NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- 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: Dec 10, 2020
To: "Nisse Clark"
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-20-3078

RE: Manuscript Number ONG-20-3078
Superior Hypogastric Plexus Block and Laparoscopic Hysterectomy: A Randomized Controlled Trial

Dear Dr. Clark:

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 Dec 31, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:
Reviewer #1: The authors should be congratulated on completion of a multi-center randomized controlled trial. While a negative study, I do think the results are important and question the need for additional preemptive analgesia in the age of ERAS. The definition, description and collection of the primary outcome was somewhat confusing and inconsistent throughout the document, and I recommend an improved detailed description of the primary outcome and making sure this is consistent throughout the abstract and manuscript. There are also minor grammatical errors throughout document that should be thoroughly read through and corrected.

Specific comments:
Abstract:
Lines 44-45: Based on reading the manuscript, I think a better description of the primary outcome is warranted. Specifically, describing that you were comparing a proportion of <4 or >4 on the VAS as your primary outcome. Continuous VAS scores were not your primary outcome and this should be clarified.

Please provide additional detail on sample size calculation in the abstract.

Introduction: Well-written and concise

Lines 99-101: Please add a hypothesis for your study

Materials and Methods:

Please comment on why you chose 2 hours as your primary endpoint? This seems very early after surgery where effects of general anesthesia could still be on board. Additionally, patients are often still very "groggy" 2 hours postoperatively.

Lines 142-149. I have some concerns about the technique. How do you know that this technique is actually anesthetizing any nerves? Has this technique used previously with evidence demonstrating its effectiveness? And if yes, did you use the same technique as described in prior studies? Based on the description and Figure 1, it seems to me the bupivacaine would just enter the presacral space. Is the idea to just let the SHP "soak" in the bupivacaine? And at what level of the sacrum? Figure 1 almost seems as though you are at the sacral promontory, however the SHPB should be located caudad to this. If truly injected at the level of the promontory, this could potentially explain the negative findings.

Lines 169-175: As mentioned above for the abstract, additional clarification needed here that your primary outcome was...
not comparing the continuous VAS score. Rather, your primary outcome is a dichotomized VAS score. Additional clarification in this section will help reader understand the sample size calculation in the subsequent paragraphs.

It also says the VAS score was assessed by the PACU nurse. I want to clarify - did the nurses ask how much pain the patient was experiencing and record the pain score? Or did the patient actually have a piece of paper or tablet with the VAS and the patient herself mark on the indicated line? If the former, I have serious concerns about the primary outcome as this would not represent a true VAS score assessment (if it were not completed by the patients themselves). Please clarify.

Line 206: Please add a citation for this prior work used to calculate the sample size

Lines 211-214 are somewhat confusing. Previously, the authors report the VAS score at 2 hours was utilized as the primary outcome. However, here it seems as though the VAS score was a mean. Please provide further clarification or edit this sentence for improved understanding. If a mean or median value was used for the primary outcome, this should be clarified in the primary outcome description.

Results:

Lines 246-247: Great that you did not have any complications related to the SHPB. I worry this would not be the case if the surgeons are not fellowship trained and not as familiar with anatomy. The generalizability of this approach may be limited by surgical expertise and I would be sure to discuss later in the manuscript.

Line 272: "Differ" should be changed to "different." There are similar grammatical errors throughout document.

Discussion:

Line 320: Please add a reference

Lines 336-338: One of the theories behind preemptive analgesia is that is reduces the downstream pain cascade. Thus, while the immediate impact of bupivacaine may have worn off by 2 hours after surgery, a downstream dulling of the pain response should still occur if indeed the intervention is effective. Consider expanding on this discussion of preemptive analgesia with appropriate references.

Limitations section Line 356-361: As noted above, please also discuss the generalizability of this procedure itself. It does not seem that a SHPB would be generalizable to low volume gynecologic surgeons. Additionally, while mentioned in other parts of the discussion section, I would reiterate here that the use of multiple other modes of preemptive analgesia (including the preoperative cocktail and ERAS) may have masked the ability to see any differences in your cohorts. You listed using ERAS as a strength, which I agree with, but it could also be a weakness in that it may mask any differences between treatment arms. Lastly, I would also comment that you were not powered to detect a difference in secondary outcomes. Specifically, you were only powered to detect the difference in the proportion of dichotomized VAS scores, not continue VAS scores (other secondary outcomes).

Lines 365-366: I very much agree with this statement. With more negative preemptive analgesia studies since ERAS, it begs the question whether additional preemptive analgesia techniques for any gynecologic procedures will add further benefit to the improved pain control already afforded by ERAS protocols.

Line 366-368: This sentence seems to come out of left field as it is the first mention of liposomal bupivacaine in the manuscript. I understand your statement (because of its longer half-life), however if going to include in a conclusion statement, I would recommend discussing in more detail earlier in the discussion section. Additionally, a limitation to the use of liposomal bupivacaine is its much higher cost. Thus, I am not sure this belongs in your closing remarks.

Tables

I would add the full terminology of "Superior Hypogastric Plexus Block" somewhere to all tables and potentially to the column headings. The word "block" is vague and could refer to any sort of nerve block if not read in context with the article.

Table 3. Inconsistency with description of data and how data being presented. The rows state "Mean" however the parenthesis state median (IQR) - yet the data seem to be reported as mean SD. This needs clarification and to be corrected. Are the authors presenting means or medians? Please correct in all tables and ensure also correct in text. If the VAS scores were not normally distributed, the median (IQR) should be reported and should be used for statistical analyses where appropriate. If reporting IQR, this should be a range. Please make sure you are correctly describing the data you are reporting (or that you are reporting the desired data).

Reviewer #2: I would like to commend the authors on a well written manuscript and well designed study. The manuscript
describes a multi-center, randomized, single blind controlled trial comparing patients who received a superior hypogastric block plexus (SHPB) at the start of laparoscopic hysterectomy with those who did not. The primary objective measure is their visual analogue pain scores following the procedure. The study question is relevant because although superior hypogastric block has been shown to be beneficial in open hysterectomy, it has not been studied in the form of a RCT for laparoscopic hysterectomy. I do have some comments, questions and suggestions for the authors.

* **Abstract:**
  - It appears that the final study sample participants were selected from a large original population of possible participants. What were the differences between those who enrolled and those that were approached and not enrolled? CC of pain? Age? Why was there such a significant difference in these numbers?
  - Would also recommend this be included in the body of the manuscript

* **Introduction:**
  - Succeeds in stating primary and secondary aims but does not discuss hypothesis
  - We recommend the authors include more information about previous findings of the referenced, non-RCT study findings and how these studies influenced the study design and power calculation.

* **Methods:**
  - Line 114: grammar error with comma (pre USA needs comma)
  - Lines 137-138: please clarify, was the member of the research team that made the randomization envelopes also someone that enrolled and consented patients or were they separate?
  - Line 149: "performed similarly in all patients" - does this mean all trained at the same institution? Or was there a review for investigators to ensure that steps were standardized? We feel that this answer could affect the reproducibility of the study.
  - Line 155-158: Were pre-operative prep medication administration times standardized (half-life could factor in)?
  - Line 181: please clarify how the patients were contacted to remind them about the daily diary. What were specifics regarding how missed messages were dealt with.
  - Line 155-158: Were pill counts conducted after completion of the study to assess opioid use?
  - Lines 198-199: How was the clinically significant score "deemed"?
  - How did the authors decide on the timing of injection especially if a RCT on abdominal hysterectomy showed benefit when injected at the end of the procedure?
  - Since the injection was prior to hysterectomy, depending on how long the case was, the effects could have worn off by the time the participants were assessed. How was this considered in the study design? Any benefit to after hysterectomy. If so, how do we know this.

* **Results:**
  - Line 241: elaborate on "pre sacral space not accessible"? (8% seems high for this).
  - Interesting that the 4 in the treatment arm were removed from the study but not the four in the control arm that had the same issue (for the as-treated analysis). Can the authors discuss this further?
  - Lines 273-275: For MME used in post days 1-6, how was narcotic usage reported? Did patients receive same pre-op counseling about pain medication post op
  - Lines 283-285: was the study powered for these subgroup analyses?

* **Figure/Table Legends:**
  - Figure 2 - boxes next to allocation both say "allocated to no SHPB"

* Although less relevant with negative results, I am concerned that sham injection could exclude the possibility of volume in this space resulting in anesthetic outcome secondary to pressure resulting in a question regarding need for Bupivicane versus just volume. Can the authors describe in further detail why they feel that single blind design excludes need for sham.

Reviewer #3:

The authors present a multi-institutional RCT looking at the impact of superior hypogastric plexus block with Bupivacaine during laparoscopic hysterectomy. The primary outcome of interest was Visual Analog Pain Score (VAS) at the 2-hour postoperative mark. The study was well designed. My major criticism is missed opportunity for double blinding including the surgeon by using NS for intended SHPB.

**Abstract:**

Well written concise abstract. Easy to understand what was done. As written results section supports the conclusion.
Introduction:

Line 79  The citation Am J Obstet Gynecol. 2017;216:557-67 was a recent systematic review. They stated only positive finding was paracervical block for TVH. This may be important to expand upon because I did not see this in the materials and method section and could have confounded results depending on variability of removal of specimen and closure of the cuff.

Line 88  The citation listed included some cancer patients and disruption of the SHP at various levels along the presacral nerve pathway including both pre- and post-synapse. This would include the LUNA procedure. Expand upon the physiology and the location of the various blocks and data for short and long term pain relief.

Line 90-97 This is a good pharmacologic review of Bupivacaine. Given the metabolism and maximum blood levels, it does make one wonder why it was not done at the completion of the procedure. This would better standardize the primary outcome of pain at the 2 hour postoperative mark from when the block was given.

Materials and Methods:

Line 105  Why not double blind as stated in the objectives above?

Line 142  Was there as standardized port entry? ie Veres needle, open and port sizes. Was an NG or OG routinely documented or used? This can be a problem if ERAS medications are suctioned out during the surgery and confound pain assessment.

Line 158-159  Was bupivacaine given pre-incision, post-incision, or both?

Line 160  Was there a standardize regiment and or triggers on pain scales used for nursing and anesthesia to give narcotic postoperatively?

Line 162-163  I did a quick MME calculator for the discharge medications. A 2 mg dose of hydromorphone was 8, 5 mg oxycodone 7.5 and 5 mg hydrocodone was 5 MME. I do see a total MME was calculated however this may have impacted short term pain scores both immediately postoperatively and the first day vs total MME and opioid use.

Line 187  If available give more details about the procedure related to suture material, paracervical block, and cuff closure. These may confound the results.

Line 198-208  This is a thorough and concise explanation of why a VAS score of < 4 and power calculation were chosen.

Results:

Table 1

What were the indications for sub total hysterectomy? Patient preference vs surgical difficulty? I assume subtotal = supracervical hysterectomy.

Table 3

The statistically significant pain at 1 hour 18 (36.0) 31 (62.0) <0.01 may have been a function of the time of the block and length of surgery. It is hitting the maximum benefit at the 1 hour mark vs 2 hr.

Discussion:

Line 295-305  The comparative studies listed all used SHBP after hysterectomy. The timing may be the reason as acknowledged later in the discussion by the authors.

General strengths and limitations are addressed.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

Abstract: Need to conform to our RCT abstract template.

lines 203-208: Since the sample size/power calculation was framed in terms of proportion of patients with VAS < 4, that is how the primary should be cited in Abstract and in Tables. The format of OR and aOR can be added as secondary
outcomes.

Table 1: Need units for age.

Table 2: Since there were protocol deviations (moreso in the block cohort in Table 1), should report the per protocol results as well as the ITT results.

EDITOR 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. 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.

4. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the article (after the References section).

5. 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-definition 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.

6. 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 print appendixes) but exclude references.

7. 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.
8. 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. Please provide a word count.

9. Abstracts for all randomized, controlled trials should be structured according to the journal’s standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.

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 construction 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).

15. Figures 1-2: The current figure files may be resubmitted with the revision.

16. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at https://wkauthorservices.editage.com/open-access/hybrid.html.
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 Dec 31, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Dwight J. Rouse, MD, MSPH

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.
December 31st, 2020

Dear Editors of Obstetrics & Gynecology,

We sincerely thank you for your thorough review and ongoing consideration of our manuscript, “Superior Hypogastric Plexus Block and Laparoscopic Hysterectomy: A Randomized Controlled Trial,” for publication in Obstetrics & Gynecology.

We have read the Instructions for Authors and provided a point-by-point response to the reviewers and editors comments below. All responses are italicized in this letter and all revisions are tracked in the revised manuscript. Line references in our response refer to the tracked manuscript. Our revised manuscript includes an improved Introduction outlining the use and technique of a superior hypogastric plexus block, clarification of our primary outcome, further details of our study methods, and an expanded Discussion noting some important limitations of our work. Several additional modifications have been made in accordance with the reviewers’ and editors’ suggestions. We believe these edits have resulted in a high-quality manuscript that will be of interest to your readers. While a negative study, the findings underscore that added techniques to reduce postoperative pain may not be effective in the setting of minimally invasive surgery and enhanced recovery pathways.

The authors would like to reiterate that we intend to solely submit to Obstetrics & Gynecology. The manuscript is not under consideration elsewhere and will not be submitted elsewhere unless a final negative decision is made by the Editors of Obstetrics & Gynecology. The clinical trial is registered at https://clinicaltrials.gov/, identifier NCT03283436.

The protocol described in the manuscript and performed in the trial are identical to the protocol documented on the trial registry. The trial was approved by the Institutional Review Boards at Brigham and Women’s Hospital, the University of North Carolina Medical Center, and the George Washington University Hospital School of Medicine.
and Health Sciences. The data reported were entered manually by research specialists at each institution and validated by both the statistician and first author.

The study was presented at the American Association of Gynecologic Laparoscopists Global Congress in Vancouver, British Columbia, Canada, in November 2019.

As the lead author, I affirm that this revised 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 registered have been explained. Thank you for your ongoing consideration.

Sincerely,

Nisse Clark, MD MPH

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REVIEWER COMMENTS:

Reviewer #1: The authors should be congratulated on completion of a multi-center randomized controlled trial. While a negative study, I do think the results are important and question the need for additional preemptive analgesia in the age of ERAS. The definition, description and collection of the primary outcome was somewhat confusing and inconsistent throughout the document, and I recommend an improved detailed description of the primary outcome and making sure this is consistent throughout the abstract and manuscript. There are also minor grammatical errors throughout document that should be thoroughly read through and corrected.

Thank you for your review and comments. We agree that our primary outcome should be well-defined and consistent throughout our manuscript. Our primary outcome was the proportion of patients with a mean VAS score less than 4 within 2 hours postoperatively. This has been clarified in the Abstract, the Materials and Methods, and the Results (lines 48-49, 231-233, 366-369). We have reviewed the manuscript carefully and corrected any grammatical errors.

Specific comments:

Abstract:

Lines 44-45: Based on reading the manuscript, I think a better description of the primary outcome is warranted. Specifically, describing that you were comparing a proportion of <4 or >4 on the VAS as your primary outcome. Continuous VAS scores were not your primary outcome and this should be clarified.

We have revised the manuscript to include a better description of the primary outcome (lines 48-49, 231-233)

Please provide additional detail on sample size calculation in the abstract.

We have included further details of the sample size calculation in the Abstract while keeping the Abstract within the 300 word limit (lines 51-54).

Introduction: Well-written and concise

Lines 99-101: Please add a hypothesis for your study

We hypothesized that a SHPB performed during laparoscopic hysterectomy reduces postoperative pain. We have added this hypothesis to the manuscript (lines 151-152).

Materials and Methods:

Please comment on why you chose 2 hours as your primary endpoint? This seems very
We chose 2 hours after surgery as this was felt to be within the window of time that the block would still be effective and a time point at which all patients were still present in the recovery unit. It is also a common time point when patients’ pain is being assessed to determine if they are prepared for discharge (lines 281-290).

Lines 142-149. I have some concerns about the technique. How do you know that this technique is actually anesthetizing any nerves? Has this technique used previously with evidence demonstrating its effectiveness? And if yes, did you use the same technique as described in prior studies? Based on the description and Figure 1, it seems to me the bupivacaine would just enter the presacral space. Is the idea to just let the SHP "soak" in the bupivacaine? And at what level of the sacrum? Figure 1 almost seems as though you are at the sacral promontory, however the SHPB should be located caudad to this. If truly injected at the level of the promontory, this could potentially explain the negative findings.

We used a SHPB technique similar to that described in the three prior studies examining SHPB at the time of abdominal or laparoscopic hysterectomy, all of which did identify some benefit of the block in reducing postoperative pain. The technique is intended to deposit local anesthesia near to the superior hypogastric plexus, without intraneural injection, using anatomic landmarks to locate the plexus. The superior hypogastric plexus is a retroperitoneal midline structure anterior to the lower third of L5 and upper third of S1, immediately caudad to the aortic bifurcation and vena cava confluence, and overlying the sacral promontory. Image-guided percutaneous blockade of the plexus is performed in a similar manner whereby vertebral and vascular landmarks are used to locate the presacral space, and contrast used to fill and confirm the space before injecting the block. This percutaneous method was first shown to be effective in reducing pain by Plancarte et al. in 1990 and studies that followed. We did exclude patients requiring presacral dissection for other purposes (e.g. those undergoing sacrocervicopexy) as this was felt to prevent concentration of the block in the presacral space. The Introduction has been expanded to describe the technique (lines 125-132).

Lines 169-175: As mentioned above for the abstract, additional clarification needed here that your primary outcome was not comparing the continuous VAS score. Rather, your primary outcome is a dichotomized VAS score. Additional clarification in this section will help reader understand the sample size calculation in the subsequent paragraphs.

Our primary outcome has been clarified (lines 48-49, 231-233).

It also says the VAS score was assessed by the PACU nurse. I want to clarify - did the nurses ask how much pain the patient was experiencing and record the pain score? Or did the patient actually have a piece of paper or tablet with the VAS and the patient herself mark on the indicated line? If the former, I have serious concerns about the
primary outcome as this would not represent a true VAS score assessment (if it were not completed by the patients themselves). Please clarify.

*Patients and the PACU staff were provided a study-specific worksheet that included the VAS and time intervals when the VAS should be collected after surgery. We have revised the Materials and Methods to detail how the VAS scores were recorded (lines 235-239).*

Line 206: Please add a citation for this prior work used to calculate the sample size

*The prior work used to calculate the sample size is cited (line 294).*

Lines 211-214 are somewhat confusing. Previously, the authors report the VAS score at 2 hours was utilized as the primary outcome. However, here it seems as though the VAS score was a mean. Please provide further clarification or edit this sentence for improved understanding. If a mean or median value was used for the primary outcome, this should be clarified in the primary outcome description.

*We appreciate that the use of mean and median to report VAS scores is confusing and have attempted to clarify this in our Materials and Methods. Mean VAS scores at varying time intervals were collected for individual patients to generate a consistent datapoint for each time period of interest. Additionally, means were used as there were few VAS score values to summarize for each time period and the distribution could not be well determined. The mean VAS scores for all patients in a treatment group were summarized using medians as it was clear the mean VAS scores were not normally distributed across the larger groups. We have clarified this in our manuscript and added a note to the Table 3 to clarify this (lines 304-308, 369-372).*

Results:

Lines 246-247: Great that you did not have any complications related to the SHPB. I worry this would not be the case if the surgeons are not fellowship trained and not as familiar with anatomy. The generalizability of this approach may be limited by surgical expertise and I would be sure to discuss later in the manuscript.

*We appreciate this limitation and have noted it in the Discussion (lines 498-501).*

Line 272: "Differ" should be changed to "different." There are similar grammatical errors throughout document.

*We have fixed this error and carefully reviewed and revised the manuscript (line 380).*

Discussion:

Line 320: Please add a reference
A reference has been added (line 442).

Lines 336-338: One of the theories behind preemptive analgesia is that it reduces the downstream pain cascade. Thus, while the immediate impact of bupivacaine may have worn off by 2 hours after surgery, a downstream dulling of the pain response should still occur if indeed the intervention is effective. Consider expanding on this discussion of preemptive analgesia with appropriate references.

This is an excellent point. Preemptive analgesia is intended to work immediately, for the duration of the procedure and for some period after the procedure by inhibiting central sensitization in response to painful stimuli. We have included this in our Discussion (lines 462-466).

Limitations section Line 356-361: As noted above, please also discuss the generalizability of this procedure itself. It does not seem that a SHPB would be generalizable to low volume gynecologic surgeons. Additionally, while mentioned in other parts of the discussion section, I would re-iterate here that the use of multiple other modes of preemptive analgesia (including the preoperative cocktail and ERAS) may have masked the ability to see any differences in your cohorts. You listed using ERAS as a strength, which I agree with, but it could also be a weakness in that it may mask any differences between treatment arms. Lastly, I would also comment that you were not powered to detect a difference in secondary outcomes. Specifically, you were only powered to detect the difference in the proportion of dichotomized VAS scores, not continue VAS scores (other secondary outcomes).

We have expanded the Discussion to include these important limitations (lines 496-498, 505-506).

Lines 365-366: I very much agree with this statement. With more negative preemptive analgesia studies since ERAS, it begs the question whether additional preemptive analgesia techniques for any gynecologic procedures will add further benefit to the improved pain control already afforded by ERAS protocols.

Line 366-368: This sentence seems to come out of left field as it is the first mention of liposomal bupivacaine in the manuscript. I understand your statement (because of its longer half-life), however if going to include in a conclusion statement, I would recommend discussing in more detail earlier in the discussion section. Additionally, a limitation to the use of liposomal bupivacaine is its much higher cost. Thus, I am not sure this belongs in your closing remarks.

We agree and have removed the final sentence. We have replaced the sentence with a comment highlighting the potential limitations of additional preemptive analgesia in the setting of ERAS (lines 511-513).

Tables
I would add the full terminology of "Superior Hypogastric Plexus Block" somewhere to all tables and potentially to the column headings. The word "block" is vague and could refer to any sort of nerve block if not read in context with the article.

_All tables have been revised to include the full terminology “Superior Hypogastric Plexus Block.”_

Table 3. Inconsistency with description of data and how data being presented. The rows state "Mean" however the parenthesis state median (IQR) - yet the data seem to be reported as mean SD. This needs clarification and to be corrected. Are the authors presenting means or medians? Please correct in all tables and ensure also correct in text. If the VAS scores were not normally distributed, the median (IQR) should be reported and should be used for statistical analyses where appropriate. If reporting IQR, this should be a range. Please make sure you are correctly describing the data you are reporting (or that you are reporting the desired data).

_We have clarified the use of means and medians to summarize VAS scores in the Materials and Methods (lines 304-308, 369-372). We have also added a note to Table 3._

Reviewer #2: I would like to commend the authors on a well written manuscript and well designed study. The manuscript describes a multi-center, randomized, single blind controlled trial comparing patients who received a superior hypogastric block plexus (SHPB) at the start of laparoscopic hysterectomy with those who did not. The primary objective measure is their visual analogue pain scores following the procedure. The study question is relevant because although superior hypogastric block has been shown to be beneficial in open hysterectomy, it has not been studied in the form of a RCT for laparoscopic hysterectomy. I do have some comments, questions and suggestions for the authors.

* Abstract:
  o It appears that the final study sample participants were selected from a large original population of possible participants. What were the differences between those who enrolled and those that were approached and not enrolled? CC of pain? Age? Why was there such a significant difference in these numbers?
  o Would also recommend this be included in the body of the manuscript

_Eighty-six patients were eligible for the study but declined to participate. Data is available for 46 of these 86 patients (all from Brigham and Women’s Hospital). Compared to patients who were enrolled in the study, eligible patients who were not enrolled were older (median age 48 compared to 45, p<0.05), had a lower BMI (27.0 compared to 29.5, p=0.04), were more likely to be Asian (13.0% compared to 4.0%,p=0.04) and more likely to have a primary indication of fibroids (65.2% compared to 45.0%, p=0.02). There were no other significant differences between the two groups. Specifically, there was no significant difference in the proportion of patients with a primary indication of pelvic pain between the two groups (19.6% of patients in the
unenrolled group had a primary indication of pelvic pain and 28.0% of patients in the enrolled group had a primary indication of pelvic pain, p=0.28). Without the data for the remaining 40 unenrolled patients, we do not believe it is meaningful to include this comparison in the manuscript, as any differences may be related to the single site for which this information was available, instead of something inherently different between the unenrolled and enrolled patients. It is also difficult to draw any conclusions about why the two groups may be different other than that certain patient characteristics may have been associated with unwillingness to participate in the study.

* Introduction:
  o Succeeds in stating primary and secondary aims but does not discuss hypothesis

* We have added our hypothesis (lines 115-152).

* We recommend the authors include more information about previous findings of the referenced, non-RCT study findings and how these studies influenced the study design and power calculation.

We have added more information regarding prior studies on SHPB for chronic pelvic pain and post-procedural pain. We have also detailed the prior RCT on SHPB performed during abdominal hysterectomy and the findings that guided our sample size calculation (lines 100-123).

* Methods:
  o Line 114: grammar error with comma (pre USA needs comma)

Noted and edited (line 168).

* Lines 137-138: please clarify, was the member of the research team that made the randomization envelopes also someone that enrolled and consented patients or were they separate?

A separate member of the research team made the randomization envelopes. This has been clarified in the Materials and Methods (lines 181-183).

* Line 149: "performed similarly in all patients" - does this mean all trained at the same institution? Or was there a review for investigators to ensure that steps were standardized? We feel that this answer could affect the reproducibility of the study.

All participating surgeons were experienced in performing a SHPB and were educated on the exact study protocol (lines 206-208). Surgeons were not trained at the same institution.

* Line 155-158: Were pre-operative prep medication administration times standardized (half-life could factor in)
Unfortunately, it was not possible to standardize the exact timing of the preoperative medications given the diverse staff and institutions represented in the study. All preoperative medications were given in the preoperative area prior to surgery.

- Line 181: please clarify how the patients were contacted to remind them about the daily diary. What were specifics regarding how missed messages were dealt with.

Patients were contacted by telephone after surgery to remind them to complete the diary. If they did not answer the initial telephone call, two additional attempts were made. This has been clarified in the Materials and Methods (lines 259-262).

- Was patient recall and reporting all that was used once discharged?

Patient recall and reporting on a templated diary were all that were used to assess VAS pain scores and opioid consumption after discharge. The diary included instructions for recording VAS pain scores and opioid use. Patients were contacted by telephone after surgery to remind them to complete the diary. We recognize that this limits the accuracy of some of the results but as these longer-term outcomes were not our primary outcome of interest, we did not implement a more rigid measurement system.

- Were pill counts conducted after completion of the study to assess opioid use?

Pill counts were not conducted after the study. Patients were responsible for reporting their opioid consumption on days 1 through 6 in the diary.

- Lines 198-199: How was the clinically significant score "deemed"?

We have expanded upon our choice of a primary outcome in the Materials and Methods (lines 280-291).

- How did the authors decide on the timing of injection especially if a RCT on abdominal hysterectomy showed benefit when injected at the end of the procedure?

We chose to administer the block at the start of the procedure as a means of preemptive analgesia. The pharmacokinetics of Bupivacaine also suggest that it will still be active for some time after a laparoscopic hysterectomy, which on average, took around two hours in our study.

- Since the injection was prior to hysterectomy, depending on how long the case was, the effects could have worn off by the time the participants were assessed. How was this considered in the study design? Any benefit to after hysterectomy. If so, how do we know this.

The effect should not have worn off based on the pharmacokinetics of Bupivacaine and the goal of preemptive analgesia. There was heterogeneity in procedure length however all but one were within the time period during which the medication should still be active.
The Introduction and Discussion review these points (lines 135-139, 462-466)

* Results:
   o Line 241: elaborate on "pre sacral space not accessible"? (8% seems high for this).

The presacral space was not accessible for patients with a very large uterus or adhesions obscuring the space (lines 346-347). The study included patients of surgeons with fellowship-training in MIGS and therefore includes many patients with uterine enlargement, endometriosis, or a prior surgical history that increases their surgical complexity. This may account for the larger-than-anticipated proportion of patients with an inaccessible presacral space.

- Interesting that the 4 in the treatment arm were removed from the study but not the four in the control arm that had the same issue (for the as-treated analysis). Can the authors discuss this further?

If there was no intent to perform a SHPB for patients in the control arm, it is difficult to determine who in that group would have not received the SHPB if they were in fact randomized to the treatment arm. Certainly those with an inaccessible presacral space may have not been eligible for a SHPB but there are additional unpredictable factors that could have prevented patients in the control arm from receiving the intervention in this hypothetical scenario. We felt it important to simply compare those who did and did not receive the SHPB in our as-treated analysis. It is assumed that an as-treated analysis has inherent bias in that there may be disparate characteristics that result in protocol deviation.

   o Lines 273-275: For MME used in post days 1-6, how was narcotic usage reported? Did patients receive same pre-op counseling about pain medication post op

Postoperative narcotic usage for days 1 through 6 was reported by patients using a study-specific diary. The diary including instructions and a template for reporting daily VAS pain scores and opioid consumption in milligrams of oxycodone, hydrocodone or hydromorphone. These values were standardized to MME for the analysis. Patients were provided a standard opioid prescription and instructions for use after surgery. Please see lines 241-244 and 224-227 for clarification in our Materials and Methods.

   o Lines 283-285: was the study powered for these subgroup analyses?

Our sample size was not chosen for the subgroup analyses and therefore the analyses are potentially underpowered. We have included this as a limitation in our Discussion (lines 505-506).

* Figure/Table Legends:
   o Figure 2 - boxes next to allocation both say "allocated to no SHPB"
* Although less relevant with negative results, I am concerned that sham injection could exclude the possibility of volume in this space resulting in anesthetic outcome secondary to pressure resulting in a question regarding need for Bupivacaine versus just volume. Can the authors describe in further detail why they feel that single blind design excludes need for sham.

We recognize that this study could have included a sham block to blind the surgeons and operating room staff. We chose not to include a sham block given the potential risk to study subjects in accessing the presacral space without anticipated benefit. Moreover, the surgeons and operating room staff were not present or responsible for collection of the primary or secondary outcomes, helping to avoid any bias related to knowledge of the subject’s treatment arm.

Reviewer #3:

The authors present a multi-institutional RCT looking at the impact of superior hypogastric plexus block with Bupivacaine during laparoscopic hysterectomy. The primary outcome of interest was Visual Analog Pain Score (VAS) at the 2-hour postoperative mark. The study was well designed. My major criticism is missed opportunity for double blinding including the surgeon by using NS for intended SHPB.

Thank you for your review and positive comments. We have included our rationale for conducting a single blind trial in response to Reviewer 2 as above.

Abstract:

Well written concise abstract. Easy to understand what was done. As written results section supports the conclusion.

Introduction:

Line 79 The citation Am J Obstet Gynecol. 2017;216:557-67 was a recent systematic review. They stated only positive finding was paracervical block for TVH. This may be important to expand upon because I did not see this in the materials and method section and could have confounded results depending on variability of removal of specimen and closure of the cuff.

No additional blocks (aside from the SHPB for subjects randomized to receive it, and the standardized incisional anesthetic) were performed as part of the hysterectomy. Some specimens were extracted intact through the colpotomy while others required manual morcellation via the colpotomy or a minilaparotomy if a subtotal (supracervical) hysterectomy was performed or the specimen was too large to deliver intact vaginally. The cuff closure method was not recorded during data collection. As this study only
included patients undergoing laparoscopic hysterectomy, and we unaware of literature demonstrating a difference in postoperative pain with different routes of specimen removal and cuff closure for laparoscopic hysterectomy, we do not feel that this potential variation significantly impacted our results. A prior study by some of the authors demonstrated no difference in postoperative pain by extraction site following laparoscopic hysterectomy. We also purposefully included multiple surgeons at different institutions performing laparoscopic hysterectomy using their own techniques for any indication and with most concomitant procedures (excluding those that disrupted the presacral space), to encompass a real-world cohort of patients undergoing laparoscopic hysterectomy. Our sample size was increased to account for this heterogeneity.

Line 88  The citation listed included some cancer patients and disruption of the SHP at various levels along the presacral nerve pathway including both pre- and post-synapse. This would include the LUNA procedure. Expand upon the physiology and the location of the various blocks and data for short and long term pain relief.

We have expanded the introduction to outline prior literature on short-term blockade of the superior hypogastric plexus for post-procedural pain, long-term blockade of the plexus for chronic cancer-related pelvic pain, and surgical transection of the plexus for relief of dysmenorrhea (lines 100-123). The laparoscopic uterosacral nerve ablation (LUNA) procedure targets the uterovaginal plexus and has not been shown to alleviate chronic pelvic pain according to a large randomized controlled trial. We have chosen not to include this procedure in the introduction as it aims to transect a different plexus and has not been shown to be effective.

Line 90-97  This is a good pharmacologic review of Bupivacaine. Given the metabolism and maximum blood levels, it does make one wonder why it was not done at the completion of the procedure. This would better standardize the primary outcome of pain at the 2 hour postoperative mark from when the block was given.

We chose to administer the block at the start of the procedure as a means of preemptive analgesia. Bupivacaine’s effect can last up to 8 hours therefore should remain active after most laparoscopic hysterectomies, which were, on average, 2 hours long. Please see lines 135-139 and 462-466.

Materials and Methods:

Line 105  Why not double blind as stated in the objectives above?

We chose not to conduct a double blind study as this would expose patients in the control arm to potential risk without anticipated benefit.

Line 142  Was there as standardized port entry? ie Veres needle, open and port sizes. Was an NG or OG routinely documented or used? This can be a problem if ERAS medications are suctioned out during the surgery and confound pain assessment.
We did not standardize laparoscopic entry method, port size, or the use of a nasogastric or orogastric tube. We chose not to standardize these variables in our protocol as they are surgeon-dependent and may vary according to other procedural factors. By not restricting these variables, the cohort better represents a real-world sample of patients undergoing laparoscopic hysterectomy.

Line 158-159 Was bupivacaine given pre-incision, post-incision, or both?

*Incisional Bupivacaine was given either before, after, or both before and after the incisions, depending on the surgeon’s preference.*

Line 160 Was there a standardize regiment and or triggers on pain scales used for nursing and anesthesia to give narcotic postoperatively?

*Nursing and anesthesia employed their usual assessment tools to determine when postoperative pain medication was needed. There was no standard regimen for postoperative narcotic use.*

Line 162-163 I did a quick MME calculator for the discharge medications. A 2 mg dose of hydromorphone was 8, 5 mg oxycodone 7.5 and 5 mg hydrocodone was 5 MME. I do see a total MME was calculated however this may have impacted short term pain scores both immediately postoperatively and the first day vs total MME and opioid use.

*We agree that intraoperative and postoperative opioid use has the potential to impact postoperative pain. For this reason we calculated both intraoperative and postoperative MME and found there was no significant difference between the two groups.*

Line 187 If available give more details about the procedure related to suture material, paracervical block, and cuff closure. These may confound the results.

*We do not have this information available.*

Line 198-208 This is a thorough and concise explanation of why a VAS score of < 4 and power calculation were chosen.

Results:

Table 1

What were the indications for sub total hysterectomy? Patient preference vs surgical difficulty? I assume subtotal = supracervical hysterectomy.

A subtotal hysterectomy was performed for some patients as per the patient’s preference following surgical counseling.
Table 3

The statistically significant pain at 1 hour 18 (36.0) 31 (62.0) <0.01 may have been a function of the time of the block and length of surgery. It is hitting the maximum benefit at the 1 hour mark vs 2 hr.

There were significantly more patients with less pain in the first and fourth, but not the second and third, hour after surgery. It is hard to draw strong conclusions from this secondary outcome when the intervening hours did not find a benefit of the block.

Discussion:

Line 295-305 The comparative studies listed all used SHBP after hysterectomy. The timing may be the reason as acknowledged later in the discussion by the authors.

This is an important point and we have expanded upon it in our Discussion (lines 457-469).

General strengths and limitations are addressed.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

Abstract: Need to conform to our RCT abstract template.

The abstract has been revised in accordance with the reviewers’ suggestions. The sample abstract has also been reviewed and is in compliance with the template.

lines 203-208: Since the sample size/power calculation was framed in terms of proportion of patients with VAS < 4, that is how the primary should be cited in Abstract and in Tables. The format of OR and aOR can be added as secondary outcomes.

The primary outcome has been clarified in the Abstract and Materials and Methods. The Abstract and Results have been revised to highlight the primary outcome (lines 48-49, 231-233).

Table 1: Need units for age.

Noted and revised.

Table 2: Since there were protocol deviations (more so in the block cohort in Table 1), should report the per protocol results as well as the ITT results.
We chose to conduct a secondary as-treated analysis, whereby patients were analyzed according to whether or not they received a SHPB, as this was our primary intervention of interest. A per-protocol analysis excluding patients who received a different SHPB dose, different SHPB timing or different perioperative medications, was not performed, as these were less frequent events or were not felt to have a large impact on the study findings. If this is important to the editor we will need more time to perform additional statistical analyses.

EDITOR 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.

   We OPT-IN and agree to have our point-by-point response letter included as supplemental digital content.

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.

   The authors have no disclosures in their eCTA.

3. 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 (e.g., 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.

_Race was analyzed as a variable using the categories White, Black, Hispanic, Asian and Other. White, Black, Hispanic and Asian were pre-specified race classifications retrieved from the medical record. Patient race was classified as “Other” when it did not fall in one of these four categories. The Materials and Methods section and Table 1 have been revised to detail this classification (lines 271-272)._

4. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (e.g., study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Responses to the five bullet points should be provided in a box at the end of the article (after the References section).

_A data sharing statement is included at the end of our manuscript (lines 607-614)._

5. 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](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](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.

_We do not find use of the reVITALize definitions to be problematic in our manuscript._

6. 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 print appendixes) but exclude references.

_Our text has been reviewed and all numbered pages (including the title page, précis, abstract, text, tables, and figure legends; excluding references) is less than 5,500 words_
7. 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).

We acknowledge that the findings presented in this paper were presented at the American Association of Gynecologic Laparoscopists’ Global Congress in Vancouver, B.C., Canada, in November 2019 (lines 26-28). We have no other relevant acknowledgements.

8. 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. Please provide a word count.

The Abstract has been reviewed and revised such that the primary outcome and sample size calculation are further clarified. There are no inconsistencies between the Abstract and the manuscript. Our conclusion is clear and supported by the paper. Our Abstract word count is 300 words.

9. Abstracts for all randomized, controlled trials should be structured according to the journal’s standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your
abstract as needed.

The Abstract has been revised in accordance with the reviewers’ suggestions. The primary outcome and the sample size calculation have been clarified. In order to comply with the 300 word limit, the continuous VAS score results were omitted from the abstract, as they were not the primary outcome of interest. The sample abstract has been reviewed and we believe our Abstract is in compliance with the standard.

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.

Abbreviations and acronyms are spelled out the first time they are used in the abstract and again in the body of the manuscript. Given the frequency with which Superior Hypogastric Plexus Block (SHPB) and Visual Analog Scale (VAS) are used throughout the manuscript, we have chosen to use their acronyms, after initially spelling them out.

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.

The virgule symbol is not used in the text.

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").

The abstract, manuscript results and tables have been reviewed with the primary outcome reported using unadjusted and adjusted odds ratios with confidence intervals. A number need to treat is not relevant to our study findings. The data has been standardized throughout the manuscript with P values to two decimal places and percentages to one decimal place.
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.

The Table Checklist was reviewed and Tables 1 through 3 conform to the journal style.

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.

The Referencing Formatting Instructions were reviewed. The reference list has been revised to include DOI with any journal articles for which it is relevant. The two websites references have been revised to include the accessed date.

15. Figures 1-2: The current figure files may be resubmitted with the revision.

Both figures have been slightly revised. Figure 1 was cropped to exclude the perimeter of the screen shot used to capture the image. Figure 2 was corrected to the allocation groups “Allocated to no SHPB” and “Allocated to SHPB.”

Response References:


