

Peer Review File

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Reviewer A

Thanks for your submission, but there are many issues with this review, and little to no novel concepts, strategies, or perspectives presented. I am specifically concerned about the lack of discussion around ways to prevent complications.

This review presents no new ideas, perspectives, strategies, or information over older reviews. There are also major omissions in many sections, and the review doesn't actually follow through with the purported aim of helping readers not just list, but also prevent, identify, and manage complications.

I was surprised to see how little emphasis there was on the differences between glycine and isotonic solutions, the absence of tranexamic acid in this manuscript, the absence of any suggestions for how to reduce complications like perforation (ex. pencil grip of instruments, specific types of dilators etc) or gas embolism (ex. keep the sheath in the cervix/uterus and only withdraw the resecting element and scope when performing loop resection) etc etc. How to manage a patient with suspected gas embolism (ex. Trendelenberg, lateral tilt etc)

I have included many comments/notes in my annotated review.

Reply:

We extended each section with more details on the prevention, identification, and management of each complication, as you, the Reviewer, rightly pointed out.

We added more lines about the differences between hypotonic and isotonic solutions for better clarity, as advised. *(Please check lines 176-182; 185-190)*

We also discussed the role of tranexamic acid in hysteroscopic myomectomy, as suggested. *(Please check lines 264-270)*

Unfortunately, we tried very hard to crack all the comments and notes that you, Reviewer A, wrote down by hand in red on our manuscript. We succeeded in deciphering the majority but not all of them. We modified the manuscript as suggested in the parts that were clear to us. Please feel free to report again any notes that we could not understand from your handwritten notes, we will be glad to receive any further helpful advice to improve the quality of our manuscript.

Reviewer B

Comment 1: *“line 92-93: how is relevancy of other articles determined? how many total articles were found, what were the basis for including them in this review?”*

Reply 1: We conducted our research on Pubmed and Embase databases using keywords and matching them into pairs. Only articles published since November 1st, 1993 were included in our research. Our research resulted in 473 articles found matching the words “Hysteroscopy and Myomectomy”; 2502 for “Hysteroscopy and Complications”; 290 for “Hysteroscopy and Uterine perforation”; 16 for “Hysteroscopy and Intravascular Absorption Syndrome”; 7 for “Hysteroscopy and Venous Intravasation”; 2335 for “Hysteroscopy and Bleeding”; 330 for “Hysteroscopy and infection”; 804 for “Hysteroscopy and Adhesions”.

The relevancy of the articles that have been included in this review was determined based on intrinsic characteristics of the studies, such as the study design: Systematic reviews, Meta-Analyses, and Clinical randomized trials have been preferably reviewed. The inclusion criteria of each study have been verified, as well as the primary outcome (complication rate). Articles dealing with hysteroscopic myomectomy were preferably chosen. All the articles dealing with other intrauterine pathologies than submucous myomas (e.g., endometrial polyps, uterine septa, Retained Products of Conception, etc.) were excluded from this review.

Changes in the text: We added some details on our methods and specified these aspects in the Material and Methods section for greater clarity. *(Please check lines 69-75)*

Comment 2: *“line 106-108: the wording is confusing, and would benefit from stating the rate of perforation in “literature”, which should also be cited.”*

Reply 2: The rate of uterine perforation in literature varies slightly depending on the study under consideration. AAGL statistics from 1988, 1991 and 1993 showed uterine perforations in 1,1-1,4% of all hysteroscopic procedures (PMID: 2359057, PMID: 9050544). Other studies reported a perforation rate between 0,87 and 1,2% (doi: 10.1016/s1074-3804(96)80106-x). Compared with these studies, the multicentric study that we cited showed a lower overall incidence of uterine perforation (0,12%). Nevertheless, hysteroscopic myomectomy was the procedure with the highest rate of uterine perforation (0,15%).

Changes in the text: we cited the perforation rate we found from the analysis of many past studies, as suggested by the reviewer, for better clarity. *(Please check lines 87-89)*

Comment 3: *“line 119-120: would like to hear more about how thermal injury occurs without perforation”*

Reply 3: As explained in “doi: 10.1097/GRF.0000000000000146”, thermal injury can occur to intraperitoneal structures both with or without the perforation of the myometrium and the serosal surface. Even if thermal injury without uterine complete perforation is extremely less frequent, such an injury can still occur if an organ such as a bowel loop is deeply adherent to the serosal surface and deep myometrial electrosurgical technique is used. Moreover, when using a monopolar instruments, the “capacitative coupling” effect (also known as “current diversion”) regardless of the transmitted amount of energy, the monopolar current can be diverted to another path, resulting in an area of high current density on the vagina or vulva, with a possible undesired electrosurgical trauma, as also explained in PMID: 32696024.

Changes in the text: We added some lines about the capacitative coupling effect and added a reference (doi: 10.1016/j.ogc.2010.05.007) to better clarify this aspect about electrosurgical injuries. *(Please check lines 119-132)*

Comment 4: *“line 175: either keep ‘evidence’ or ‘data’ in the sentence”*

Reply 4: Thank you for your suggestion.

Changes in the text: We have modified this sentence as suggested.

Comment 5: *“line 176: consider using the word “depth” instead of degree of plunge into the myometrium”*

Reply 5: Thank you for your suggestion.

Changes in the text: We have modified this sentence as suggested.

Comment 6: *“line 189: why is embolism the primary symptom to be watching out for when so much of what was previously discussed has been about fluid overload”*

Reply 6: Thank you for your correct specification.

Changes in the text: We have modified this sentence for better clarity, as suggested.

Comment 7: *“line 201 - 202: would be helpful to outline how vasopressin helps and what the effects seen in the studies were”*

Reply 7: Thank you for your suggestion.

Changes in the text: We added some lines about the effect of the intralesional vasopressin injection during a hysteroscopic myomectomy. *(Please check lines 212-216)*

Comment 8: *“line 230 - 232: any data on how shrinking fibroids with lupron pre-operatively can make hysteroscopy more difficult if the fibroids are too small to see”*

Reply 8: While some Authors have suggested that the shrinking of the fibroids after the pre-treatment with GnRH-a may lead to a more difficult discernment of the lesion, resulting in a missed identification of the disease, other data suggested that the evidence of fibroid “recurrence” (after a missed identification) in the literature is equivocal, while the advantages of the hormonal treatment in reducing operative time, blood loss and the complication rate have been clearly demonstrated.

Changes in the text: We added some lines about this topic and two more references. *(Please check lines 251-257)*

Comment 9: *“line 237: what uterotonics is the author referring to? there is data to suggest that not all uterotonics (such as Pitocin) works in the non-pregnant uterus”*

Reply 9: According to our research, the existing evidence on the use of uterotonics in reducing and managing blood loss during myomectomy is still limited, but some data showed that oxytocin appears to be the most effective in reducing the need for blood transfusion and blood loss.

Changes in the text: We clarified this in the text and added a reference about this topic. *(Please check line 262)*

Comment 10: *“line 255-257: this is not a common practice”*

Reply 10: According to our research, we found different articles about the use of hyaluronic gel in reducing the recurrence of IUAs after hysteroscopic surgery. Although it may not be very common, data showed that its routine application after a hysteroscopic myomectomy should be recommended, especially after multiple myomectomy (Grade 1B recommendation).

Changes in the text: none.

Comment 11: *“line 276 -279: this wording is confusing. and compared to the bipolar loop the morcellator is removed from the patient fewer times per surgery”*

Reply 11: Thank you for your suggestion.

Changes in the text: We removed those lines for better clarity.

Reviewer C

Comment 1: *“I believe there’s a typo in this sentence, lines 106-107. Please address: “A multicenter study conducted on 21676 patients, even if registering a lower incidence of uterine perforation if compared to literature, showed that hysteroscopic myomectomy”*

Reply 1: Thank you for your suggestion.

Changes in the text: We modified that sentence for better clarity, as suggested. *(Please check lines 87-89)*

Comment 2: *“In the “distention fluid-related complications” section, the specific risks of hypotonic vs isotonic solutions should be more thoroughly presented, and the section should be better organized. I recommend having a paragraph on the specific risks of each solution type rather than trying to begin with the overlapping risks common to both solutions. Isotonic solutions are much safer and easier to use than hypotonic solutions, and this should be the conclusion of this section.”*

Reply 2: Thank you for your advice. As well suggested by you, in lines 184-186 we had already specified that the isotonic solutions are safer than the hypotonic ones in reducing the risk of OHIA.

Changes in the text: We added more lines to extend this section and better describe the differences between the two categories of solutions, as suggested. *(Please check lines 176-190)*

Comment 3: *“In the venous gas embolism section and the last paragraph on carboxyhemoglobin, I recommend you include this paper which describes a prospective trial: doi:10.1016/j.jmig.2022.09.002”*

Reply 3: Thank you for your recommendation.

Changes in the text: We included this paper as a reference in our work, as suggested. *(Please check lines 233-236)*

Comment 4: *“Sentence structure in line 313 is both too informal and awkward for scientific paper “Speaking of HM, IOUS increases”*

Reply 4: Thank you for your suggestion.

Changes in the text: We modified that sentence, as suggested.