Peer Review File

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Reviewer A

Major points:

Comment 1: Introduction page 2 line 38: I believe this should be reactive hypertrophy rather than reactive fibrosis of the surrounding smooth muscle.

Reply 1: Thank you for this comment, we have amended this to read "reactive hypertrophy" on page 3 line 38 of the manuscript.

Comment 2: Introduction page 2 line 46: Because the "junctional zone" isn't a phrase most pathologists are familiar with, I would suggest defining it here.

Reply 2: Thank you for this comment, we have now included a definition for the junctional zone on page 3 line 45 of the manuscript.

Comment 3: Page 4 line 82: Replace "endometrial tissue" with "Mullerian rests" per review of the cited article.

Reply 3: Thank you for this comment, we have replaced "endometrial tissue" with "Mullerian rests" as advised, on line 82 page 7 of the manuscript.

Comment 4: Page 4 line 88: To avoid later confusion, I would recommend changing "…two different pathophysiological processes…" to "…three…" Reference 13 describes three subtypes of adenomyosis based on MRI findings, with a fourth group

not meeting strict criteria for the other three. Intramural adenomyosis without involvement of the junctional zone or serosa is postulated to represent the result of metaplasia.

Reply 4: Thank you, we have amended "two" to "three" as advised, on line 88 page 8 of the manuscript.

Comment 5: Page 6 line 123: "… women with focal adenomyosis (often referred to as intramural adenomyomas by pathologists) …"

Reply 5: Thank you, we have amended as advised on line 121 page 14 of the manuscript.

Comment 6: Page 7 line 151: Recommend rephrasing to "Recent advances in ultrasound and MRI technology have facilitated the [minimally invasive? Noninvasive?] diagnosis of adenomyosis, avoiding the need for surgical excision to make a diagnosis."

Reply 6: Thank you, we have re-phrased as advised to "Recent advances in ultrasound and MRI technology have facilitated the non-invasive diagnosis of adenomyosis, avoiding the need for surgical excision to make a diagnosis." on line 148 page 16 of the manuscript.

Minor points:

Comment 1: In the abstract, recommend writing out "heavy menstrual bleeding" at

the first mention.

Reply 1: Thank you, we have now written out “heavy menstrual bleeding” in the abstract.

Comment 2: Page 4 line 73: It may be appropriate to include the caveat that adenomyosis was previously diagnosed almost exclusively at the time of hysterectomy, whereas modern ultrasound techniques allow for noninvasive diagnosis.

Reply 2: Thank you for this comment. We have now included this aspect on line 152 page 16 of the manuscript and therefore have not made any change to line 73 of the manuscript.

Comment 3: Page 5 line 103: Recommend adding “(as discussed below)” after the “distinct clinical presentations.”

Reply 3: Thank you, as advised we have now added “as discussed below” after the “distinct clinical presentations.” On line 105 page 10 of the manuscript.

Comment 4: Page 5 line 116: Recommend being more consistent about using “inner and outer adenomyosis” or “internal and external adenomyosis.”

Reply 4: Thank you for pointing this out. We have now consistently used “inner and outer adenomyosis” instead of “internal and external adenomyosis” throughout the manuscript.

Comment 5: Page 6 line 137: "... have been suggested to explain the negative impact of adenomyosis on fertility ..."

Reply 5: Thank you for pointing this out, we have amended the wording accordingly on line 136 page 14 of the manuscript.

Comment 6: Reference 3: Human Reprod. 2021;36(2):349-357.

Reply 6: Thank you for pointing this out, we have amended reference 3 accordingly.

Reviewer B

This study was very interesting for me, because this review provided "Treatment part" including latest methods, so-called Uterine-sparing surgery such as adenomyomectomy. In Cochrane Reviews, surgical managements were not included (Hormonal treatment for uterine adenomyosis). So, I think the adoption may be dependent on the balances of other researches in this journal. And I could only point out two requests as follows:

Comment 1: In Clinical presentation part, you explained about co-existing leiomyomas and endometriosis. In the latter, you showed the specific probabilities, but you did not show in the former. I want to know these probabilities.

Reply 1: Thank you for this comment. The probability of co-existing leiomyomas in

women with adenomyosis is included in the “Epidemiology” section – “The coexistence of endometriosis and fibroids was common, at 18% and 47%, respectively” on line 72 page 7 of the manuscript.

Comment 2: In Treatment part, you said “Combing surgery with GnRH analogue treatment may improve its effectiveness”. I want to know the specific difference when performing ART for these patients with surgical treatments for adenomyomas.

Reply 2: Thank you for this comment. The usefulness of combination of GnRH therapy with surgery is not clear. In one report it has been suggested that combining surgery with GnRH analogue treatment may improve its effectiveness for symptom relief of dysmenorrhea and menorrhagia (Wang P-H, Liu W-M, Fuh J-L, Cheng M-H, Chao H-T. Comparison of surgery alone and combined surgical-medical treatment in the management of symptomatic uterine adenomyoma. Fertil Steril. 2009;92(3):876–85.) However, there is currently any data specifically relating to GnRH analogue and surgical treatment of adenomyoma with subsequent ART outcomes.