OBSTETRICS & GYNECOLOGY

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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*
- Email correspondence between the editorial office and the authors*

*The corresponding author has opted to make this information publicly available.

Personal or nonessential information may be redacted at the editor's discretion.

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office:

obgyn@greenjournal.org.

Date: Dec 14, 2018
To: "Mary M Mullen" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-2065

RE: Manuscript Number ONG-18-2065

Wound Complication Rates after Vulvar Excisions for Premalignant Lesions

Dear Dr. Mullen:

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).

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 Jan 04, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Abstract: well written overall. IN results I would mention that there were no significant differences in other predisposing factors (diabetes, BMI etc..)

Introduction: overall good description of background and hypothesis.

Methods: Was there a power or sample size calculation done?

Did you look to see if the use of antibiotics was correlated with higher risk patients (ie: were abx used more often in smokers, diabetics, obese women or those on immunosuppression) and could these correlations impact your analysis? Were there any correlations in your regression?

Results: lines 134-6: does this statement relate to the antibiotic group only, or is it for the entire study group? Can you make that clear?

Discussion: lines 196-202: it may be that the surgery was less aggressive in a second excision due to the previous surgery.

Reviewer #2: Overall a worthwhile investigation with interesting findings. The major flaw in this manuscript is that the results section needs to be restructured significantly. Major revisions and then re-review will be required.

Introduction:

1. Lines 62-64: Are the patients in the referenced studies cancer patients? Or what were the indications for the surgeries in the referenced studies? Is the risk of SSI for benign vulvectomy known?

2. Line 63: 58% wound infection rate after radical and modified vulvectomy was found in another review. (Leminen A, Forss M, Paavonen J. Wound complications in patients with carcinoma of the vulva. Comparison between radical and modified vulvectomies. Eur J Obstet Gynecol Reprod Biol 2000;93: 193-197)

3. Line 64-65: It is not accurate to state that antibiotics are "routinely" administered for vulvectomy. In fact, in this study, a substantial number of patients did not receive antibiotic prophylaxis. If a specific type of vulvectomy is intended, this should be clarified

4. Line 65-69, 75-78: Sentences are awkward

5. Line 70-74: Has been updated to ACOG Practice Bulletin No. 195, which suggests that antibiotic prophylaxis can be considered for vulvectomy, despite the absence of good data.

6. Lines 74-81: Doesn't make sense to address antibiotic prophylaxis, discuss other risk factors for infection, and then return to antibiotic prophylaxis in the next paragraph. Sentences regarding antibiotic prophylaxis should be consolidated/adjacent to each other

Results:

7. The result section needs to be restructured significantly. It would make most sense to structure this section as if this were a trial comparing antibiotic prophylaxis versus none for vulvectomy. Table 1 should be comparison of demographic/pre-operative/operative characteristics in women in these 2 groups (pre-op antibiotics versus none).

8. Table 2 should compare outcomes in women who received antibiotics versus none (currently Table 3)

9. Table 3 should compare characteristics of women who had wound complications versus none (currently Table 2)

10. Table 4 should be multivariate analysis (as it is now)

11. The text should be restructured around tables as described above

13. Lines 127-129: Demographic characteristics should precede the results described here. Demographic characteristics/narrative summary of Table 1 should precede further description of the results in a full paragraph. Rate of wound complication among women who did not receive antibiotics should be immediately followed by statement wound infection rate among women who did receive antibiotics.

14. Line 131-132: What were the other indications for vulvectomy other than VIN? I note that final path is included in Table 1 footnote, but preop indications should be summarized in text

15. Line 132: Did immunosuppressed patient have HIV or use immunosuppressing medications? For patients with HIV, what was median CD4?

16. Line 134-135: What other antibiotics were used? I note they are included in table but brief description should be included in text. Is there any indication how it was determined who should receive antibiotics, and how specific antibiotics were chosen? Did it differ depending on attending physician or time period? Did it differ depending on indication for surgery? Did it differ depending on comorbidities such as immunosuppression or diabetes? Were smokers or other women with risk factors more likely to receive antibiotics? Currently some of this info is contained in Supplemental table 1 but should be summarized in text in lines 144-148.

17. Line 134-136: Again the order of reporting the results does not seem logical here. Why is this result in the same paragraph as the demographic characteristics? Wound outcomes and factors associated with wound outcomes should follow demographics and then other descriptors of the predictor variables.

18. Line 134-136: Are these the results among all patients, or among those who did not receive prophylactic antibiotics?

19. Were wound infection and breakdown analyzed separately as outcomes? This would be interesting and should be included.

20. Table 1:

a* It is not clear what the denominator for these percentages is. For example, for classification of race: 131 women with a wound complication were white (85%). 315 of women without a wound complication were white (82%). This makes sense. However, same logic of reading the table cannot be applied to women who used immunosuppressant drugs: 5 had a wound complication. Presumably this is 5 of the 154 women who had a wound complication (same denominator as above). However, the percentage is listed 32%. 32% of what?

b* In most manuscripts, table 1 serves as a descriptor for demographic characteristics, and is not used for reporting study outcomes. Most readers will use table 1 to see if 2 comparator groups differed. It would make more sense to me to restructure table 1 to contain the following columns:

Characteristic Overall rate in population Received preop antibiotics Didn't receive preop antibiotics p

c* Supplemental Table 1 is structured approximately this way. I would use this as the actual/main Table 1

d* Some of the items in current Table 1 can be included again in Table 2 when the breakdown of columns is Wound complication vs no Wound complications

Table 2:

e* Some items can be consolidated. For example incision width and length do not need to be listed separately. Antibiotic types or suture size can be consolidated or removed

Discussion:

21. Line 174: Because the groups receiving antibiotics differed significantly by several operative characteristics (EBL, incision length/width, surgery type), one cannot conclude that antibiotic use did not have any effect on post op wound complications. The statement that "we did not find a protective impact..." should be less emphatic, perhaps stating that the effect could not be demonstrated in this study, but that this is may be due to inherent differences in the groups receiving and not receiving antibiotics. This is addressed in lines 213-221 as well, but cannot be overemphasized.

22. Line 230: Please see updated ACOG recommendations in PB No. 195

Reviewer #3:

Introduction

The introduction lays out the need for the study succinctly and clearly.

Methods

1. Explain the setting for the study and the use of anesthesia (outpatient surgicenter vs hospital OR, general versus local anesthesia).
2. End point of wound breakdown needs more specific description: separation? To what extent?
3. You call it separation in results, and breakdown in methods.

Results

4. The data forms that collected the variables in chart review seem remarkably complete. The documentation at your institution is impeccable, and not customary. How many charts were reviewed and had incomplete data set(s) and had to be excluded? This could have led to selection bias.
5. Were there any occult malignancies discovered in the cohort studied who did not receive a radical vulvectomy? Any impact on the wound condition postoperatively?
6. The use of univariate and multivariate analysis and the findings concur with studies on abdominal incisions as well. It was explained well in the manuscript.

Discussion

7. Diabetic control (preoperative glucose levels) could be another factor to analyze.
8. You briefly stated the analysis what limited regarding race and ethnicity, and I agree. Make that a separate sentence with emphasis on the limitation to those two races.

STATISTICAL EDITOR'S COMMENTS:

1. lines 132: What were the reasons for the women who were on immunosuppressive drugs? What were the results of sensitivity analysis if those women were omitted from the analysis?
2. Table 1: The counts of women who were using immunosuppressive drugs are low and there is likely insufficient power to generalize the NS of that association.
3. Table 2: There are multiple differences between those women who experienced wound complications and those who did not, including length, depth and width of incision, duration of surgery and need for reconstructive flap/graft, all of which might be associated with higher risk of complications. About 60% of women were given antibiotic prophylaxis, almost evenly distributed among those who did/did not have wound complication. What were the criteria for administering antibiotics? Those who received antibiotics were slightly older and more likely to have ASA class 3-4. What evidence is there that the study was adequately powered to address the question of antibiotic prophylaxis vs wound complications?
4. Table 3: The counts for hematoma, seroma, readmission or wound culture are all low and therefore there is low power to generalize the NS associations.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase 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, as well as subsequent author queries. 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:

1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

2. Please note that all authors need to fill out the "Disclosure of Potential Conflicts of Interest" section of their author agreement form. The relevant authors should resubmit a revised author agreement form if they filled it out erroneously the first time. All updated and missing forms should be uploaded with the revision in Editorial Manager.

3. 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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at <http://links.lww.com/AOG/A515>, and the gynecology data definitions are available at <http://links.lww.com/AOG/A935>.

4. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendices).

Please limit your Introduction to 250 words and your Discussion to 750 words.

5. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

- * All financial support of the study must be acknowledged.
- * Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
- * All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
- * If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

6. 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 limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

7. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmgr.ovid.com/ong/accounts/abbreviations.pdf>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

8. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

9. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

10. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

11. The American College of Obstetricians and Gynecologists' (College) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite College documents in your

manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly. If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if a College document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All College documents (eg, Committee Opinions and Practice Bulletins) may be found via the Resources and Publications page at <http://www.acog.org/Resources-And-Publications>.

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If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at <http://ong.editorialmanager.com>. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

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

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 Jan 04, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982

2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

In compliance with data protection regulations, please contact the publication office if you would like to have your personal information removed from the database.

REVIEWER COMMENTS:

Reviewer #1:

Abstract: well written overall. IN results I would mention that there were no significant differences in other predisposing factors (diabetes, BMI etc..)

This has been added to the abstract (Line 45-46).

Introduction: overall good description of background and hypothesis.

Methods: Was there a power or sample size calculation done?

The power analysis has been included in the methods (Line 129-132).

Did you look to see if the use of antibiotics was correlated with higher risk patients (ie: were abx used more often in smokers, diabetics, obese women or those on immunosuppression) and could these correlations impact your analysis? Were there any correlations in your regression?

Spearman's rank correlation coefficient was used to evaluate if high risk patients were more likely to receive prophylactic antibiotics. There was no association between high risk patients and the administration of prophylactic antibiotics making it unlikely that this would bias our results. This has been added to the methods as well as the results (Line 138-143, Line 181-184).

Results: lines 134-6: does this statement relate to the antibiotic group only, or is it for the entire study group? Can you make that clear?

This refers to the entire study group. This has been clarified in the text (Line 206).

Discussion: lines 196-202: it may be that the surgery was less aggressive in a second excision due to the previous surgery.

Repeat excisions were similar in volume to primary excisions (15.5 vs 14.3cm³, P=0.822) (Line 233-234).

Reviewer #2: Overall a worthwhile investigation with interesting findings. The major flaw in this manuscript is that the results section needs to be restructured significantly. Major revisions and then re-review will be required.

Introduction:

1. Lines 62-64: Are the patients in the referenced studies cancer patients? Or what were the indications for the surgeries in the referenced studies? Is the risk of SSI for benign vulvectomy known?

These studies specifically evaluated patients with a cancer diagnosis. The risk of SSI following vulvar excision for benign or premalignant indications is unknown. This information has been added to the manuscript (Line 64, 67-68).

2. Line 63: 58% wound infection rate after radical and modified vulvectomy was found in another review. (Leminen A, Forss M, Paavonen J. Wound complications in patients with carcinoma of the vulva. Comparison between radical and modified vulvectomies. Eur J Obstet Gynecol Reprod Biol 2000;93:193-197)

This 58% wound infection rate reported in this paper includes patients who underwent radical en block vulvectomy (RV). Given this procedure is no longer traditionally used we simply reported the infection rate for modified radical vulvectomies which is the more common practice.

3. Line 64-65: It is not accurate to state that antibiotics are "routinely" administered for vulvectomy. In fact, in this study, a substantial number of patients did not receive antibiotic prophylaxis. If a specific type of vulvectomy is intended, this should be clarified

[This statement specifically refers to modified radical vulvectomies. This has been clarified in the text \(Line 66\).](#)

4. Line 65-69, 75-78: Sentences are awkward

[These sentences have been clarified \(Line 68-75\).](#)

5. Line 70-74: Has been updated to ACOG Practice Bulletin No. 195, which suggests that antibiotic prophylaxis can be considered for vulvectomy, despite the absence of good data.

[This reference has been added to the manuscript and the ACOG recommendations have updated per the following statement "In the 195th practice bulletin addressing the "Prevention of Infection after Gynecologic Procedures", ACOG recognizes the paucity of literature regarding SSI after a wide local excision or partial/complete vulvectomy. However, they identified a vulvectomy as similar to other clean-contaminated procedures and therefore report that antibiotic prophylaxis is acceptable despite the absence of data" \(Line 78-82\).](#)

6. Lines 74-81: Doesn't make sense to address antibiotic prophylaxis, discuss other risk factors for infection, and then return to antibiotic prophylaxis in the next paragraph. Sentences regarding antibiotic prophylaxis should be consolidated/adjacent to each other

[We have edited the introduction to flow more appropriately.](#)

Results:

7. The result section needs to be restructured significantly. It would make most sense to structure this section as if this were a trial comparing antibiotic prophylaxis versus none for vulvectomy. Table 1 should be comparison of demographic/pre-operative/operative characteristics in women in these 2 groups (pre-op antibiotics versus none).

[Table 1 has been changed as suggested.](#)

8. Table 2 should compare outcomes in women who received antibiotics versus none (currently Table 3)

[Table 2 has been changed as suggested.](#)

9. Table 3 should compare characteristics of women who had wound complications versus none (currently Table 2)

[Table 3 has been changed as suggested.](#)

10. Table 4 should be multivariate analysis (as it is now)

[Table 4 is the multivariate analysis as suggested.](#)

11. The text should be restructured around tables as described above

[The text has been appropriately restructured.](#)

13. Lines 127-129: Demographic characteristics should precede the results described here. Demographic characteristics/narrative summary of Table 1 should precede further description of the results in a full paragraph. Rate of wound complication among women who did not receive antibiotics should be immediately followed by statement wound infection rate among women who did receive antibiotics.

The results section has been rearranged as suggested.

14. Line 131-132: What were the other indications for vulvectomy other than VIN? I note that final path is included in Table 1 footnote, but preop indications should be summarized in text

This information was added to the manuscript (Line 157-160).

15. Line 132: Did immunosuppressed patient have HIV or use immunosuppressing medications? For patients with HIV, what was median CD4?

The text has been clarified to state "Thirty-eight percent were obese and 6.1% used immunosuppressant medications including tacrolimus, mycophenolate mofetil, or disease-modifying antirheumatic drugs" (Line 161-163). We do not have data available regarding CD4 counts in HIV patients.

16. Line 134-135: What other antibiotics were used? I note they are included in table but brief description should be included in text. Is there any indication how it was determined who should receive antibiotics, and how specific antibiotics were chosen? Did it differ depending on attending physician or time period? Did it differ depending on indication for surgery? Did it differ depending on comorbidities such as immunosuppression or diabetes? Were smokers or other women with risk factors more likely to receive antibiotics? Currently some of this info is contained in Supplemental table 1 but should be summarized in text in lines 144-148.

The antibiotic choices are included in the manuscript as well as the statement "The choice of antibiotic was based on the patient's allergies and surgeon preference." Additional statistics were run to evaluate the association between antibiotic use and patients at high risk for infection as well as the association between type of antibiotic administered and surgeon, date of surgery, and indication for surgery. "Antibiotic choice was correlated with the surgeon ($P=0.013$)" (Line 166-169).

17. Line 134-136: Again the order of reporting the results does not seem logical here. Why is this result in the same paragraph as the demographic characteristics? Wound outcomes and factors associated with wound outcomes should follow demographics and then other descriptors of the predictor variables.

The results section has been edited as suggested.

18. Line 134-136: Are these the results among all patients, or among those who did not receive prophylactic antibiotics?

These results apply to all patients. This has been clarified (Line 206).

19. Were wound infection and breakdown analyzed separately as outcomes? This would be interesting and should be included.

This was analyzed separately and included in the results section (Line 194-195).

20. Table 1:

a* It is not clear what the denominator for these percentages is. For example, for classification of race: 131 women with a wound complication were white (85%). 315 of women without a wound complication were white (82%). This makes sense. However, same logic of reading the table cannot be applied to women who used immunosuppressant drugs: 5 had a wound complication. Presumably this is 5 of the 154 women who had a wound complication (same denominator as above). However, the percentage is listed 32%. 32% of what?

We apologize for the confusion. This was a mistake. The percent is 3.2%. This has been edited in Table 3.

b* In most manuscripts, table 1 serves as a descriptor for demographic characteristics, and is not used for reporting study outcomes. Most readers will use table 1 to see if 2 comparator groups differed. It would make more sense to me to restructure table 1 to contain the following columns:

Characteristic	Overall rate in population	Received preop antibiotics	Didn't receive preop antibiotics
p			

Table 1 has been changed to include demographics of patients who received antibiotics compared to those who did not.

c* Supplemental Table 1 is structured approximately this way. I would use this as the actual/main Table 1

Supplemental Table 1 has been made Table 1.

d* Some of the items in current Table 1 can be included again in Table 2 when the breakdown of columns is Wound complication vs no Wound complications

These tables have been consolidated.

Table 2:

e* Some items can be consolidated. For example incision width and length do not need to be listed separately. Antibiotic types or suture size can be consolidated or removed

These tables have been consolidated.

Discussion:

21. Line 174: Because the groups receiving antibiotics differed significantly by several operative characteristics (EBL, incision length/width, surgery type), one cannot conclude that antibiotic use did not have any effect on post op wound complications. The statement that "we did not find a protective impact..." should be less emphatic, perhaps stating that the effect could not be demonstrated in this study, but that this is may be due to inherent differences in the groups receiving and not receiving antibiotics. This is addressed in lines 213-221 as well, but cannot be overemphasized.

The following was added to the discussion "A protective effect of antibiotics was not demonstrated in this study, but this could be due to inherent differences in the groups receiving and not receiving prophylactic antibiotics" (Line 239-241).

22. Line 230: Please see updated ACOG recommendations in PB No. 195

The discussion has been updated to include the recommendations from the new practice bulletin (Line 302-303).

Reviewer #3:

Introduction

The introduction lays out the need for the study succinctly and clearly.

Methods

1. Explain the setting for the study and the use of anesthesia (outpatient surgicenter vs hospital OR, general versus local anesthesia).

This has been clarified in the methods (Line 116-117).

2. End point of wound breakdown needs more specific description: separation? To what extent?
This has been clarified in the text- "This was defined as the presence of wound separation of any extent, infection, or both documented in the surgeon's follow-up postoperative visit note" (Line 123-124).

3. You call it separation in results, and breakdown in methods.
This has been corrected in the methods section as noted above (Line 123-124).

Results

4. The data forms that collected the variables in chart review seem remarkably complete. The documentation at your institution is impeccable, and not customary. How many charts were reviewed and had incomplete data set(s) and had to be excluded? This could have led to selection bias.
In total 645 charts were initially reviewed. Upon collection of data it was revealed that procedures completed prior to 1/2007 had inadequate documentation due to paper charts. Therefore, 61 procedures done prior to 1/2007 were excluded. Forty seven procedures performed 1/2007-1/2017 were radical vulvectomies, and therefore these were also excluded from analysis. This resulted in a total of 537 patients to be evaluated. Documentation for these patients was completed not only by the surgeon but also the anesthesia team. Per hospital policy, standardized documentation was required for all surgical procedures resulting in thorough and reliable documentation. Given cases were excluded based on an entire time period and on a surgery that was not being evaluated in this study as opposed to excluding individual cases based on missing information we do not believe there was any selection bias.

5. Were there any occult malignancies discovered in the cohort studied who did not receive a radical vulvectomy? Any impact on the wound condition postoperatively?
All patients with malignancy noted on final pathology were excluded (Line 114-115) and therefore we are unable to draw conclusions regarding this patient population.

6. The use of univariate and multivariate analysis and the findings concur with studies on abdominal incisions as well. It was explained well in the manuscript.
Thank you for the comment.

Discussion

7. Diabetic control (preoperative glucose levels) could be another factor to analyze.
We agree this would be a beneficial analysis, but we do not have adequate record of preoperative glucose measurements or hemoglobin A1Cs on these patients to include in the analysis.

8. You briefly stated the analysis what limited regarding race and ethnicity, and I agree. Make that a separate sentence with emphasis on the limitation to those two races.
This has been emphasized in the results with the statement- "Second, this study had minimal racial and ethnic diversity with >80% of patients included in the study being white which limited our observations" (Line 294-296).

STATISTICAL EDITOR'S COMMENTS:

1. lines 132: What were the reasons for the women who were on immunosuppressive drugs? What were the results of sensitivity analysis if those women were omitted from the analysis?

The immunosuppressive medications taken by patients in this study have been added to the manuscript (Line 161-163). Sensitivity analysis excluding women on immunosuppressive drugs demonstrated no significant differences in wound complications between those who received prophylactic antibiotics and those who did not ($P=0.359$) (Line 144-146, 192-193).

2. Table 1: The counts of women who were using immunosuppressive drugs are low and there is likely insufficient power to generalize the NS of that association.

This has been added to the discussion in the limitations section- "The absolute number of patients using immunosuppressive drugs as well as the number of women with hematomas, seromas, wound cultures, or requiring readmission was low, and therefore there is low power to generalize these nonsignificant associations between patients who received preoperative antibiotics and those who did not" (Line 296-300).

3. Table 2: There are multiple differences between those women who experienced wound complications and those who did not, including length, depth and width of incision, duration of surgery and need for reconstructive flap/graft, all of which might be associated with higher risk of complications. About 60% of women were given antibiotic prophylaxis, almost evenly distributed among those who did/did not have wound complication. What were the criteria for administering antibiotics? Those who received antibiotics were slightly older and more likely to have ASA class 3-4. What evidence is there that the study was adequately powered to address the question of antibiotic prophylaxis vs wound complications?

Criteria for administration of antibiotics as well as correlations between antibiotic administered, patient comorbidities, surgeon, indication for surgery, or year of surgery were included in the results (Line 166-169).

The power analysis was included in the methods (129-132).

4. Table 3: The counts for hematoma, seroma, readmission or wound culture are all low and therefore there is low power to generalize the NS associations.

This has been added to the discussion in the limitations section as mentioned above (Line 296-300).

Daniel Mosier

From: Mullen, Mary [REDACTED]
Sent: Wednesday, January 16, 2019 5:13 PM
To: Daniel Mosier
Subject: RE: Manuscript Revisions: ONG-18-2065R1
Attachments: 18-2065R1 ms (1-15-19v2) MM 1-15.docx; Response to Editor 1-15.docx

Daniel,

Thank you so much for your thorough comments. We really appreciate the opportunity to have our article considered for publication in *Obstetrics and Gynecology*.

We have addressed each comment and tracked our changes in the manuscript and the response to the editor attached.

Please let us know if you have any questions or if there is anything further you need from us.

Thanks,
Maggie

Mary M. Mullen, MD
Gynecologic Oncology Fellow (PGY5)
Barnes Jewish Hospital/Washington University in St. Louis
[REDACTED]

From: Daniel Mosier [mailto:dmosier@greenjournal.org]
Sent: Tuesday, January 15, 2019 2:23 PM
To: Mullen, Mary [REDACTED]
Subject: Manuscript Revisions: ONG-18-2065R1

Dear Dr. Mullen,

Thank you for submitting your revised manuscript. It has been reviewed by the editor, and there are a few issues that must be addressed before we can consider your manuscript further:

1. Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes.
2. LINE 23: Dr. Matthew Powell will need to complete our electronic Copyright Transfer Agreement, which was sent to them through Editorial Manager.
3. LINE 27: Please provide the city, state, and dates of the meeting.
4. LINE 42: The n's in table 1 add up to 537. Is 534 correct? Please be sure this is stated in the body of your paper. Statements and data that appear in the Abstract must also appear in the body text for consistency.
5. LINE 64: It is unclear what is meant here: 'partial' radical vulvectomy? Typically vulvectomy is either simple or radical and complete or partial – so please either clarify what 'modified' is intended to mean or use a different term here and also line 73
6. LINE 86: The unfamiliar reader might falsely assume these are 3 different procedures. It would be better to rewrite this sentence to point out the interchangeable terms simple partial vulvectomy and WLE both

representing the same operation. It could be argued that you should exclude the complete vulvectomies all together (n = 4)

7. LINE 89 (Deleted text): The retrospective nature of this study does not allow for causal statements, only possible associations.
8. LINE 90: Please reword to better describe what you were looking at (identify predictors? Risk factors?)
9. LINE 102: See comment above to reword for clarity
10. LINE 122: Citation here
11. LINE 124: Unclear here whether you are proposing this sample size to be able to detect a 0.5% reduction in wound complication rate? This seems implausible. Please clarify
12. LINE 144 (Deleted Text): This is restated in line 156-157 and flows better there.
13. LINE 164: Confusing here to say 154 pts, but then 37+140 = 167. Better to just keep it simple. Following sentence unnecessary.
14. LINE 172: Should clarify former or current smokers – it is not clear where the 60.6 and 76.6 are coming from.
15. LINE 183: This volume exceeds the upper limit of the ranges previously described and must be erroneous(?)
16. LINE 210: This is entirely speculative. Please reword to first state the association you observed, while pointing out the possibility this is not a valid finding, could be because of familiarity with postop care routine, or some other reasons.
17. LINE 231: This would be the most convenient place to clarify this is a clinically irrelevant difference in EBL with total estimation
18. LINE 241: It is also a limitation that you did not distinguish where on the vulva the surgery occurred – ie near the anus would be higher risk than anterior
19. LINE 250: You should point out here that even though your data did not suggest ANY benefit, this is an entirely hypothesis-generating study design and not intended to definitively answer the question. Yet, due to high rate of wound complications and inconsistent use of antibiotics that you observed with little other data to guide future practice, a prospective study is indicated.

Please let me know if you have any questions. Your prompt response to these queries will be appreciated; please respond no later than COB on **Thursday, January 17th**.

Sincerely,

-Daniel Mosier

Daniel Mosier

Editorial Assistant

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