Author’s response to reviews

Title: Do endometrial lesions require removal? A retrospective study

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Author’s response to reviews:

Reviewer 1

Thank you for your valuable comments.

1. This group indicted proliferative/secret-ory/atrophy in table 3, they are not pathological.

2. Thank you for your valuable comments.

①Because hysteroscopy is the gold standard for endometrial carcinoma. Avoid the situation of missed diagnosis due to d&c.

②The endometrial benign and malignant diseases have certain characteristics under hysteroscopy, but this is not the focus of our major objective. Hysteroscopy is an invasive investigation. What we want to do is to pass the characteristics of ultrasound, suggesting that we are good. Malignant diseases increase the detection rate of malignant diseases and reduce unnecessary surgery.
③ Ultrasound prompted endometrial thickening, may be simple endometrial thickening, or endometrial polyps. We could treated with hysteroscopic biopsy or polypectomy with micro-scissors. If it is the former, hysteroscopic sampling will be performed. If it is the latter, divide it with micro-shear.

3. Thank you for your suggestion. All choose hysteroscopy, because hysteroscopy is the gold standard for diagnosis of endometrial cancer, in order to avoid missing cases) caused by d&c. The cut-off value of the endometrium is to predict the probability of endometrial malignant lesions by ultrasound. The thicker the endometrium, the higher the possibility of endometrial cancer, especially in postmenopausal women. It is not our primary goal to simply assess the sensitivity and specificity of hysteroscopy.

4. Material and methods should be detailed:

Inclusion criteria: Premenopausal endometrial inhomogeneity or uterine cavity lesions. On the 3-5th day of menstruation next month, review the ultrasound if there is still uneven endometrium or uterine cavity lesion; Postmenopausal endometrium ≥ 5mm or uterine cavity lesion. Exclusion criteria: The growth stage patients with thicker endometrium were followed up by the clinic. Hysteroscopic treatment was required if there was abnormal uterine bleeding. And all the hysteroscopic surgery for abnormal uterine bleeding is beyond our scope of discussion. We detailed the methods in the 3th paragraph.

Results were expressed as means±standard deviation (SD) or standard error of mean (SEM). Data were analysed by SPSS 22.0 (Chicago, IL, USA). The comparison between the two groups was performed with the chi-square test and P < 0.05 indicates statistically significance. A multi-logistic regression analysis was applied to study the risk factors for malignancy in patients with asymptomatic endometrial lesions. We detailed the methods in the 4th paragraph.

5. Discussion should be written detailed:

Thank you for your valuable comments. In our clinical work, most patients were reviewed in the clinic one month after surgery, and then converted to regular gynecological examination. If the patient does not come to see a doctor, it is difficult to follow up whether it relapses or not. So we check some literatures to clarify that recurrence rate and malignant transformation rate of the polyps. And we detailed this part in the discussion.

Hysteroscopic surgery for large EPs using bipolar resectoscopes, hysteroscopic morcellators or shavers are considered equally efficient and safe under general anaesthesia. Recurrence rate of EPs after resection is unknown to our knowledge. The recent advances in TVU and hysteroscopy, however, should provide an accurate diagnosis and effective treatment of polyp in the female reproductive tract with minimal recurrence or surgery complications. The
significantly increased incidence of colorectal polyps in cohorts that also had EPs might indicate that patients with EPs should be also referred for colonoscopy. EPs have the lowest incidence of malignant transformation as compared to colon, urinary bladder, oropharyngeal, nasal and laryngeal carcinomas. [Int J Surg. 2017 Jul;43:7-16. doi: 10.1016/j.ijsu.2017.05.012. Epub 2017 May 5. The management of polyps in female reproductive organs. Tanos V1, Berry KE2, Seikkula J3, Abi Raad E4, Stavroulis A5, Sleiman Z6, Campo R7, Gordts S8.]

The prevalence of polyp among women who underwent diagnostic hysteroscopy was more common in the age group of 40-49 years. There was one uterine perforation, one cervical tear, one false passage and one patient had mild bleeding after the procedure. In the study, in the mean follow-up period of 37.57±28.12 months, 3.9% (7 women) had recurrence. In the follow-up period of 16.56±18.96 months, 78.9% women didn't have recurrence. [J Clin Diagn Res. 2016 Jun;10(6):QC01-4. doi: 10.7860/JCDR/2016/18173.7983. Epub 2016 Jun 1. Clinical Study of Endometrial Polyp and Role of Diagnostic Hysteroscopy and Blind Avulsion of Polyp. Kanthi JM1, Remadevi C1, Sumathy S2, Sharma D3, Sreedhar S4, Jose A5.]

The incidence of premalignant and malignant endometrial disorders increases during the postmenopausal period. In the literature, endometrial disorders are usually discussed in the context of menopausal status. But there are limited data regarding endometrial disorders in geriatric patients. Early diagnosis of endometrial cancers with aggressive behaviour that increases during the geriatric period may allow simpler treatment options and also decrease the treatment-associated morbidity risks. Records of geriatric patients who underwent an endometrial histopathological evaluation between 2011 and 2016 were evaluated. Clinical findings, transvaginal ultrasonography findings, endometrial sampling methods, and histopathological results were evaluated. A total of 188 patients were included in the study (mean age 70.3 ±5.6 years). The most common histopathological results were endometrial polyp, atrophic endometrium, and surface epithelium (26.6%, 22.3%, and 12.8%, respectively). None of the 57 patients without vaginal bleeding had endometrial cancer. In 131 patients with vaginal bleeding, mean endometrial thickness was 9.8 ±8.1 mm (2-49 mm) and the rate of endometrial disorders was 56.5% (74 patients). Endometrial cancer was diagnosed in 19 patients (10.1%), and 36.8% of them had non-endometrioid cancers. The presence of vaginal bleeding was significantly associated with the diagnosis of endometrial cancer and any endometrial disorder (p = 0.001 and p = 0.000, respectively). The incidence of non-endometrioid endometrial cancers increased in the geriatric period. An endometrial histopathological examination should be considered, especially for patients with a history of vaginal bleeding. Further investigation of the endometrial thickness cut-off levels in the geriatric period will contribute to the literature. [Prz Menopauzalny. 2018 Mar;17(1):18-21. doi: 10.5114/pm.2018.74898. Epub 2018 Apr 11. Endometrial histopathology results and evaluation of endometrial cancer risk in geriatric women. Günakan E1, Atak Z1, Albayrak M1, Kurban Y1, Şimşek GG1.]

We discussed the detailed issue in the discussion section.
Reviewer 2

Thank you very much for your help informations.

1. Premenopausal endometrial insufficiency or uterine cavity abnormality. On the 3-5th day of menstruation next month, review the ultrasound if there is still uneven endometrium or uterine cavity lesion; Postmenopausal endometrium ≥ 5mm or uterine cavity lesion. The growth stage patients with thicker endometrium were followed up by the clinic. Hysteroscopic treatment was required if there was abnormal uterine bleeding. And all the hysteroscopic surgery for abnormal uterine bleeding is beyond our scope of discussion. We detailed the methods in the 3th paragraph. And none of our patients had a history of previous hysteroscopic surgery.

2. Asymptomatic means free of bleeding in our study, because it is the main symptom of endometrial carcinoma.

3. Thank you for your suggestion. Because hysteroscopy is the gold standard for endometrial carcinoma. Avoid the situation of missed diagnosis due to d&c. So all patients were received hysteroscopic. Results were expressed as means±standard deviation (SD) or standard error of mean (SEM). Data were analysed by SPSS 22.0 (Chicago, IL, USA). The comparison between the two groups was performed with the chi-square test and P < 0.05 indicates statistically significance. A multi-logistic regression analysis was applied to study the risk factors for malignancy in patients with asymptomatic endometrial lesions. We detailed the methods in the 4th paragraph.

4. We agree with the opinion of the conclusion would be better limited to the Chinese population. And a multi-logistic regression analysis was applied to study the risk factors for malignancy in patients with asymptomatic endometrial lesions. The results revealed that age and ET were correlated with malignancy, whereas other factors such as BMI, obesity, diabetes and hypertension were not correlated with malignancy.

5. According to current practice, all of our patients underwent uterine surgery and signed an informed consent procedure prior to surgery. The purpose of our study is also to reduce unnecessary surgical intervention in most patients and to improve the detection rate of endometrial cancer.

If a patient has an expectant management or is lost to follow-up for some reason, wouldn't that worsen her prognosis? This point is relevant and is not discussed by authors:
Thank you for your valuable comments. In our clinical work, most patients were reviewed in the clinic one month after surgery, and then converted to regular gynecological examination. If the patient does not come to see a doctor, it is difficult to follow up whether it relapses or not. So we check some articles to clarify that recurrence rate and malignant transformation rate of the polyps. And we detailed this part in the discussion.

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We detailed this part in the discussion.

Reviewer 3

Thank you very much for your suggestion.

1. Thank you very much for your help informations. The background of our article is mainly based on the guidelines. The main purpose of the article is to compare current guidelines and advocate for unnecessary surgery. The guide itself is a comprehensive study of large-scale research, relatively simple, if you list other documents, it seems that the article is
cumbersome and complicated. And we have added citations in the background and discussion section.

In a study included 112 women with endometrial polyps, which were expectantly managed over a median period of 22.5 months (range, 6-136). There was no association between women's demographic characteristics or polyps' morphology and their growth rates. Spontaneous regression appeared to occur more frequently in premenopausal women (P = 0.016) and in those who presented with abnormal uterine bleeding at diagnosis (P = 0.004); however, the differences did not reach statistical significance after correction for multiple comparisons. [Hum Reprod. 2017 Feb;32(2):340-345. doi: 10.1093/humrep/dew307. Epub 2016 Dec 18. The natural history of endometrial polyps. Wong M1, Crnobrnja B2, Liberale V3, Dharmarajah K1, Widschwendter M1, Jurkovic D4.]

2. Results were expressed as means±standard deviation (SD) or standard error of mean (SEM). Data were analysed by SPSS 22.0 (Chicago, IL, USA). The comparison between the two groups was performed with the chi-square test and P < 0.05 indicates statistically significance. A multi-logistic regression analysis was applied to study the risk factors for malignancy in patients with asymptomatic endometrial lesions. We detailed the methods in the 4th paragraph.

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3. Because hysteroscopy is the gold standard for endometrial carcinoma. Avoid the situation of missed diagnosis due to d&c.

4. Thank you for your comments, we have made amendments accordingly.

5. The point we want to make here is that the cut-off value for endometrium thickness is crucial for clinicians in Chinese patients.