



Maurizio Salvadori, MD, Professor
Editor in Chief,
World Journal of Transplantation
August 7th, 2016

Jin-Xin Kong and Xue-Mei Gong,
Science Editors, Editorial Office

Re: ESPS Manuscript 27222 entitled "Incidence of Kidney Stones in Kidney Transplant Recipients: A Systematic Review and Meta-analysis"

Dear Editor,

Thank you for the thoughtful input and review of our manuscript. The reviewers' inputs are extremely helpful. We believe as a result of this review, our study would have more value for your readers. We revised the manuscript based on the reviewer's suggestions. We have attached our point by point response.

Thank you for your time and consideration. We look forward to hearing from you.

Sincerely,

Wisit Cheungpasitporn, M.D.

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Response to Science Editor, Editorial Office

Comment 1:

Please revise your article according to the reviewers' comments/suggestions and provide point to point responses to each in the letter format specified in the attached files. Please highlight the change according to the comments.

Response: We thank you for reviewing our manuscript. We really appreciated your and reviewers' input. We have revised our manuscript as your and reviewers' suggestions.

Response to Reviewer#1

Reviewer's code: 00503255

Reviewer's country: Japan

Science editor: Xue-Mei Gong

Date sent for review: 2016-05-18 15:14

Date reviewed: 2016-06-03 16:33

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

Response: We thank you for reviewing our manuscript. We really appreciated your input and found your suggestions very helpful. We revised the manuscript based on your suggestions.

COMMENTS TO AUTHORS

The authors performed systematic review and meta-analysis on studies about kidney stones in kidney transplant recipients to evaluate the incidence and characteristics of these patients and reported that the incidence of kidney stones in patients after kidney transplantation was 0.9%, and struvite stone were not uncommon in these patients. The paper is well-written and provides valuable information.

One point question: 1. The authors described that patients with CKD or ESRD may encounter less stone disease in the introduction. Are there any studies on incidence of kidney stones in patients CKD or ESRD?

Response: Thank you for raising an important point to strengthen our manuscript. We have added reference of lowered incidence of kidney stones in patients with CKD/ESRD in the manuscript. The following text in **bold** has been added to introduction part of our manuscript.

Previous studies have shown that stone recurrence rates may be lower, when glomerular filtration rate (GFR) reduced^[9, 10]. **Thus, patients with advanced chronic kidney disease (CKD) or end stage kidney disease (ESRD) may encounter less stone disease^[10], reported being as low as 0.68%^[11].** After successful kidney transplantation, ESRD patients subsequently have significant improvement in renal function resulting in urinary excretion of metabolites that increases risk of stone disease. Studies have identified kidney stones in allograft kidney as one of the serious problems in kidney transplant recipients^[12-35]. However, unlike the general population, the incidence and characteristics of kidney stones in kidney transplant recipients are not well studied. The objective of this meta-analysis was to evaluate the incidence and types of kidney stones after kidney transplantation.

Response to Reviewer#2

Reviewer's code: 00503322

Reviewer's country: United Kingdom

Science editor: Xue-Mei Gong

Date sent for review: 2016-05-18 15:14

Date reviewed: 2016-06-19 23:42

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

Response: We thank you for reviewing our manuscript. We really appreciated your input and found your suggestions very helpful. We revised the manuscript based on your suggestions.

COMMENTS TO AUTHORS

Comment #1

The authors have conducted a systematic review and meta-analysis and examined the incidence of renal calculi after renal transplantation, but have not identified successfully any risk factors for the calculi formation; which has diluted the significance of the paper. A random-effect meta-analysis should have some conclusions, which is missing.

Response: We thank you for reviewing our manuscript. We agreed with the reviewer that risk factors for the calculi formation are important. Despite limited data on urinary supersaturation and risk factors for kidney stones, we provided available information on risk factors for kidney stones in kidney transplant recipients as the following:

"Risk factors for Kidney Stones in Kidney Transplant Recipients

Despite limited data on urinary supersaturation and risk factors for kidney stones, studies reported increased risk of kidney stones in kidney transplant recipients with hyperparathyroidism, hypercalciuria, hypocitraturia, hypophosphatemia, and urinary

tract infection[28, 38]. Harper et al.[38] found that urinary excretion of magnesium and phosphate was at the lower range for all kidney transplant recipients with kidney stones. Uncommonly, urinary outflow obstruction and foreign bodies were also found as risk factors for kidney stones in kidney transplant patients[28, 48].”

Comment #2

Although huge number of patients are included in the study, kidney stone and its relationship to other outcomes following transplantation are not analyzed, which should have been done. In essence, the paper adds minimum to the existing body of knowledge on this subject.

Response: Reviewer raised a very important comment and we agree that outcomes following transplantation in kidney transplant patients with kidney stones are important. Thus, we reviewed the existing literature and added the available information on outcomes of allograft failure in kidney transplant recipients with kidney stones. The following text in **bold** has been added.

“Allograft Failure in Kidney transplant Recipients with Kidney Stones

As in general patient populations, kidney stones can also cause acute kidney injury in kidney transplant recipients[49-52]. Since kidney transplant recipients can have obstructed kidney stones without any symptom of pain[26, 28], prompt diagnosis and the removal of obstructed stones are the keys to preventing renal allograft failure[18]. Rezaee-Zavareh et al.[29] reported no significant association between kidney stones after transplantation and graft survival (OR 1.04; CI 0.71-1.54). With the prompt removal of stones, Kim et al.[18] found no significant changes in renal allograft function at diagnosis and after removal of kidney stones.”

Response to Reviewer#3

Reviewer's code: 00503339

Reviewer's country: United States

Science editor: Xue-Mei Gong

Date sent for review: 2016-05-18 15:14

Date reviewed: 2016-07-01 00:01

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Duplicate publication	publication
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	language polishing	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Fully detailed, clear report of the prevalence of renal calculi discovered in kidney transplant recipients. The understandably unanticipated finding of a lower than 1% prevalence of renal calculi may stimulate further studies of why this might happen. Overall, a worthy, well-structured advance of our understanding to life after kidney transplantation.

Response: We thank you for reviewing our manuscript. We really appreciated your kind comments. We are hoping that our study will be helpful for future research studies.

Sincerely,

Wisit Cheungpasitporn, M.D.

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