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LETTER

Comments on a meta-analysis and systematic review of the clinicopathological significance of CDH1 in gastric cancer

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Dear editor

With great interest, we read an article entitled "The clinicopathological significance of CDH1 in gastric cancer: a meta-analysis and systematic review" by Zeng et al,[1] which was published in *Drug Design, Development and Therapy* in April 2015. In this meta-analysis, the investigators systematically reviewed the studies on correlation between CDH1 hypermethylation and gastric cancer (GC), and concluded that CDH1 hypermethylation levels in GC and adjacent gastric mucosa are both significantly higher when compared with normal gastric mucosa. Meanwhile, CDH1 hypermethylation is found markedly correlated with *Helicobacter pylori* status. Taken together, CDH1 hypermethylation is positively associated with overall GC risk and the *H. pylori*-positive GC risk.[1] It is a valuable study. Nevertheless, there are several queries that we would like to communicate with the authors.

Only three electronic databases (PubMed, Embase, Web of Science) were systematically searched for eligible studies.[1] The small number of acquired trials could be regarded as a flaw of this meta-analysis. From our perspective, any effort to minimize the bias should be valued; therefore, other common databases including the Cochrane Library, Cochrane Central Register of Controlled Trials, Scopus, CINAHL, CNKI, and CBM disc should be systematically searched as well.

With respect to the data extraction and quality assessment of the included studies, the investigators clarified that two researchers independently collected the information and summarized the data in Table 1,[1] while actually most of the extracted data, including year, sexual status, smoking history, pathological types, clinical staging, differentiation degree, lymph node metastasis, EGFR status, and prognostic conditions, were not displayed in that table. We are wondering why these data were absent. Furthermore, the authors claimed that they appraised the methodological quality of each trial according to REMARK guidelines[1,2] and the European Lung Cancer Working Party quality scale.[3] However, the detailed scores for these selected studies were also not presented in this meta-analysis.

The authors described that heterogeneity between GC tissues and adjacent gastric mucosa/normal mucosa tissues was significant (I^2>50%). To make this meta-analysis more credible, subgroup meta-analysis should be performed to further explore the sources of heterogeneity. Moreover, the investigators clarified that "publication bias was detected by the Begg's test" in the "Methods" section. However, the results of

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Begg's test were not shown in this systematic review. In our opinion, the authors should provide us all the statistical results of publication bias tests to increase its legibility and credibility.

There are some obvious mistakes in this meta-analysis. Firstly, the authors demonstrated that "a systematic literature search was performed using Pubmed, Embase, and Web of Science without any language restriction" in the "Methods" section. However, the authors clarified that "the search strategy was restricted to articles published in English" in the "Discussion" section. Besides, they also claimed that only "Pubmed and Embase databases were searched" for literature retrieval in the "Abstract" section.[1] We are confused by these inconsistent statements and are eager to know the possible reason for these discrepancies. Secondly, there is an obvious typographic error in Figure 1,[1] in which the "Records excluded (n=24)" should be replaced by "Records excluded (n=34)". Thirdly, it is appropriate to adopt random-effects model to calculate the pooled odds ratio in Figure 4, since the heterogeneity between adjacent gastric mucosa and normal gastric mucosa tissues is not significant (I^2=0).[1] As far as we know, it would be much better to use fixed-effects model in this circumstance.

We compliment the investigators for their contribution in supplying us with an assessment on the clinicopathological significance of CDH1 in GC. However, these results should be interpreted with caution, since there are several methodological deficiencies in this meta-analysis. In addition, prospective studies with larger sample sizes are still needed to further confirm these findings.

Disclosure

The authors declare no conflicts of interest in this communication.

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