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.*

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Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office: obgyn@greenjournal.org.

Date: Jan 07, 2020
To: "Xinghui Liu" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-2291

RE: Manuscript Number ONG-19-2291

Internal Iliac Artery Balloon Occlusion for Placenta Previa Accreta: A Randomized Controlled Trial

Dear Dr. Liu:

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

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

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jan 28, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: "Internal iliac artery balloon occlusion for placenta previa accreta: a randomized controlled trial" is a well designed and described project that will carry great interest to readers of the journal.
There are small suggestions that I will detail below. The study design is similar to Salim et al 2015 - an RCT on the same subject matter published in Obstetrics and Gynecology. The rationale and conclusions are similar though this current study has a larger sample size.

Introduction: would benefit from highlighting current scope of the problem. Hypothesis is not clearly stated.

Methods: Good job of explaining diagnosis and management though the term "green channel" may not be familiar to many readers. Non-blinded study with subjective quantification of blood loss - observer bias should be acknowledged in discussion. Sample size calculation is similar to prior Salim study and appears appropriate.

Results: Deliveries included scheduled CD 34-36.6 weeks. ACOG suggests 34-35.6 weeks. The average gestational age in this study was 36.4 and 36.1 for balloon and no balloon respectively. I would be curious as to the average transfusion comparing < 36 weeks and > 36 weeks.

There were 9 cases of post-operative fever (18%) in the balloon group though on 4 cases are explained: 1 intrauterine infection, 1 UTI, 2 causes of PNA. Given this adverse outcome in the intervention group, elaboration on etiologies would be appropriate.

Discussion: well done and highlights previous work in the area. Would acknowledge potential weakness of subjective EBL and the decision to transfuse. Authors mention that decision to provide hysterctomy as made intraoperatively and at discretion of surgeon. Same should be made of transfusion which was primary outcome.

Reviewer #2: Thank you for your work.
A general comment: why did you choose pRBC transfused as your primary outcome instead of EBL? Is this in accordance with previous studies on the subject? I would bring this up in intro so we understand why you designed the way you did.

Abstract: overall well written, I would mention in the results the fact that there was a significant proportion of these patients treated without C-hysterectomy as this is outside of general practice, and might impact blood loss.

Introduction:
I would mention in this section that there are previous RCTs and what they show.

Lines 66-8 I would add here your hypothesis that you were working from.

Methods:
Line 81: explain what a "green channel" is.
Lines 120-22 I am assuming they were left in place but deflated, correct? And was this true in all omwen who did not have a hysterctomy and were in this group?

Line 172: Is c-hysterectomy an appropriate outcome measure, as the decision was influenced by patient desire not only by clinical situation?

Results:
In general you do not need to repeat numbers presented in tables in the text, just refer to the tables.

Can you present data on how many patients required additional hemostatic maneuvers in each group, especially given your high rate of not performing c-hysterectomy?

Lines 241-2 this may not be there case, we do not know what other hemostatic maneuvers were undertaken including medications (such as misoprostil which can cause temp elevations) and intrauterine tamponade.

Discussion: your discussion of limitations and review of previous literature is good.
Lines 272-6 this statement would need to be backed up with data.

Reviewer #3: This is a prospective randomized study performed to investigate the effect of intraoperative balloon occlusion of internal iliac arteries in women with scheduled cesarean delivery for placenta previa and antenatally suspected placenta accreta. Authors conclude that intraoperative balloon occlusion of internal iliac arteries did not reduce packed RBC units transfused in women with placenta previa and antenatally suspected placenta accreta.
There are in my opinion some major limitations:

1-Ultrasonographic characteristics: Bladder wall interruption (Loss or interruption of the bright bladder wall -the hyperechoic band or "line" between the uterine serosa and the bladder lumen) was not evaluated. This sign suggests bladder invasion. Cases with bladder invasion/ placenta percreta might be those more likely to benefit from prophylactic placement of balloon catheters in the iliac arteries. In this study only 38/100 women underwent caesarean hysterectomy (CH) and 31/38 had placenta percreta. A study performed by Cali et al (Cali G, Forlani F, Giambanco L et al. Prophylactic use of intravas- cular balloon catheters in women with placenta accreta, increta and percreta. Eur J Obstet Gynecol Reprod Biol 2014; 179: 36-41.) assessed the efficacy of using prophylactic intra-arterial catheters in the internal iliac arteries in cases of planned CH. This cohort study included 30 cases and 23 controls, all with antenatally diagnosed PAS (placenta accreta spectrum) disorders. The authors showed a significantly lower estimated blood loss and lower blood product transfusion requirement in cases as compared to controls (0.8 vs 1.2 L, and 0.5 vs 2.0 blood product units). A subset analysis showed this significant difference persisted with analysis isolated to those with only percreta but not with accreta or increta.
In my opinion it would make more sense to evaluate the role of prophylactic placement of balloon catheters in women with placenta previa and antenatally suspected bladder invasion/placenta percreta. This study is underpowered to assess this issue

2-Manual removal of the placenta was performed in about 70% of cases in both groups. Authors performed the "extirpative technique" in order to perform conservative management of PAS disorders. This procedure consists of forcibly removing the placenta manually in an attempt to empty the uterus at delivery. The aim of this approach is to avoid leaving retained placental tissues in the uterine cavity. In case of PAS disorders this procedure is often associated with massive obstetric hemorrhage and overall, not disturbing the accreta portion of the placenta is associated with more than a 50% reduction in blood loss and need for transfusions. Most of the experts advice against this procedure, making the results of the study poorly generalizable
In how many patient was manual removal of the placenta successful? How many had emergency/unplanned hysterectomy because of unstoppable maternal hemorrhage after attempted manual removal of the placenta? How many patients had uterine preservation attempted? In how many cases CH was the planned treatment?

3-criteria to define PAS in women who had caesarean hysterectomy or conservative management should be listed. First of all authors should clarify how the diagnosis of placenta accreta was confirmed in cases where the uterus was preserved. The authors should clearly explain the following sentence: page 20, line 281: "98% of participants had a surgical diagnosis of placenta accreta while 70% had a histological confirmation of accreta or percreta".

4-indications for blood transfusion should be clearly stated

STATISTICAL EDITOR'S COMMENTS:

1. Abstract: Should conform to our RCT format (include expected SD, along with difference of 2 units).

2. lines 106-110: How was the randomization procedure performed to assure exactly 50 women in each cohort?

3. Table 1: Gravidity, parity, prior uterine curettage can only have integer values, so should format as median(range or IQR) or as categories, not as mean/SD. Since each group had total = 50, should round all %s to nearest integer, not to nearest 0.1% precision.

4. Table 2: Same comment re: rounding % to nearest integer, rather than to 0.1% precision. Should clearly separate the primary outcome (RBC units transfused), from the secondary outcomes. Need to clarify which stats test was used for various comparisons. For example, EBL and length of stay are usually non-normally distributed, and thus would require non-parametric tests.

5. Table 3: Same comment re: rounding of % to nearest integer.

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. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. 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. 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).

4. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Materials and Methods section, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Materials and Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

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 and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. 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.
* 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).

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

9. 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.

10. 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.

11. 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%").

12. 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.

13. 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 via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

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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.

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 Jan 28, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2018 IMPACT FACTOR: 4.965
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

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[redacted]

January 17, 2020

Dear Editor:

Thanks so much for the editorial office and the reviewers' great comments to our manuscript entitled "Internal iliac artery balloon occlusion for placenta previa accreta: a randomized controlled trial" (ONG-19-2291).

We have revised this manuscript carefully according to all comments and would like to submit the revised manuscript which we wish to be considered for publication in Green Journal. Our point by point response appears in the flowing page of this letter and all responses are marked in red.

This study was approved by Ethics Committee of West China Second University Hospital of Sichuan University (M-2017-033) and registered with Chinese Clinical Trial Registry (ChiCTR-IOR-17012244). This manuscript is not under consideration elsewhere and will not be submitted elsewhere until a final decision is made by the Editors of Green Journal.

Thank you very much for your consideration.

Sincerely,

Xinghui Liu, M.D.

Department of Obstetrics and Gynecology

West China Second University Hospital

Sichuan University

Point by point response

REVIEWER COMMENTS:

Reviewer #1: "Internal iliac artery balloon occlusion for placenta previa accreta: a randomized controlled trial" is a well designed and described project that will carry great interest to readers of the journal.

There are small suggestions that I will detail below. The study design is similar to Salim et al 2015 - an RCT on the same subject matter published in Obstetrics and Gynecology. The rationale and conclusions are similar though this current study has a larger sample size.

Thanks very much and we really appreciate your comments.

Introduction: would benefit from highlighting current scope of the problem. Hypothesis is not clearly stated.

We add our hypothesis in the INTRODUCTION section. (Lines 70-72)

Methods: Good job of explaining diagnosis and management though the term "green channel" may not be familiar to many readers. Non-blinded study with subjective quantification of blood loss - observer bias should be acknowledged in discussion. Sample size calculation is similar to prior Salim study and appears appropriate.

We explain the “green channel” in the revised manuscript. The “green channel” ensured that women with placenta previa and suspected accreta who did not receive routine antenatal care in our hospital could transfer to our hospital as soon as possible, no matter whether they agreed or refused to participate in this trial. (Lines 91-94)

Observer bias is discussed in the DISCUSSION section. (Lines 283-284)

Results: Deliveries included scheduled CD 34-36.6 weeks. ACOG suggests 34-35.6 weeks. The average gestational age in this study was 36.4 and 36.1 for balloon and no balloon respectively. I would be curious as to the average transfusion comparing < 36 weeks and > 36 weeks.

Although ACOG suggests scheduled CD at 34-35.6 weeks for placenta accreta, timing of delivery for women with accreta is still under debate. For example, RCOG suggests 35+0 to 36+6 weeks (Jauniaux ERM, Alfirevic Z, Bhide AG, Belfort MA, Burton GJ,

Collins SL, et al on behalf of the Royal College of Obstetricians and Gynaecologists. Placenta Praevia and Placenta Accreta: Diagnosis and Management. Green-top Guideline No. 27a. BJOG 2018; https://doi.org/10.1111/1471-0528.15306.) and FIGO suggests 36-37 weeks for women who are stable (Allen L, Jauniaux E, Hobson S, Papillon‐Smith J, Belfort MA for the FIGO Placenta Accreta Diagnosis and Management Expert Consensus Panel. FIGO consensus guidelines on placenta accreta spectrum disorders: Nonconservative surgical management,. Int J Gynecol Obstet 2018;140:281-290. doi:10.1002/ijgo.12409).

In our hospital, a scheduled late preterm CD at 34-36 6/7 weeks was performed for women with placenta previa accreta who were stable.

In this trial there were 30 participants who delivered at < 36 weeks while 70 delivered at ⩾ 36 weeks, both the mean and median packed RBC units transfused (mean 5.3 vs 4.9, median 3.0 vs 3.0) and the mean and median blood loss (mean 2694 mL vs 2310 mL, median 1660 mL vs 1896 mL) were similar (P > .05). We do not add these results in the revised manuscript because these are not our intended outcomes.

There were 9 cases of post-operative fever (18%) in the balloon group though on 4 cases are explained: 1 intrauterine infection, 1 UTI, 2 causes of PNA. Given this adverse outcome in the intervention group, elaboration on etiologies would be appropriate.

The potential causes of postpartum fever are presented in the revised manuscript. (Lines 240-249)

Discussion: well done and highlights previous work in the area. Would acknowledge potential weakness of subjective EBL and the decision to transfuse. Authors mention that decision to provide hysterectomy as made intraoperatively and at discretion of surgeon. Same should be made of transfusion which was primary outcome.

We have discussed the potential observer bias caused by the subjectiveness of EBL and blood transfusion in this unblinded trial in the DISCUSSION section. (Lines 283-284)

Reviewer #2: Thank you for your work.

A general comment: why did you choose pRBC transfused as your primary outcome instead of EBL? Is this in accordance with previous studies on the subject? I would

bring this up in intro so we understand why you designed the way you did.

Thanks very much for your comments.

We used packed RBC transfused in units as our primary outcome because this was a relatively objective outcome which was easy to be calculated and compared. And this was similar to that in Salim and colleagues's trial (Salim R, Chulski A, Romano S, Garmi G, Rudin M, Shalev E. Precesarean prophylactic balloon catheters for suspected placenta accreta: a randomized controlled trial. Obstet Gynecol 2015;126:1022-8.).

We explain this in the MATERIALS AND METHODS section. (Lines 187-189)

Abstract: overall well written, I would mention in the results the fact that there was a significant proportion of these patients treated without C-hysterectomy as this is outside of general practice, and might impact blood loss.

We provide the data in Table 2 and in the RESULTS section (Lines 232-233), and discuss this in detail in the DISCUSSION section rather than mentioning that in the ABSTRACT section, because this was not the primary outcome in this study. (Lines 284-292)

Introduction:

I would mention in this section that there are previous RCTs and what they show.

We have cited the previous RCT and its results in the INTRODUCTION section. (Lines 60-64)

Lines 66-8 I would add here your hypothesis that you were working from.

We add our hypothesis in the INTRODUCTION section. (Lines 70-72)

Methods:

Line 81: explain what a "green channel" is.

We explain the "green channel" in the revised manuscript. The "green channel" ensured that women with placenta previa and suspected accreta who did not receive routine antenatal care in our hospital could transfer to our hospital as soon as possible, no matter whether they agreed or refused to participate in this trial. (Lines 91-94)

Lines 120-22 I am assuming they were left in place but deflated, correct? And was this true in all women who did not have a hysterectomy and were in this group?

Yes, catheters were left in situ with balloons deflated in women who did not have

hysterectomy for the convenience of postoperative uterine artery embolization. (Lines 133)

Line 172: Is c-hysterectomy an appropriate outcome measure, as the decision was influenced by patient desire not only by clinical situation?

In this trial, the decision to perform hysterectomy was based on both the clinical situation and the patient's desire to preserve the uterus, and mainly on the clinical situation. (Lines 150-169) Actually, all women in this trial had the desire to preserve their uteri. Additionally, many other previous studies also considered it as an outcome for women with placenta accreta. (Salim R, Chulski A, Romano S, Garmi G, Rudin M, Shalev E. Precesarean prophylactic balloon catheters for suspected placenta accreta: a randomized controlled trial. Obstet Gynecol 2015;126:1022-8. Shahin Y, Pang CL. Endovascular interventional modalities for haemorrhage control in abnormal placental implantation deliveries: a systematic review and meta-analysis. Eur Radiol. 2018;28:2713-26.)

Results:

In general you do not need to repeat numbers presented in tables in the text, just refer to the tables.

We have deleted the repeated numbers in the RESULTS section.

Can you present data on how many patients required additional hemostatic maneuvers in each group, especially given your high rate of not performing c-hysterectomy?

We provide these data in Table 2.

Lines 241-2 this may not be there case, we do not know what other hemostatic maneuvers were undertaken including medications (such as misoprostol which can cause temp elevations) and intrauterine tamponade.

Yes, we can not state that "the increased incidence of postoperative fever may be associated with the placement of balloon catheters", since uterotonics and intrauterine tamponade may influence this outcome. Therefore, we have changed our statement here. (Lines 266-267)

Discussion: your discussion of limitations and review of previous literature is good.

Lines 272-6 this statement would need to be backed up with data.

We have changed our statement and cite a reference to address this issue. (Rac MW, Dashe JS, Wells CE, Moschos E, McIntire DD, Twickler DM. Ultrasound predictors of placental invasion: the Placenta Accreta Index. Am J Obstet Gynecol 2015;212(3):343e1-7.) (Lines 301-302)

Reviewer #3: This is a prospective randomized study performed to investigate the effect of intraoperative balloon occlusion of internal iliac arteries in women with scheduled cesarean delivery for placenta previa and antenatally suspected placenta accreta. Authors conclude that intraoperative balloon occlusion of internal iliac arteries did not reduce packed RBC units transfused in women with placenta previa and antenatally suspected placenta accreta.

There are in my opinion some major limitations:

Thank you very much for your great comments.

1-Ultrasonographic characteristics: Bladder wall interruption (Loss or interruption of the bright bladder wall -the hyperechoic band or "line" between the uterine serosa and the bladder lumen) was not evaluated. This sign suggests bladder invasion. Cases with bladder invasion/ placenta percreta might be those more likely to benefit from prophylactic placement of balloon catheters in the iliac arteries. In this study only 38/100 women underwent caesarean hysterectomy (CH) and 31/38 had placenta percreta. A study performed by Cali et al (Cali G, Forlani F, Giambanco L et al. Prophylactic use of intravascular balloon catheters in women with placenta accreta, increta and percreta. Eur J Obstet Gynecol Reprod Biol 2014; 179: 36-41.) assessed the efficacy of using prophylactic intra-arterial catheters in the internal iliac arteries in cases of planned CH. This cohort study included 30 cases and 23 controls, all with antenatally diagnosed PAS (placenta accreta spectrum) disorders. The authors showed a significantly lower estimated blood loss and lower blood product transfusion requirement in cases as compared to controls (0.8 vs 1.2 L, and 0.5 vs 2.0 blood product units). A subset analysis showed this significant difference persisted with analysis isolated to those with only percreta but not with accreta or increta. In my opinion it would make more sense to evaluate the role of prophylactic placement of balloon

catheters in women with placenta previa and antenatally suspected bladder invasion/placenta percreta. This study is underpowered to assess this issue.

The reviewer suggests the evaluation of the role of prophylactic placement of balloon catheters in women with placenta previa and antenatally suspected bladder invasion or placenta percreta. This is a very good idea although the results may be less generalizable. Actually, we evaluated the ultrasonographic signs of bladder wall interruption but we did not provide data in Table 1. In the revised manuscript, we add these data in Table 1. According to the reviewer's suggestion, we conduct a post hoc analysis comparing packed RBC units transfused (7.4 vs 10.5, P=.15) and EBL (3272 mL vs 3648 mL, P=.50) in women with placenta percreta between two groups (17 in the balloon group and 14 in the control group), and find no significant differences. In those with hysterectomy and no attempt to remove the placenta (15 in the balloon group and 14 in the control group), the results were similar. In Cali and colleagues' retrospective study, there were 18 cases in the balloon group and 13 cases in the control group and the authors found that the blood products transfused and EBL were lower in the balloon group. However, the results should be explained with caution because cases in the two groups were collected in 2004-2009 (control group) and 2009-2013 (balloon group) respectively. Potential bias might be present in this study since surgical skills (which could impact blood loss) could be improved year by year.

2-Manual removal of the placenta was performed in about 70% of cases in both groups. Authors performed the "extirpative technique" in order to perform conservative management of PAS disorders. This procedure consists of forcibly removing the placenta manually in an attempt to empty the uterus at delivery. The aim of this approach is to avoid leaving retained placental tissues in the uterine cavity. In case of PAS disorders this procedure is often associated with massive obstetric hemorrhage and overall, not disturbing the accreta portion of the placenta is associated with more than a 50% reduction in blood loss and need for transfusions. Most of the experts advice against this procedure, making the results of the study poorly generalizable. In how many patient was manual removal of the placenta successful? How many had emergency/unplanned hysterectomy because of unstoppable maternal hemorrhage after

attempted manual removal of the placenta? How many patients had uterine preservation attempted? In how many cases CH was the planned treatment?

All data mentioned by the reviewer have been added in the revised manuscript in Table 1.

Actually, in 38 hysterectomy cases (31 with percreta and 7 with increta), only 9 were managed with manual removal of placenta and conservative management but underwent emergent hysterectomy because of heavy bleeding, while most of them were managed with hysterectomy without attempt to remove the placenta as guidelines suggested.

Planned cesarean hysterectomy for every woman with antenatally suspected accreta was not the routine practice in our hospital and in the present study concerning the possibility of false positive of the diagnostic methods. In fact, many women in our study had their uteri preserved, similar to the results of a previous RCT (Salim R, Chulski A, Romano S, Garmi G, Rudin M, Shalev E. Precesarean prophylactic balloon catheters for suspected placenta accreta: a randomized controlled trial. Obstet Gynecol 2015;126:1022-8.).

3-criteria to define PAS in women who had caesarean hysterectomy or conservative management should be listed. First of all authors should clarify how the diagnosis of placenta accreta was confirmed in cases where the uterus was preserved. The authors should clearly explain the following sentence: page 20, line 281: "98% of participants had a surgical diagnosis of placenta accreta while 70% had a histological confirmation of accreta or percreta".

We have explained both the surgical and pathological diagnosis of placenta accreta in the MATERIALS AND METHODS section. Placenta accreta was surgically confirmed with the failure of detachment by a gentle attempt to remove the placenta (Lines 177-178), while the pathological diagnosis of placenta accreta and percreta were made by microscopically observation of placental villi invading into the myometrium and invading through the myometrium (Lines 180-183). In some women who were conservatively managed just with manual removal of the placenta and local clamping and suturing, pathological examination was not performed because a resected specimen

was unavailable. (Lines 183-186)

4-indications for blood transfusion should be clearly stated.

There was no universal indications for blood transfusion for postpartum hemorrhage, the decision to transfuse blood products was made intraoperatively by the anesthesiologists and surgeons in our hospital, depending on the patient's hemodynamic status, the amount of blood loss and the results of hematological assessment. (Lines 172-176)

STATISTICAL EDITOR'S COMMENTS:

Thanks very much for the Editor's comments.

1. Abstract: Should conform to our RCT format (include expected SD, along with difference of 2 units).

We add SD in the METHODS SECTION in our ABSTRACT. (Line 34)

2. lines 106-110: How was the randomization procedure performed to assure exactly 50 women in each cohort?

The random allocation sequence was computer-generated and the randomization results in numbered opaque envelopes (including 50 in the treatment group and 50 in the control group) were kept in a closed box. Although we intended to assigned eligible women to study groups at the day before cesarean delivery after written informed consent was obtained, the envelope was opened and the allocation was unsealed until the morning of surgical day. (Lines 116-121) This procedure would lower the dropout rate in our study.

3. Table 1: Gravidity, parity, prior uterine curettage can only have integer values, so should format as median(range or IQR) or as categories, not as mean/SD. Since each group had total = 50, should round all %s to nearest integer, not to nearest 0.1% precision.

We have revised Table 1 according to the editor's requirements.

4. Table 2: Same comment re: rounding % to nearest integer, rather than to 0.1% precision. Should clearly separate the primary outcome (RBC units transfused), from the secondary outcomes. Need to clarify which stats test was used for various

comparisons. For example, EBL and length of stay are usually non-normally distributed, and thus would require non-parametric tests.

We have revised Table 2 according to the editor's requirements.

5. Table 3: Same comment re: rounding of % to nearest integer.

We have revised Table 3 according to the editor's requirements.

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.

A. Yes, please publish my point-by-point response letter.

2. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. 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.

Yes, we have carefully checked with coauthors and we confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. 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).

We provide Authors' Data Sharing Statement box in the revised manuscript.

4. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Materials and Methods section, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB website outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Materials and Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

Our study was approved by Ethics Committee of West China Second University Hospital of Sichuan University. This was documented in our cover letter and in the Materials and Methods 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 and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and- Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Thanks, we use reVITALize definitions without any problem.

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.

The revised manuscript has 4,492 words excluding 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.

* 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).

Our manuscript obeys the abovementioned rules.

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

We have carefully checked the abstract and the entire manuscript. Word count of the abstract is 238.

9. 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.

Our manuscript obeys the abovementioned rules.

10. 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.

We do not use virgule symbol in the manuscript.

11. 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.

We have provided relative risks where appropriate in our manuscript.

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.

Yes, we express the outcome of the comparison in U.S. dollar amounts in the revised manuscript.

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%").

Our manuscript obeys the abovementioned rules.

12. 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.

Tables in our manuscript conform to Green Journal's style.

13. 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 via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

We have cited the updated ACOG documents in our manuscript.

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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.

Yes, we would like to receive an email from the editorial office for choosing a

publication route (traditional or open access) if our article is accepted.

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.

We confirm that we have read the Instructions for Authors and a point-by-point response to each of the received comments has been provided in the cover letter.

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

Yes, the revised manuscript has been developed in consultation with our coauthors and each author has given approval to the final form of the revision.