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Letter to the Editor

Comment on "Impact of insulin use on outcomes of diabetic breast cancer patients: a systematic review and meta-analysis"

Dear Editor,

With great interest, we read the article by Wang et al[1] published in 2021 in the Eur Rev Med Pharmacol Sci. The authors performed a meta-analysis and concluded that "Diabetic breast cancer patients on insulin have increased mortality and recurrence rates as compared to insulin non-users". At the outset, we would like to congratulate the authors for writing an informative article with novelty. Nevertheless, we have several suggestions and queries that we would like to communicate with the authors.

There are several flaws in the study design that are worth mentioning. First and foremost, the authors mentioned that PubMed, Embase, and CENTRAL were searched in this study, but they were not enough. It would make the outcomes more convincing if the authors included other databases, like clinicaltrials.gov, Web of Science, NLM Gateway, and BIOSIS previews, to obtain more literature. Furthermore, two important studies which published online in 2012 (Redaniel et al[2] 2012) and 2019 (Baglia et al[3] 2019) were missed. This was possibly related to the improper search strategy used in the meta-analysis. Identifying and aggregating as many eligible studies as possible are the keys to improving the quality of meta-analysis.

Another concern of us is about the high heterogeneities in the results. High inter-study heterogeneity could not result in a definite conclusion according to Cochrane Handbook for Systematic Reviews. With such large heterogeneities found in this meta-analysis, sensitivity analysis had been conducted to explain the source of heterogeneity. As far as we know, a more robust model, named Inverse Variance Heterogeneity (IVhet) model, has been introduced in the study of Doi et al[4]. They examined an improved alternative to the random effects (RE) model for meta-analysis of heterogeneous studies. It was shown that the known issues of underestimation of the statistical error and spuriously overconfident estimates with the RE model could be resolved by the use of an estimator under the fixed effect model assumption with a quasi-likelihood-based variance structure – the IVhet model[4]. Thus, we subsequently used the IVhet model to re-analyze the outcomes in this meta-analysis. Most of the re-analysis outcomes were consistent with the authors, however, no statistically significant difference was detected for the all-cause mortality between the groups (HR = 1.30, 95% CI 1.00 to 1.69) (Figure 1).

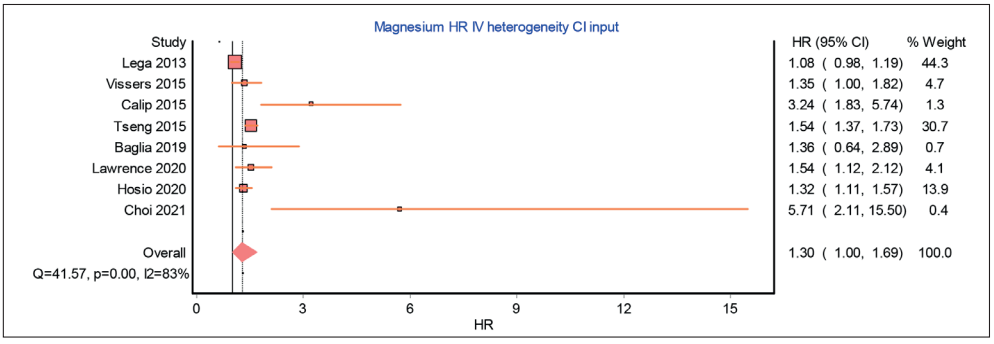

Figure 1. Forest plot of re-analysis for the all-cause mortality between insulin users vs. non-users.

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Most of the included studies were not randomized controlled trials, and there were significant biases in this paper, which should be pointed out in the discussion. Finally, different doses and types of insulin therapy may affect the accuracy of the results, thus further subgroup analyses may be necessary. Overall, Wang et al[1] analyzed a valuable issue but the results of this meta-analysis should be interpreted with caution due to the limitations mentioned above.

Conflict of Interest

All authors declare no Conflicts of Interests for this study.

Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent

For this type of study, formal consent is not required.

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L.-L. Wang and D.-Q. Yue contributed equally to this study.

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