random-effects model. We agree that the IVhet model could improve the heterogeneity issue. Nevertheless, the DerSimonian and Laird random-effects model we used is reasonable as the Cochrane Handbook [2] mentioned that the difference between the random-effects model and other advanced models is similar—“In practice, the difference in the results is likely to be small unless there are few studies.” In addition, most of the outcomes reanalyzed by Cui et al using the IVhet model were consistent with ours, with only 1 exception, the incidence of transfusion. However, the result remained to favor the high-intensity focused ultrasound group. Overall, because there was no major change in the outcomes and the conclusions, the DerSimonian and Laird random-effects model we used was sufficient enough.

To summarize, we appreciated the comment made by Cui et al and agreed that the search of databases and the use of appropriate statistical models are essential to meta-analysis studies. We agreed that high-quality studies with larger sample sizes are still needed in the future to confirm these conclusions. Nevertheless, our research strategies have addressed the research questions appropriately for the time being.

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References

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Regarding “Optimal Dose of Pituitrin in Laparoscopic Uterine Myomectomy: A Prospective, Double-Blinded, Randomized Controlled Trial”

To the Editor:

I congratulate the authors on completing a randomized controlled trial (RCT); this methodology is the gold standard for investigations of treatment efficacy. However, to generate valid and generalizable data, studies must adhere to the tenets of a well-designed, executed, and analyzed RCT.

Equipoise is one of these tenets. Here, there was not equipoise between randomization arms. Guo et al [1] randomized patients to placebo and 3 doses of Pituitrin. There was preexisting evidence from old [2,3] and recent [4] RCTs and other studies [3] that vasopressin reduces blood loss at the time of myomectomy, and Pituitrin is simply a combination of oxytocin and vasopressin. Including a placebo group unnecessarily exposed participants to potential harm from excessive blood loss. Future investigations of hemostasis prophylaxis at laparoscopic myomectomy should not include a placebo arm unless there is true equipoise, and alternate methods known to reduce blood loss are used [5].

To be generalizable, the primary outcome must be described in sufficient detail to allow for reproducible assessment. There is no definition of “...satisfactory surgical field,” and even if there was, it would be too subjective to reproduce. Transfusion or measured blood loss is a more objective primary outcome for similar investigations.

Finally, statistical analysis must be clear. Was analysis performed by intent to treat, by protocol, as treated, or “other”? Given that crossover was allowed at the surgeons’ discretion, this could markedly affect interpretability. There seemed to be a dose-response relationship in the primary and secondary outcomes, but misclassification may have diluted or amplified intergroup differences depending on number of crossover events and method of statistical analysis. It is also problematic that there was no consideration of preoperative medical therapies such as leuprolide acetate or antiocoagulation. Although we might assume that randomization balanced these potential confounders known to affect intraoperative bleeding, this should be demonstrated in Table 1 [1].

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References

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Author’s Reply

To the Editor:

We thank Dr. Devon Evans for his comments on our recently published study titled “Optimal Dose of Pituitrin in
Laparoscopic Uterine Myomectomy: A Prospective, Double-Blinded, Randomized Controlled Trial [1].” We appreciate the opportunity to respond to the issues raised by Dr. Devon Evans in his letter.

We do agree with his viewpoints that clinical study must adhere to the tenets of a well-designed, executed, and analyzed randomized controlled trial. However, we do not think there was not equipoise, one of the tenets, between randomization arms in our study [1]. Including a placebo group would provide more exact information on the effects (both treat effects and adverse effects) of Pituitrin with a range of different doses including 0 IU. Of course, participants in the placebo group could have potential harm from excessive blood loss in theory. However, hemostasis prophylaxis with Pituitrin at laparoscopic myomectomy has not been mandatory in clinical procedure so far. In addition, a patient with the number of main myomas of >3 and maximal diameter of >10 cm was excluded from our study. Moreover, effective rescue strategies were available for all participants. Therefore, the potential harm from excessive blood loss of the patients in the placebo group could be well controlled and should not be an ethical problem.

Satisfactory surgical field, which refers to satisfactory surgical condition, was evaluated by the surgeon who performed the laparoscopic myomectomy using the visual analog score (VAS), which has been elaborated in the article. Several similar studies also have described VAS to evaluate and quantify the surgical condition [2,3]. Despite of its subjectivity, the VAS rating the surgical condition is still a general and widely accepted methodology. Fortunately, the results of estimated blood loss supported the results of the VAS of satisfactory surgical field in our study, which also suggested the VAS is a valid tool for such a study.

Regarding the balanced randomization, we preset strict inclusion and exclusion criteria and used a well-accepted randomization method. Please refer to the Methods section of our paper.

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