

## Peer Review File

Article information: <http://dx.doi.org/10.21037/tau-21-195>

**Reviewer A:** The authors paid special attention to the cystoscopic findings in women with lower urinary tract symptoms (LUTS). In this study, 84 women underwent cystoscopy with hydrodistension (CWHD) were investigated. As results, they found the frequency of glomerulations in women with minimally symptomatic women was eight-fold lower compared to that with highly symptomatic women. In addition, extensive glomerulations are rare in women with minimal symptoms. Finally, they showed the importance of evaluating objective evidence on CWHD.

I think that their study has important results to discuss the evaluation of LUTS. However, I have several question and opinion before publication.

### Major

**Comment 1:** In Introduction, you showed that “glomerulations are non-specific for IC/BPS”. I also agree with your opinion. However, many urologists may believe glomerulations are specific finding for IC/BPS. Therefore, please add more detailed information about it into Introduction.

**Reply 1:** We have added further details regarding this  
Changes in the text: Background. Page 4, 5

**Comment 2:** Do you recommend the CWHD for patients with LUTS as routine examinations? I am afraid that its clinical benefit is not clear. I would like to know your opinion.

**Reply 2:** While we do not recommend routine CWHD routinely. I believe that whether or not glomerulations are pathologic or not should be further explored. In patients with complex pelvic pain symptoms, where the contribution of bladder sensitivity is uncertain, that significant glomerulations on CWHD may prompt clinicians to focus more on the bladder as a source of pain.  
Changes in the text: Discussion. Page 13.

**Comment 3:** Are there any complications in your study population. Please add information about them into Results section.

**Reply 3:** There were no complications related to cystoscopy with hydrodistension that were identified. Complication data otherwise not collected  
Changes in the text: Results. Page 10

### Minor

**Comment 4:** I think that sentences about strength of the study are too much in Discussion. Please simplify or delete a part of them.

**Reply 4:** We have removed a significant portion of this.  
Changes in the text: Discussion. Page 14

**Reviewer B:** There is significant deficiency in the design, description, and presentation of this research. I encourage authors to discuss and edit major defects from this paper before another submission.

Several items need further clarification:

Title page

**Comment 1:** Line 9 – First author’s affiliation should be labeled #1 superscript, not 2.

**Reply 1:** Thank you. Appropriate change has been made.

Changes in text: Page 1, line 9

**Comment 2:** Line 21 – Saint Louis University School of Medicine? Or just School as intended to be?

**Reply 2:** Thank you. Appropriate change has been made to Saint Louis University School of Medicine

Changes in text: Page 1, line 21

Abstract

**Comment 3:** Line 72: 3.0% versus 23.5% vs 3.05 – this is poorly structured. Please re-write.

**Reply 3:** The error has been corrected and has been restructured

Changes in text: Abstract. Page 3, lines 72-73

**Comment 4:** Line 72-26: This run-on sentence is extremely confusing. Where is the data for no glomerulation? Is the  $p > 0.05$  for difference between 10+ glomerulation to – glomerulation, or 10+ glomerulation in highly vs minimally symptomatic women?

**Reply 4:** I removed this from the abstract. Agree that it ends up being too confusing.

Changes in text: Page 3, lines 72-76

**Comment 5:** Line 79: how does another study “contrast” your study when your findings are consistent with existing studies?

**Reply 5:** This references the Waxman 1998 study which is frequently cited when discussing glomerulations in asymptomatic women which is referenced in the manuscript.

Changes to text: None at this time- if the answer above is sufficient.

**Comment 6:** Line 81: How does cystoscopic evaluation change your management in management of IC/BPS as the glomerulation finding seems to be parallel to their symptoms.

**Reply 6:** It does not change management at this time. But this finding contributes to the understanding of which bladder findings are pathologic, in the setting of our

evolving discussion regarding bladder health. If other studies substantiate that glomerulations, while not specific to IC/BPS, are pathologic, findings on cystoscopy with hydrodistention may help unravel the relative contribution of bladder-related pathology to a patient with pelvic pain.

Changes to text: page 3, line 82

### Introduction

**Comment 7:** Line 97-98: award to have a self-imposed question in a manuscript. You may rephrase to, "It is unknown that ..."

**Reply 7:** We have made the change.

Changes to text: Background, page 5, lines 127-128

### Methods

**Comment 8:** Line 147: what is the rationale to develop this scale in this categorization fashion?

**Reply 8:** > 10 glomerulations in 3 or 4 quadrants was selected to represent the NIDDK research criteria. > 10 glomerulations in 1 or 2 quadrants was selected at the discretions of the authors.

Changes to text: Methods, page 7-8, line 179-185

**Comment 9:** Line 149: what does glomerulations occurring at a lower rate mean?

**Reply 9:** We made changes in the manuscript to describe that this represents glomerulations occurring at an lower rate than >10 glomerulations in 1 or 2 quadrants

**Comment 10:** Line 169: This is a secondary analysis of a prior study. Not a prospective study of glomerulation in IC/BPS patients. If it was a prospective study for glomerulation, power analysis would've been carried out. The authors needs to understand the difference between a prospective study versus a secondary analysis.

**Reply 10:** This distinction has been made.

Changes to the text: Methods. Page 6, lines 138-148.

**Comment 11:** Line 178: please explain how authors came to determine to include these variables.

**Reply 11:** The variables included in our model were minimal symptomatology, self-reported gastroesophageal reflux disease (GERD), recurrent urinary tract infection (rUTI), and history of endometriosis. These were selected as they were statistically significant differences in between the minimally and maximally symptomatic group and were considered to be clinically significant potential confounders.

Changes to the text: Methods, page 9, lines 219-222

### Results

**Comment 12:** This is a secondary analysis of a prospective study. There is no description of the parent study either. Or the characteristics of those included and excluded.

**Reply 12:** The collection of the prospective data set is now described in methods. However, analysis was performed on all participants in the data set. It was treated as a database collection.

Changes to the text: Results, page 10, line 230-231