available in our database and due to retrospective nature of our study, access to these data is not feasible.” I recommend the authors add this point in paper and make a brief discussion and mention this as a limitation.

This matter was partly discussed in the second part of the study’s limitations; as requested, it is now further talked about.

5-I asked the authors to add p-values for comparison between low and normal BMD subgroups in table 1. But they added a phrase to legend as: “P-Values less than 0.05 considered to be significant.” There is no p-value for comparison in table. We know that the p-value lower than 0.05 is significant. Please add p values for comparison in table1. In addition, it is better the authors add exact p value in all table. P 0.05).” This sentence is not enough. If there is no considerable correlation between BMD with other variables, and they

can not make a good prediction for BMD based on mentioned variables, they should mention clearly this point in the paper and the sentence about age and sex is not enough in this regard. The authors mentioned this sentence in response: “Linear regression analysis and correlation coefficient were utilized for analysis of the probable predictor role of urinary biometrics on BMD. However, no predictive effect was noted (P- value > 0.05).” this sentence should be mentioned in paper.

P-values for all of the requested variables are now added to all of the Tables. Furthermore, the requested sections of the article are now edited to better convey the findings.

7-I asked: “The ANOVA based methods need post hoc tests to determine if an ANOVA test is significant, which groups are statistically different. Please add post hoc tests results to the paper.” but the authors only reported using scheffe test and mentioned P value of ANOVA. They should report post hoc result. If ANOVA is meaningful, we should know which groups are statistically different.*

All post-hoc values are now added to the article for the Table-3; as for the Table-4, we included post-hoc results for the values between the stone size and the mean HU subdomain, as the rest of the values did not prove statistically significant through ANOVA. We also made structural adjustments to the Table-4 to better suit the paper's format.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (2) — 11 Dec 2020

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Associate Editor | **Revision** (2) — 12 Dec 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: Reviewer | **Revision** (2) — 15 May 2021

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Associate Editor | **Revision** (2) — 1 Jun 2021

Dear EIC,
Comments for the authors:
1- the authors mentioned: “any general populations” what is the meaning of general population? It seems we can write this part as: “any population”
2- x-rays should be X-rays.
3- this sentence is unclear: “Obtaining data through CT imaging for urolithiasis minimized the need for additional, cost and radiation burden for the patients(5)” the unclear part is “additional, cost” maybe the authors mean “additional cost”
4- what is the meaning of “opportunistic screening”? why opportunistic?
5- please replace: “removed from the study” with: “excluded from the study”
6- please complete the manufacturer data of IBM SPSS.

7- please correct: 48.80 ± (14.11) as “48.80 ± 14.11” or “48.80 (± 14.11)”
8- line 138; part: “in stone size groups” could be written as: “in different groups determined based on stone size”
9- “urinary exerted citrate” seems to be: “urinary excreted citrate”
10- line 142 and line 153; “post-hoc values” seems to be “(post-hoc P-values”
11- in line 187, “reduces BMD” seems to be “reduced BMD”
12- line 203: “this current study” could be: “current study” or “this study”
13- line 213, “24 h” should be “twenty-four-hour”.
14- please delete: “6. Conclusion” and replace it with: “In conclusion” at the beginning of the paragraph.
15- line 262, part: “and hyperoxaluria and are shown” seems to be: “and hyperoxaluria are shown”
16- table 1 legend could be written as: “distribution of Basic characteristics between low and normal BMD subgroups”
17- please complete the columns heading in table 1. <160 HU is unclear. it could be written as:
“Low BMD [HU<160] and normal BMD [HU>160]” please apply such correction to table 2.
18- please explain in the paper what anatomical region was the reference for the assessment of HU and determining low BMD vs. normal BMD based on the cut-off of 160. Explain this as a footnote in Table 1.
19- in table 4, the authors have mentioned Mean HU but it is unknown HU of where? Please add the location of assessment of HU. [for example bone mineral HU or bone mineral attenuation]
Thanks.

REFEREE: EIC | **Revision (2)** 2 Jun 2021

Dear Authors,
Your article needs Minor Revision.
Regards

OPEN PEER REVIEW

Revision (3)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

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We would like to express our gratitude for the evaluation and suggestions made by reviewers about our manuscript **“The Correlation between CT-based bone mineral density and kidney stone size, and their association with 24-hours urinary analysis biometrics in urinary stone patients”.**

Revisions made are listed as follows which also marked using yellow color highlight in the text; on the basis of reviewer’s comments and suggestions.

We wish to resubmit the revised version of our manuscript to be evaluated for publication in the journal.

Sincerely yours

Associate Editor 2:

1-the authors mentioned: “any general populations” what is the meaning of general population? It seems we can write this part as: “any population”

The requested change has been applied to the article.

2- x-rays should be X-rays.

The requested change has been applied to the article.

3-this sentence is unclear: “Obtaining data through CT imaging for urolithiasis minimized the need for additional, cost and radiation burden for the patients(5)” the unclear part is “additional, cost” maybe the authors mean “additional cost”

The requested change has been applied to the article.

4-what is the meaning of “opportunistic screening”? why opportunistic?

Opportunistic screen is a kind of screen that relies on early detection of disease in patients who present to health care providers for other complaints.

5-please replace: “removed from the study” with: “excluded from the study”

The requested change has been applied to the article.

6-please complete the manufacturer data of IBM SPSS.

The name and the version of the program has been added to the article.

7- please correct: 48.80 ± (14.11) as “48.80 ± 14.11” or “48.80 (± 14.11)”

The requested change has been applied to the article.

8-line 138; part: “in stone size groups” could be written as: “in different groups determined based on stone size”

The requested change has been applied to the article.

9-“urinary exerted citrate” seems to be: “urinary excreted citrate”

The requested change has been applied to the article.

10-line 142 and line 153; “post-hoc values” seems to be “post-hoc P-values”

The requested change has been applied to the article.

11-in line 187, “reduces BMD” seems to be “reduced BMD”

The requested change has been applied to the article.

12-line 203: “this current study” could be: “current study” or “this study”

The requested change has been applied to the article.

13-line 213, “24 h” should be “twenty four hour”.

The requested change has been applied to the article.

14-please delete: “6. Conclusion” and replace it by: “In conclusion” at the beginning of the paragraph.

The requested change has been applied to the article.

15-line 262, part: “and hyperoxaluria and are shown” seems to be: “and hyperoxaluria are shown”

The requested change has been applied to the article.

16-table 1 legend could be written as: “distribution of Basic characteristics between low and normal BMD subgroups”

The requested change has been applied to the article.

17-please complete the columns heading in table 1. <160 HU is unclear. it could be written as: “Low BMD [HU<160] and normal BMD [HU>160]” please apply such correction to table 2.

The requested change has been applied to the article.

18-please explain in paper what anatomical region was the reference for assessment of HU and determining low BMD vs. normal BMD based on the cut off of 160. Explain this as footnote in table 1.

The process of identifying a ROI for bone mineral attenuation measurements has been discussed in the section 3.2 of the article. A footnote for Table-1 is added to the article as per request.

19-in table 4, the authors have mentioned Mean HU but it is unknown HU of where? Please add the location of assessment of HU. [for example bone mineral HU or bone mineral attenuation]

The requested change has been applied to the article.

OPEN PEER REVIEW

Revision (3)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (3) 12 Jun 2021

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (3) 13 Jun 2021

Dear authors,
Your article is acceptable for the publication in IJR.
Regards