Comment on "Associations Between Tea and Cancer Risk in Two Umbrella Reviews"

Dear Editor:

With great interest we read the article entitled "Tea consumption and risk of cancer: an umbrella review and meta-analysis of observational studies" by Kim et al. (1). Currently, a lot of misleading, unnecessary, and conflicted meta-analyses and systematic reviews have been published. Therefore, an umbrella review is needed to systematically collect and integrate data, evaluate information on all clinical outcomes, and provide an expanded view of the evidence (2, 3). We appreciate the efforts made by the authors to assess the epidemiological support for cancer outcomes being associated with tea consumption using an umbrella review. Previously, we conducted an umbrella review assessing the association between tea consumption and multiple health outcomes, in which we also assessed the cancer risk related to tea consumption (4).

In the present umbrella review, 64 observational studies with 25 types of cancer outcomes were included. In our previous umbrella review, 68 meta-analyses with 21 types of cancer outcomes were identified. In both umbrella reviews, high consumption of tea was related to reduced risks of biliary tract cancer, leukemia, oral cancer, ovarian cancer, and thyroid cancer, and when considering the types of tea, high consumption of green tea was associated with reduced risks of breast cancer, endometrial cancer, and liver cancer. Additionally, the present umbrella review by Kim et al. identified the protective role of tea against gastric cancer and lung cancer, and of green tea against colorectal cancer. However, only the negative association between tea consumption and risk of oral cancer was supported by convincing evidence. Our previous umbrella review also assessed the association between tea consumption and cancer mortality and found that consumption of black tea could reduce the risk of cancer mortality significantly (HR: 0.79; 95% CI: 0.65, 0.97) (5).

However, our previous umbrella review suggested that when the temperature of the tea consumed was >55–60°C, the associations become harmful for gastric (6) and esophageal cancer (7). Similarly, drinking very hot tea (>60°C) was significantly associated with an increased risk of esophageal cancer (HR: 1.62; 95% CI: 1.15, 2.22) from a cohort during an average 10 y of follow-up (8). The mechanism might be the impairment of barrier function of the esophageal epithelium by thermal injury, the inflammatory process associated with chronic irritation of the esophageal mucosa by hyperthermia, and mutations like higher rates of transitions of somatic G to A in CpG dinucleotides of the *Tp53* gene, which were related to nitric oxide synthase activity (9).

In conclusion, although current evidence has suggested the protective role of tea for several cancers, we do not recommend that individuals consume very hot tea.

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References

1. Kim TL, Jeong GH, Yang JW, Lee KH, Kronbichler A, van der Vliet HJ, Grosso G, Galvano F, Aune D, Kim JY, et al. Tea consumption and risk of cancer: an umbrella review and meta-analysis of observational studies. Adv Nutr 2020;11:1437–52.
2. Ioannidis JP. Integration of evidence from multiple meta-analyses: a primer on umbrella reviews, treatment networks and multiple treatments meta-analyses. Can Med Assoc J 2009;181:488–93.
3. Aromataris E, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. Int J Evid Based Healthc 2015;13:132–40.
4. Yi M, Wu X, Zhuang W, Xia L, Chen Y, Zhao R, Wan Q, Du L, Zhou Y. Tea consumption and health outcomes: umbrella review of meta-analyses of observational studies in humans. Mol Nutr Food Res 2019;63(16):1900389.
5. Tang J, Zheng JS, Fang L, Jin Y, Cai W, Li D. Tea consumption and mortality of all cancers, CVD and all causes: a meta-analysis of eighteen prospective cohort studies. Br J Nutr 2015;114(5):673–83.
6. Huang Y, Chen H, Zhou L, Li G, Yi D, Zhang Y, Wu Y, Liu X, Wu X, Song Q, et al. Association between green tea intake and risk of gastric cancer: a systematic review and dose-response meta-analysis of observational studies. Public Health Nutr 2017;20(17):3183–92.
7. Zheng JS, Yang J, Fu YQ, Huang T, Huang YJ, Li D. Effects of green tea, black tea, and coffee consumption on the risk of esophageal cancer: a systematic review and meta-analysis of observational studies. Nutr Cancer 2013;65(1):1–16.
8. Sheikh M, Poustchi H, Pourshams A, Etemadi A, Islami F, Khoshnia M, Gharavi A, Hashemian M, Roshandel G, Khademi H, et al. Individual and combined effects of environmental risk factors for esophageal cancer based on results from the Golestan Cohort Study. Gastroenterology 2019;156(5):1416–27.

9. Li ZG, Shimada Y, Sato F, Maeda M, Itami A, Kaganoi J, Komoto I, Kawabe A, Imamura M. Promotion effects of hot water on N-nitrosomethylbenzylamine-induced esophageal tumorigenesis in F344 rats. Oncol Rep 2003;10:421–6.

Reply to Yi M et al.

Dear Editor:

We deeply appreciate the interest and considerate comments of Yi et al. regarding our article entitled "Tea consumption and risk of cancer: an umbrella review and meta-analysis of observational studies," which was published in November 2020 in this Journal (1, 2). Also, we appreciate that Yi and the team emphasized the importance of the research design of umbrella reviews and conducted a similar review on the effects of tea consumption on several diseases other than cancer (3). Similar to their study, we summarized the outcomes from the previous meta-analyses on the association between tea consumption and the risk of cancer, and combined all the individual studies, and reanalyzed them, drawing the final outcomes with the predefined level of evidence (2).

Yi et al. commented that the risk of upper gastrointestinal tract cancer (esophageal cancer and gastric cancer) associated with tea consumption should be evaluated considering the temperature of the tea (1). Our team agrees that this is a critical comment because the carcinogenic risk of thermal injury to the upper gastrointestinal tract, such as the esophagus, is well known and information on temperature should be taken into account. Several studies suggest that drinking high-temperature beverages can cause squamous cell carcinoma of the esophagus or stomach by inducing inflammatory processes or damaging the barrier of these organs (4, 5). The authors of the individual meta-analyses on the association between these types of cancer have also commented that there is a need to consider the temperature effect to elucidate the true effect (6, 7).

For example, the World Cancer Research Fund Network/American Institute for Cancer Research reports have stated that drinking maté increases the risk of esophageal cancer (risk estimate: 1.16; 95% CI: 1.07, 1.25); that was graded as "probable" evidence (8). They attributed the risk to the high temperature of maté but failed to give a similar conclusion with other nonalcoholic drinks including coffee and tea. Our fundamental problem is the scarcity of studies on how high tea temperature affects cancer risk, while it is also unclear whether other hot drinks such as coffee can equally be carcinogenic due to high temperature.

In the case of esophageal cancer, unlike the other umbrella review that included only 1 study on the association between tea consumption and cancer risk, we included 3 eligible studies to derive the final result. We also separated the study design used in meta-analyses by case-control studies and cohort studies, which can broaden the reader's perspective to understand the association. Six meta-analyses from 3 studies were finally included for umbrella review and reanalysis. Of 6 meta-analyses, 1 meta-analysis of case-control studies conducted by Zheng et al. (6) was statistically significant, whereas others showed nonsignificant results. However, these outcomes should be carefully interpreted for 2 reasons: 1) the statistically significant meta-analysis only includes the case-control studies, which are subject to unknown biases; and 2) not all of the results from the individual studies considered the temperature effect. Because the high temperature has the opposite effect to the tea on the risk of cancer, the anticarcinogenic effect of tea might be rather underestimated. In spite of these limitations, by integrating all the individual studies, we presented the most updated meta-analyses on the risk of cancer and tea consumption, but we did not evaluate temperature as a confounder, partially due to lack of sufficient data.

In conclusion, as Yi et al. suggested, a temperature effect on the association between tea consumption and cancer risk cannot be concluded by our findings but remains plausible. This underlines the need for further studies to provide more conclusive evidence.

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