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Correspondence

Response to comment on: Comparison of diagnostic accuracy between endometrial curettage and aspiration biopsy in patients treated with progestin for endometrial hyperplasia: a Korean Gynecologic Oncology Group study

▸ See the letter "Letter to editor in response to: Comparison of diagnostic accuracy between endometrial curettage and aspiration biopsy in patients treated with progestin for endometrial hyperplasia: a Korean Gynecologic Oncology Group study" in volume 31, e88.

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
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We would like to thank Dr. Sabour for his interest in our study and for taking time to express his concerns. We would also like to thank the Editor for the opportunity to respond to the issues raised in Dr. Sabour's letter and to clarify aspects of our methodology in relation to those concerns.

In his letter to the editor, Dr. Sabour notes methodological issues in evaluation of the diagnostic accuracy of endometrial aspiration biopsy. Actually, the optimal design for assessing the accuracy of a diagnostic test for endometrial pathology is considered to be an independent, prospective blind comparison, with the appropriate population and close chronological proximity between the main test and the reference test. In the literature, there is no study assessing the diagnostic accuracy of endometrial biopsy that satisfies such rigorous methodology; therefore, we must proceed with suboptimal study designs and interpret results accordingly [1-3].

The primary objective of our study was to compare the diagnostic accuracy of dilatation & curettage (D&C) versus endometrial aspiration biopsy in follow-up evaluation of patients treated with progestin for endometrial hyperplasia (EH) [4]. In principle, to compare the accuracy of the two methods, preoperative D&C and aspiration biopsy have to be performed before hysterectomy, and then, the histological findings for the subsequently obtained hysterectomy specimen (the reference test) should be compared with those obtained by the preoperative D&C and aspiration biopsy [5]. However, in our study, patients had been treated with hormonal therapy to avoid surgery, and so we could not obtain a hysterectomy specimen. Therefore, we evaluated the diagnostic accuracy of aspiration biopsy in comparison with D&C, widely considered the gold standard for endometrial assessment and routinely used [6]. The consistency of the histological results between the aspiration biopsy and the D&C was the primary outcome of this study. We estimated the diagnostic accuracy of aspiration biopsy by "agreement," which means, the consistency of the histological results between the aspiration biopsy and the D&C. Kappa statistics were used to assess the agreement. Thus, they were not used to determine reliability (precision).

Dr. Sabour suggested the use of statistical tools (i.e. sensitivity, specificity, positive and negative predictive values, likelihood ratios [LRs] and odds ratios [ORs]) for more accurate estimation. We did not use them in our study, because we could not obtain the hysterectomy specimen (the reference test). If a D&C specimen had been used as the reference test, the results of aspiration biopsy would have been as follows.

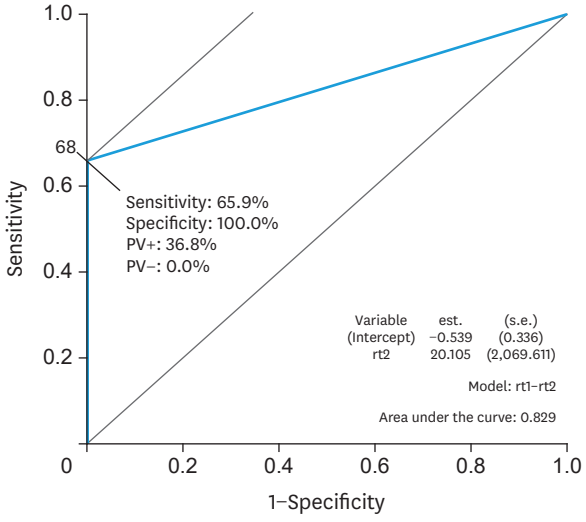
Point estimates and 95% CIs:

Apparent prevalence	0.37 (0.25–0.50)
True prevalence	0.58 (0.46–0.71)
Sensitivity	0.63 (0.46–0.78)
Specificity	1.00 (0.87–1.00)
Positive predictive value	1.00 (0.86–1.00)
Negative predictive value	0.66 (0.49–0.80)
Positive likelihood ratio	Inf (NaN–Inf)
Negative likelihood ratio	0.37 (0.24–0.56)

The LR indicates the extent to which a given aspiration biopsy either raises or lowers the probability of having EH. The positive and negative LRs for prediction of EH are infinity and 0.37. Therefore, for EH patients treated with progestin, a positive test result (i.e. detection of disease) is more accurate than a negative test result (i.e. exclusion of disease).

In the results, among the 38 cases of EH on D&C, only 24 were diagnosed with EH from aspiration biopsy, for a diagnostic concordance of 63.2% (κ=0.59). Although the diagnostic concordance was low, we cannot conclude that endometrial aspiration biopsy is a less accurate method. However, there were 14 cases of false negatives in aspiration biopsy compared with D&C, but no case of normal endometrium by D&C diagnosed as EH by aspiration biopsy. In other words, this disagreement between the two methods equates to a false negative result for aspiration biopsy. Thus, we think that the accuracy of aspiration biopsy for diagnosis of EH is inadequate.

In addition, as Dr. Sabour suggested, to evaluate the diagnostic added value, the receiver operating characteristic (ROC) curve is drawn. The McNemar test was used as appropriate (McNemar's $\chi^2 = 12.071$, df = 1, p-value = 0.000512).



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In summary, we believe that the concerns raised by Dr. Sabour have minimal impact on our derived conclusion that endometrial aspiration biopsy cannot be considered to be an appropriate method for accurate response assessment of hormonal treatment of EH.

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