

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)*

**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: Oct 15, 2020
To: "Nathan King" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-20-2446

RE: Manuscript Number ONG-20-2446

Laparoscopic Major Vascular Injuries in Benign Gynecologic Surgery: A Systematic Review

Dear Dr. King:

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 14 days from the date of this letter. If we have not heard from you by Oct 29, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

This is a systematic review regarding the incidence, location, etiology, and mortality of major vascular injuries in gynecologic laparoscopy for benign indications. I thank the editors for giving me the chance to review this manuscript and thank the authors for their contribution to the field.

Strengths:

- * This is an important descriptive question to answer, and a systematic review is the best way to answer this question given the rarity of the complication.
- * The authors wisely compare the incidence of MVI in prospective and retrospective studies to assess the risk of bias.
- * The review includes information about how the vessel injury occurred and how it was managed, where that information was included in the relevant studies.

Limitations:

- * As acknowledged by the authors, many of the studies on laparoscopic benign gynecologic surgery do not report complications in such a way that the prevalence of major vessel injuries can be extracted from their data AND/OR do not report how the vessel injury happened, so the body of useful literature from within the body of total literature on laparoscopy for benign gynecologic surgery is shockingly little.
- * The quality of studies contributing to this body of literature is not assessed or summarized in the
- * The authors do not describe how and how clearly the study had to report on MVI outcomes in order to be included.

Comments for authors by section

Abstract

- * The abstract, despite the limited word count, should clearly defined what is considered a major vessel injury. Some would consider the inferior epigastric vessels not to be "major", and some would. It should be clear from reading the abstract alone what the authors defined as a major vessel.

Introduction

- * Line 98-99: This is a picky question of precise wording, but technically for hysterectomy vaginal approach, which rarely lacerates major vessels, is the standard of care. As this article is about laparoscopic and robotically-assisted surgeries, I would reword this to clarify that laparoscopic and robotic-assisted surgeries are considered superior in patient outcomes to open abdominal surgery.
- * Line 115-116: Even though this is a descriptive primary aim, to describe the incidence of major vessel injury, a hypothesis should be stated here. Such as: we anticipated the incidence to be low (<0.5% [or something like that]) and

that most major vessel injuries would occur at abdominal entry.

Methods

* Parts of the PICOS are listed here (Population, Intervention, Comparator [if relevant], Outcomes, and Study types) and described, but there should be stricter and clearer criteria here for how it was determined that the study gave sufficient information to meet the authors' PICOS criteria. Some things need to be more clearly spelled out for the reader to know how to interpret these data. For example, what happened if a study did not mention MVI? Was it included and the MVI was assumed to be zero, or was it excluded as it did not mention vascular injury?

Results

* In general, it would be very helpful to have a count of how many studies did not include information about something being reported here, so we can have some idea how the denominators were calculated. For example, if a study was included and reported on major vessel injuries, but did not have information on how it occurred and how it was managed, there should be a sentence about the number of studies like this in the Results.

* In general, numbers (n and denominator) should be reported in addition to percentages in these results. For example, in Line 179, where it is said that 54.9% of injuries were managed by laparotomy, we need to know the number managed by laparotomy and the denominator (studies that stated how it was managed), so we know how the percentage was calculated.

Discussion

* The summary of results should also include, for a systematic review, the overall quality of the literature on the topic and how well the field is doing reporting these complications and detailing their nature of occurrence and repair. It seems from reading this review that this is poor, and the authors should comment on this from their now-expertise in the evidence on the topic.

* The authors acknowledge well the limitations of the study.

Reviewer #2:

This study does have many limitations inherent in the manuscripts included in this review.

This study DOES NOT serve as a comprehensive review of major vascular injuries during gynecologic laparoscopy for benign indication.

Unfortunately, most vascular injuries are not reported in the literature. They are reported in courts of law. I suspect that they would double your numbers at the very least.

One thousand and ninety-seven studies were screened for inclusion with 147 full-text articles reviewed.

Sixty-one studies published between 1978 and 2015 met inclusion criteria, representing 199,305 surgeries.

But case reports were not before reported. Why?

Major vascular injuries to the iliac artery or vein, aorta, and inferior vena cava represented less than half the cases.

This systematic review demonstrated a 0.090% incidence of major vascular injury during gynecologic laparoscopy for benign indications. The rate of mortality directly from an MVI was found to be exceedingly rare at 0.001%, or 1 in every 100,000 laparoscopic procedures.

But remember that major vascular injuries to the iliac artery or vein, aorta, and inferior vena cava presented less than half the time. Over half the cases involved the inferior epigastric vessels. This makes even a better case for the lawyers!

A total of 179 major vascular injuries were reported with an incidence of 0.091%.

Major vascular injuries to the iliac artery or vein, aorta, and inferior vena cava presented less than half the time.

The inferior epigastric vessels were the most commonly

injured vessel, comprising 47.5% of all injuries. Of the remaining injuries, the following vessels were involved: iliac artery or vein (12.3%, aorta (3.9%, and inferior vena cava (2.2%,). The majority occurred during abdominal entry (82.3%, while the remainder occurred during surgical dissection (17.7%.

Only two of the 179 MVIs resulted in death for an overall mortality rate from vascular injuries of 0.001%.

Conclusion: The incidence of major vascular injury in gynecologic laparoscopy for benign indication remains very low at 0.091%.

Some studies may not have considered inferior epigastric injuries as major vascular injuries and thus may not have reported them. Despite this, greater than half of the papers that reported at least one MVI included injuries to the inferior epigastric vessels. Additionally, of the two deaths reported in our review, one was the result of an epigastric vessel laceration. Sounds like a great paper!

Reviewer #3:

This manuscript summarizes a systematic review that investigates major vascular injuries in benign gynecologic laparoscopic surgeries. The authors concluded that the incidence and mortality from major vascular injury in these surgeries were extremely low and nearly half of those injuries were attributed to the inferior epigastric vessels.

Specific comments and recommendations:

- * Abstract (page 3, lines 54-56) and Results (page 7, lines 153-156): there is a discrepancy between the number of studies included and surgeries performed in these 2 sections.
- * Methods (Page 6, Lines 128-141): Did the authors include any studies pertaining to single incision laparoscopy? Since the authors reported that nearly half the injuries were from the inferior epigastric vessels, can they draw conclusion if single incision laparoscopy had lower vascular injury rates?
- * Discussion (Page 10, lines 242-244): I agree with the authors that there are inconsistencies among studies in allocating inferior epigastric vessels injury as a major vascular injury. However, are there any guidelines or evidence-based society statements that recommend it to be classified in that category? If so, please add the reference here to support your analysis.
- * Discussion (page 9, lines 218-220): While the authors cited the Cochrane review by Ahmad et al 2015 that concluded that there were no differences in vascular injuries between entry techniques, that review was different from the authors' for example in including non-gynecological surgeries. Since the authors demonstrated a high incidence of inferior epigastric vessels injury in their review, I think it would benefit the readers to understand what type of trocar system that might have contributed to this result.
- * Discussion (Page 10, lines 244-245): I recommend the authors to add the details of the 2 reported mortalities in the manuscript.
- * Table 1 (page 12): The authors included studies from a wide geographic distribution across the review period. Could the authors draw conclusion whether vascular injuries were associated with the country income level?
- * Table 3 (page 17): In a published review focused about morcellator related complications, there were 27 injuries to the vascular system from the morcellator (Milad MP, Milad EA. Laparoscopic morcellator-related complications. Journal of minimally invasive gynecology. 2014 May 1;21(3):486-91). I think it would be very informative to the readers to know the causes for the injury in the surgical phase in this review. For example, were there any morcellator related vascular injuries in the included studies?
- * Table 5 (page 19): I noticed that the authors included 1 study that included robotic hysterectomy. Can the authors confirm that for the whole period of the studies included (1978-2016) there were only 1 study for robotic hysterectomy and vascular injuries? And if so, I am confused because the authors included studies with laparoscopies where no vascular injuries were reported.

STATISTICAL EDITOR COMMENTS:

lines 61-62: The 95% CI should be 0.077%-.104%. (as in Table 2)

lines 63-65: The total number of vascular injuries in this series was 179, then subdivided by vessel injured. Those % should all be rounded to nearest integer %, along with their respective CIs, based on the number of counts, not cited to nearest 0.1% or .01%, as currently formatted.

lines 68-69: There were only 2 deaths, so the CIs should be based on either Poisson or binomial assumptions, not the usual normality assumption. As such, the 95%CI = 0 to 0.004%

Table 2: Need to make appropriate changes to precision of citing the CIs and estimates of proportions. The CI for iliac vein is incorrect, it cannot be a negative number (-0.21,3.56)%. Based on the denominator = 199,305 and the numerators given, the CI for Aorta = (0.001,.007)%, IVC = (.001,.005)%, Iliac vessels = (.007,.017)%, Iliac artery = (.005,.013)%, Iliac vein = (0, .004)%, the high proportion of other/not otherwise specified makes the estimation of the other %s imprecise and possibly biased, which should be a caveat in the discussion. The 179/199,305 results in 0.090%, or more precisely 0.0898%, which does not round to 0.091%

Tables 3, 4: As noted earlier, need to round the %s and their CIs. Need to explain to reader in footnote what is being compared and by what stats test that results in the p-values cited.

General: Omitted from the discussion is the possibility of selection bias, which may have resulted in either over or underestimation of the incidence rates. This is a large series, but is not a database of all surgeries nor of all vascular injuries.

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. 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.
- B. OPT-OUT: No, please do not publish my point-by-point response letter.

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at <http://ong.editorialmanager.com>. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, RECORD, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

4. 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.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Review articles should not exceed 25 typed, double-spaced pages (6,250 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

6. Specific rules govern the use of acknowledgments in the journal. Please note 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 response in the journal's electronic author 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).

7. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

8. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's

conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

9. 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.

10. 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.

11. 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.

12. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

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%).

13. 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.

14. Please review examples of our current reference style at <http://ong.editorialmanager.com> (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources"). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG 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 (exceptions could include manuscripts that address items of historical interest). 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 an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found at the Clinical Guidance page at <https://www.acog.org/clinical> (click on "Clinical Guidance" at the top).

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Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

If you choose to revise your manuscript, please submit your revision through Editorial Manager at <http://ong.editorialmanager.com>. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

* A confirmation that you have read the Instructions for Authors (<http://edmgr.ovid.com/ong/accounts/authors.pdf>), and

* 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 Oct 29, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

John O. Schorge, MD
Associate Editor, Gynecology

2019 IMPACT FACTOR: 5.524
2019 IMPACT FACTOR RANKING: 6th out of 82 ob/gyn journals

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/ong/login.asp?a=r>). Please contact the publication office if you have any questions.

Cover Letter

Re: Manuscript ONG-20-2446

Laparoscopic Major Vascular Injuries in Benign Gynecologic Surgery: A Systematic Review

Dear Editors:

Thank you for considering our manuscript entitled "Laparoscopic Major Vascular Injuries in Benign Gynecologic Surgery: A Systematic Review" for publication in the esteemed *Obstetrics and Gynecology*. We appreciate the time and effort that the reviewers have taken to read and provide constructive feedback on our study. We have thoroughly reviewed these recommendations and edited the manuscript to the best of our ability to comply with the journal's standard. We also followed the MOOSE guidelines for systematic review and uploaded the annotated checklist. On the following pages, please find an itemized list of queries and responses as requested. Please reach out if there are any further questions or concerns. We greatly appreciate your time and consideration.

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Sincerely,

A handwritten signature in black ink that reads "Nathan King". The signature is written in a cursive, flowing style.

Nathan King, MD

REVIEWER COMMENTS:

Reviewer #1:

Strengths:

- * This is an important descriptive question to answer, and a systematic review is the best way to answer this question given the rarity of the complication. ✓
- * The authors wisely compare the incidence of MVI in prospective and retrospective studies to assess the risk of bias. ✓
- * The review includes information about how the vessel injury occurred and how it was managed, where that information was included in the relevant studies. ✓

Limitations:

- * As acknowledged by the authors, many of the studies on laparoscopic benign gynecologic surgery do not report complications in such a way that the prevalence of major vessel injuries can be extracted from their data AND/OR do not report how the vessel injury happened, so the body of useful literature from within the body of total literature on laparoscopy for benign gynecologic surgery is shockingly little. ✓

- * The quality of studies contributing to this body of literature is not assessed or summarized in the

The comment was not received by us as a complete statement, however, from an additional comment under “Discussion” from the same reviewer, it can be assumed that the author is highlighting the lack of discussion about the quality of included studies in the discussion. This has been addressed as referenced under the reviewers similar comment below under “Discussion” and as an addition to the text (See Edit #5)

- * The authors do not describe how and how clearly the study had to report on MVI outcomes in order to be included.

Text has been added to clarify this pertinent information (See Edit#4a and #4b)

Comments for authors by section

Abstract

- * The abstract, despite the limited word count, should clearly defined what is considered a major vessel injury. Some would consider the inferior epigastric vessels not to be "major", and some would. It should be clear from reading the abstract alone what the authors defined as a major vessel.

Abstract has been edited to include this information (See Edit #14).

Introduction

- * Line 98-99: This is a picky question of precise wording, but technically for

hysterectomy vaginal approach, which rarely lacerates major vessels, is the standard of care. As this article is about laparoscopic and robotically-assisted surgeries, I would reword this to clarify that laparoscopic and robotic-assisted surgeries are considered superior in patient outcomes to open abdominal surgery.

We appreciate this insightful comment. Text has been changed to indicate that it is the laparoscopic approach specifically that have been shown to be superior to laparotomy (See Edit #2). We kept the first sentence as “minimally invasive surgery,” which includes the vaginal approach as well, given that the first sentence is referring to all gynecologic surgery for benign disease (not just hysterectomy), thus this broader definition fits what is “standard of care” more inclusively. (For example, benign gyn surgeries include many other surgeries behind hysterectomy, namely adnexal surgery, of which laparoscopy in the gold standard)

* Line 115-116: Even though this is a descriptive primary aim, to describe the incidence of major vessel injury, a hypothesis should be stated here. Such as: we anticipated the incidence to be low (<0.5% [or something like that]) and that most major vessel injuries would occur at abdominal entry.

Text has been added to reflect our team’s hypothesis prior to embarking on our review. (See Edit #3)

Methods

* Parts of the PICOS are listed here (Population, Intervention, Comparator [if relevant], Outcomes, and Study types) and described, but there should be stricter and clearer criteria here for how it was determined that the study gave sufficient information to meet the authors' PICOS criteria. Some things need to be more clearly spelled out for the reader to know how to interpret these data. For example, what happened if a study did not mention MVI? Was it included and the MVI was assumed to be zero, or was it excluded as it did not mention vascular injury?

Text has been added to clarify that only studies that specifically reported whether or not MVIs occurred were included (See Edit #4a). If a study did not specify on MVIs, it was excluded, rather than just assuming that no injuries occurred. This is essential for the accuracy of the review, so we thank the reviewer for asking for clarification.

Results

* In general, it would be very helpful to have a count of how many studies did not include information about something being reported here, so we can have some idea how the denominators were calculated. For example, if a study was included and reported on major vessel injuries, but did not have information on how it occurred and how it was managed, there should be a sentence about the number of studies like this in the Results.

Text has been added to delineate how many studies reported on the information used in each specific analysis that is denoted. See these changes throughout the results section.

* In general, numbers (n and denominator) should be reported in addition to

percentages in these results. For example, in Line 179, where it is said that 54.9% of injuries were managed by laparotomy, we need to know the number managed by laparotomy and the denominator (studies that stated how it was managed), so we know how the percentage was calculated.

Text has been added to delineate the numerator and denominator when reporting percentages of injuries as requested. See these changes throughout the results section.

Discussion

* The summary of results should also include, for a systematic review, the overall quality of the literature on the topic and how well the field is doing reporting these complications and detailing their nature of occurrence and repair. It seems from reading this review that this is poor, and the authors should comment on this from their now-expertise in the evidence on the topic.

Text has been added to comment on both the quality of evidence and the field's reporting on these complications (See Edit #5)

* The authors acknowledge well the limitations of the study. ✓

Reviewer #2:

Please note that this reviewer included many direct texts from our manuscript within his/her own comments, thus this text (from the manuscript) has been italicized to help facilitate responding to the reviewer's comments themselves.

This study does have many limitations inherent in the manuscripts included in this review.

This study DOES NOT serve as a comprehensive review of major vascular injuries during gynecologic laparoscopy for benign indication. Unfortunately, most vascular injuries are not reported in the literature. They are reported in courts of law. I suspect that they would double your numbers at the very least.

We appreciate this insightful comment. It is likely true that many vascular injuries, due to their severe nature, may prompt legal action. In accords with published guidelines for conducting systematic reviews, court records are not part of the data that can be included, especially as these individual cases would not have a denominator of total laparoscopic cases to allow calculation of incidence.

One thousand and ninety-seven studies were screened for inclusion with 147 full-text articles reviewed.

Sixty-one studies published between 1978 and 2015 met inclusion criteria, representing

199,305 surgeries.

But case reports were not before reported. Why?

Case Reports are not included in this systematic review as they do not provide information on the total number of surgeries from which the complications arose. Without this information (the denominator), these cases cannot be used to calculate incidence. If you were to add individual case reports as vascular injuries, but not add the denominator to the total number of surgeries this would falsely enlarge your incidence of MVI.

Major vascular injuries to the iliac artery or vein, aorta, and inferior vena cava represented less than half the cases.

This systematic review demonstrated a 0.090% incidence of major vascular injury during gynecologic laparoscopy for benign indications. The rate of mortality directly from an MVI was found to be exceedingly rare at 0.001%, or 1 in every 100,000 laparoscopic procedures.

But remember that major vascular injuries to the iliac artery or vein, aorta, and inferior vena cava presented less than half the time. Over half the cases involved the inferior epigastric vessels. This makes even a better case for the lawyers!

We appreciate this insightful comment. We have made sure to both highlight further the limitations of the studies included and specifically address the inclusion of inferior epigastric vessels in our study within the discussion. As noted in our discussion as well one of the two deaths was from an injury to the inferior epigastric laceration, further highlighting the importance of inclusion.

A total of 179 major vascular injuries were reported with an incidence of 0.091%.

Major vascular injuries to the iliac artery or vein, aorta, and inferior vena cava presented less than half the time.

The inferior epigastric vessels were the most commonly injured vessel, comprising 47.5% of all injuries. Of the remaining injuries, the following vessels were involved: iliac artery or vein (12.3%, aorta (3.9%, and inferior vena cava (2.2%,). The majority occurred during abdominal entry (82.3%, while the remainder occurred during surgical dissection (17.7%.

Only two of the 179 MVIs resulted in death for an overall mortality rate from vascular injuries of 0.001%.

Conclusion: The incidence of major vascular injury in gynecologic laparoscopy for benign indication remains very low at 0.091%.

Some studies may not have considered inferior epigastric injuries as major vascular injuries and thus may not have reported them. Despite this, greater than half of the papers that reported at least one MVI included injuries to the inferior epigastric vessels. Additionally, of the two deaths reported in our review, one was the result of an epigastric vessel laceration. Sounds like a great paper! ✓

Thank you!

Reviewer #3:

This manuscript summarizes a systematic review that investigates major vascular injuries in benign gynecologic laparoscopic surgeries. The authors concluded that the incidence and mortality from major vascular injury in these surgeries were extremely low and nearly half of those injuries were attributed to the inferior epigastric vessels.

Specific comments and recommendations:

* Abstract (page 3, lines 54-56) and Results (page 7, lines 153-156): there is a discrepancy between the number of studies included and surgeries performed in these 2 sections.

Corrected in the abstract to reflect accurate numbers

* Methods (Page 6, Lines 128-141): Did the authors include any studies pertaining to single incision laparoscopy? Since the authors reported that nearly half the injuries were from the inferior epigastric vessels, can they draw conclusion if single incision laparoscopy had lower vascular injury rates?

To our best knowledge from the details supplied in the studies, 2 studies included single-site laparoscopy representing a total of * procedures. Neither of these studies reported MVIs, however, owing to the very low number of studies in comparison to the total procedure number within the series, strong conclusions about how the risks of these procedures specifically differs cannot be made. Additionally, some of the included studies report a wide range of procedures, including diagnostic laparoscopy, which may have been performed through a single site without denoting this, making any analysis of this imprecise. We have added text that includes this as a limitation in our discussion (see Edit #6). We are intrigued by this interesting question that the reviewed proposes, and hope this can be examined in future, focused research as this technique becomes more widespread.**

* Discussion (Page 10, lines 242-244): I agree with the authors that there are inconsistencies among studies in allocating inferior epigastric vessels injury as a major vascular injury. However, are there any guidelines or evidence-based society statements that recommend it to be classified in that category? If so, please add the reference here to support your analysis.

Guidelines to this effect could not be identified, and text has been added to address this and recommend future guidelines to speak on it with more clarity (See Edit #7).

* Discussion (page 9, lines 218-220): While the authors cited the Cochrane review

by Ahmad et al 2015 that concluded that there were no differences in vascular injuries between entry techniques, that review was different from the authors' for example in including non-gynecological surgeries. Since the authors demonstrated a high incidence of inferior epigastric vessels injury in their review, I think it would benefit the readers to understand what type of trocar system that might have contributed to this result.

We appreciate this insightful comment. Unfortunately, given the inconsistent reporting of details of the surgeries, which rarely included the type of trocar systems used, this analysis is out of the scope of this review. We have added text to our conclusion that addresses this limitation (See Edit #6). This would be another interesting question for future research as trocar systems have advanced over the years to be more “safe.”

* Discussion (Page 10, lines 244-245): I recommend the authors to add the details of the 2 reported mortalities in the manuscript.

Text added in the results section to describe details of the two deaths (See Edit #7)

* Table 1 (page 12): The authors included studies from a wide geographic distribution across the review period. Could the authors draw conclusion whether vascular injuries were associated with the country income level?

This is an intriguing and insightful question. We have thought about this thoroughly and came to the following conclusion. We feel that doing a sub-analysis based solely on country income level may not answer the true question of interest, which we suggest is whether patients at lower socio-economic status are more susceptible to injury. We feel evaluating this by country income level alone may pose several limitations, such as the patients within a certain study may exclusively receive the highest quality care within the country, and thus perhaps not reflect the general population or average healthcare. Moreover, for instance, patients even within the US have access to hospitals with drastically different resources based solely upon their income and insurance coverage, even within the same cities. Since this information is not available in the studies included in our study, any conclusions made based on this analysis are unlikely to reflect any true affect income level has on MVI. Regardless, we feel that any research aimed at highlighting disparities between groups of patients of varying socioeconomic, racial, or cultural backgrounds is highly important. We fell all types of research looking at complication rates between different populations is important and should be pursued, but is unfortunately, outside the realm of this particular study design. We added text to include this in our limitations (See Edit #8).

* Table 3 (page 17): In a published review focused about morcellator related complications, there were 27 injuries to the vascular system from the morcellator (Milad MP, Milad EA. Laparoscopic morcellator-related complications. Journal of minimally invasive gynecology. 2014 May 1;21(3):486-91). I think it would be very informative to the readers to know the causes for the injury in the surgical phase in this review. For example, were there any morcellator related vascular injuries in the included studies?

Unfortunately, only 6/25 MVIs that occurred during surgical dissection denoted how the injuries was caused. Text has been added to the results to summarize this data (Edit #10). . Text has also been added to the discussion to discuss this limitation (See Edit #9). None of these reported injury from a morcellated, however, studies did often not supply enough details to discern how many of the total surgeries used morcellation technology, and thus this study is unable to comment on this risk in regard to this particular technology.

* Table 5 (page 19): I noticed that the authors included 1 study that included robotic hysterectomy. Can the authors confirm that for the whole period of the studies included (1978-2016) there were only 1 study for robotic hysterectomy and vascular injuries? And if so, I am confused because the authors included studies with laparoscopies where no vascular injuries were reported.

This is an interesting finding indeed. In review, there were a small number of additional studies that included robotic surgeries, but they ultimately did not meet criteria for inclusion as they did not specifically report on vascular injuries. The dearth of robotic procedures encountered may also be related to the large span of time over which studies were included, as well as the exclusion of studies on oncologic surgeries, as prevalence of robotic surgery in this field is much higher. We have added text to the discussion to highlight the limit of this study on generalizing to robotic procedures (See Edit #11).

STATISTICAL EDITOR COMMENTS:

lines 61-62: The 95% CI should be 0.077%-.104%. (as in Table 2)

Corrected

lines 63-65: The total number of vascular injuries in this series was 179, then subdivided by vessel injured. Those % should all be rounded to nearest integer %, along with their respective CIs, based on the number of counts, not cited to nearest 0.1% or .01%, as currently formatted.

Edited to match the requested formatting. Of note, in the “Editorial Office Comments” below, it states that “percentages should not exceed 1 decimal place (Example 11.1%).” This seems slightly at odds with this comment. We favored editing our manuscript to align with the statistical editor comments, however, if our interpretation is incorrect and percentages should be to one decimal place instead, please notify the corresponding author and this change can be quickly made.

lines 68-69: There were only 2 deaths, so the CIs should be based on either Poisson or

binomial assumptions, not the usual normality assumption. As such, the 95%CI = 0 to 0.004%

Corrected

Table 2: Need to make appropriate changes to precision of citing the CIs and estimates of proportions. The CI for iliac vein is incorrect, it cannot be a negative number (-0.21,3.56)%. Based on the denominator = 199,305 and the numerators given, the CI for Aorta = (0.001,.007)%, IVC = (.001,.005)%, Iliac vessels = (.007,.017)%, Iliac artery = (.005,.013)%, Iliac vein =(0, .004)%, the high proportion of other/not otherwise specified makes the estimation of the other %s imprecise and possibly biased, which should be a caveat in the discussion. The 179/199,305 results in 0.090%, or more precisely 0.0898%, which does not round to 0.091%

Data corrected as indicated. Of note, one of the studies had to be excluded (n=107 surgeries) after review of comments/revisions, and thus data has been recalculated. We have ensured that all data is consistent throughout the manuscript and abstract in terms of rounding and accuracy.

Text added to highlight bias / limitations of the reported proportions/incidences of individual major vessels due to large portion of unspecified injuries (See Edit #12).

Tables 3, 4: As noted earlier, need to round the %s and their CIs. Need to explain to reader in footnote what is being compared and by what stats test that results in the p-values cited.

% and CIs have been rounded as instructed. Footnote has been added to the table.

General: Omitted from the discussion is the possibility of selection bias, which may have resulted in either over or underestimation of the incidence rates. This is a large series, but is not a database of all surgeries nor of all vascular injuries.

Text added to specify this limitation (See Edit #13)

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4. 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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Word count for manuscript is 2653 and is noted.

Manuscript is 23 pages using double-spaced pages excluding references.

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7. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot. ✓

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Word count for abstract is 288 and is noted

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11. 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. ✓

This symbol has been removed from the manuscript texts when possible. It was, however, used in the "search terms" when performing the review, and thus was left in this portion of the manuscript to accurately reflect how the databases were searched.

12. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone. ✓

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts. ✓

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%). ✓

Edits made to comply with this standardization. There were some percentages that were so low that the first integer was in the second decimal place. For these, we referenced prior published literature in The Green Journal and left them as just one number out to the first decimal place that is not a zero. If this is incorrect, please inform the corresponding author and any necessary edits can be made quickly. Thank you!

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