

OBSTETRICS & GYNECOLOGY



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obgyn@greenjournal.org.

Date: Dec 09, 2021
To: "Koji Matsuo" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-2151

RE: Manuscript Number ONG-21-2151

Utilization and outcomes of sentinel lymph node biopsy for early endometrial cancer.

Dear Dr. Matsuo:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Please be sure to address the Editor comments (see "EDITOR COMMENTS" below) in your point-by-point response.

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Dec 30, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Utilization and outcomes of sentinel lymph node biopsy for early endometrial cancer

This study is a retrospective data base review (SEER) with the goal of examining trends, characteristic, and oncologic outcomes of SLN biopsy for endometrial cancer.

Minor issues

1. Lines 48-49: would not put data in parenthesis, would instead write a separate sentence discussing sensitivity and NPV
2. Lines 161-162: grammar issue with sentence
3. Line 239: its now 2021 so feels odd to say "by 2020" even if we don't have mature data of uptake of sLNB from 2020 yet.
4. Would discuss different techniques for sLNB detection (Tc-99/Blue vs ICG (diff sensitivity / NPV))
5. Would discuss PMID: 32349874 (showing improved outcomes in survival with sLNB)

Major issues

1. Would discuss similar study done in stage II: PMID: 34728108
2. Would also discuss Soliman et al PMID: 28528918
3. Lines 75-81: In clinical practice, sometimes one side will map and another will not in which case either a full lymphadenectomy may be performed on that side, no lymphadenectomy on one side, selective lymph node dissection or the uterus can be sent for frozen section to determine if lymph node dissection is necessary based on modified Mayo criteria. In these situations, how were the patients categorized? Is this what you mean by lines 169-170? This is the major issues I have with this data.
4. Lines 208-210: Women in the SLN biopsy group were less likely to receive postoperative external beam radiotherapy (7.1% versus 9.7%, $P<0.001$) but not chemotherapy (7.8% versus 7.4%, $P=0.350$). - Explain why in discussion. I would assume more than just due to increased cases in sLNB group with high risk histologies that are more likely to be treated with chemo and brachy.

Strengths:

1. While retrospective, this includes over 83K patients from SEER database

2. Nicely explains the uptake of sLNB over time with respect to data being published re the feasibility and sensitivity/NPV of sLNB
3. No diff in survival seen between sLNB and full LND

Reviewer #2:

Thank you for the opportunity to review " Utilization and outcomes of sentinel lymph node biopsy for endometrial cancer"

Reviewing the current literature on this topic, this work is quite similar to PMID: 32981697 the time frame this work reviews however is from 2012-2016 while the current manuscript 2005-2018 provides an additional 2 years of data on sentinel node utilization. This data adds incrementally to some of the analyses that have already been published on this topic but provides some novel information.

Unique to this study, they assessed risk of conversion to open surgery and mortality at 90 days. The prior published study uses the NCDB while the current study under review uses the SEER database. The current study also provided an assessment of tumor and patient factors associated with sentinel lymph node use as well as an assessment of endometrial cancer specific mortality associated with sentinel lymph node assessment versus lymphadenectomy. This study also provides an interesting analysis estimating a 15.3% increase in nodal evaluation based on increasing utilization of sentinel lymph node biopsy in the more recent years noting that adoption of lymph node biopsy has been highest in the low grade endometroid histology group.

Major criticism-

-Time frame of the current study reflects very similar trends to those reported in the literature already in the setting of other retrospective database studies and reported outcomes from clinical trials.

-Please include additional background literature available on utilization of sentinel lymph mapping available to date including PMID: 32981697.

-Please clarify in the methods section how the patients who had both sentinel lymph node assessment and complete lymphadenectomy were classified. It seems this group was included in the sentinel lymph node category for most analyses? How was this addressed in the endometrial cancer specific mortality analysis?

Minor criticism-

-Would encourage including additional analyses on the adoption of sentinel lymph node assessment by race and location. It would be interesting if assess if increasing rates of sentinel node biopsy and lymph node assessment of any type were the same across geographic regions and race.

Reviewer #3:

Using the NCI-SEER database, authors sought to evaluate the utilization of sentinel node biopsy (SNL) for endometrial cancer and cancer-specific mortality associated with SNL between 2003-2018. The utilization of SNL increased significantly over the study period without increased cancer specific mortality associated with SNL use.

1. Lines 38-41; need to include use of selective lymphadenopathy and briefly discuss its weaknesses.
2. The finding of no association of SNL use and excess cancer-specific mortality needs to be contextualized with a. lack of a priori sample size justification. Could this be a beta error? Post hoc power analysis may be useful. B. Important confounders are not known or adjusted for including tumor pathologic characteristics, surgeon experience etc.
3. A brief discussion on why there appears to be a health disparity in the uptake (non White vs. White) of SNL use will be useful.

STATISTICS EDITOR COMMENTS:

Figs 1, 2 & 3: The temporal trends in SLB bx are clearly non-linear, so to summarize them as annual percentage change (i.e., as a linear process, seems inappropriate. The plots appear to represent an exponential relationship, or perhaps a power relationship. Suggest using other functions to find the best fit for the data.

Fig 4: Should use a consistent scale for the x-axes, ie, increments of 12 months.

In Fig 4C and esp 4D (non-endometroid), there is a marked difference in "N" at risk (for the L and S groups) at the various time points. This becomes more discrepant in the later times, as a consequence of increasing utilization of S in later years and therefore skewed differing median follow-up times for S and L. In turn, this affects the power to discern a difference in survival in these cohorts which have generally low mortality rates. Therefore, should be more circumspect about generalizing the NS difference in HR rates.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

- A. OPT-IN: Yes, please publish my point-by-point response letter.
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2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:

- * Include your title page information in the main manuscript file. The title page should appear as the first page of the document. Add any previously omitted Acknowledgements (ie, meeting presentations, preprint DOIs, assistance from non-byline authors).
- * Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript.
- * Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
- * Name the IRB or Ethics Committee institution in the Methods section (if applicable).
- * Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

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4. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also

should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

5. Figures 1-3: okay

Figure 4: Please cite Figure 4D in the manuscript text.

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6. All submissions that are considered for potential publication are run through CrossCheck for originality. The following lines of text match too closely to previously published works.

Cite Matsuo DOI:<https://doi.org/10.1016/j.ygyno.2021.10.085> or paraphrase as applicable.

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8. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry

Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions> and the gynecology data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

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12. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words; Reviews is 300 words; Case Reports is 125 words; Current Commentary articles is 250 words; Executive Summaries, Consensus Statements, and Guidelines are 250 words; Clinical Practice and Quality is 300 words; Procedures and Instruments is 200 words. Please provide a word count.

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Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%).

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18. Figures 1-3: okay

Figure 4: Please cite Figure 4D in the manuscript text.

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- * A point-by-point response to each of the received comments in this letter. Do not omit your responses to the Editorial Office or Editors' comments.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Dec 30, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

John O. Schorge, MD
Deputy Editor, Gynecology

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

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