

Letter to the Editor

# Whether Risk Reduction of Strokes by Tofu is Possible Remains Uncertain as Long as it is not Evaluated as a Heterogeneous Nutrient

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We read with interest the article by Wang *et al.* [1] on a two-sample Mendelian randomization study of a possible causal relationship between tofu consumption and the risk of stroke and its subtypes. No causal relationship was found between stroke, in general, and tofu consumption, but there was a causal relationship between tofu consumption and the risk of intracerebral hemorrhage (ICB) [1]. The study concluded that the differential effects of tofu on different stroke subtypes emphasize the need to consider confounding dietary or lifestyle factors as a cause of this variability [1]. The study is elegant, but some ambiguities should be clarified.

First, not all tofu is the same. Tofu can be categorized into different subtypes depending on the soybean variety, the production methods, the degree of contamination with pesticides and herbicides, the number, amount and type of ingredients, and how it is processed into meals [1]. In terms of soybean type, there are more than 2500 different soybean varieties worldwide that are classified as "vegetable" (food) or "field" (oil) [2]. Accordingly, soybeans come in different colors, sizes, and with different nutritional profiles [2]. Soybeans range in size from a mustard seed to the largest edamame varieties [2]. Soybeans can be white, yellow, green, red, brown, black, or speckled [2]. The protein content in soybeans can range from 36 to 48 g [2]. Soybeans can be processed into soy milk, tofu, soy sauce, or miso paste. In terms of pesticide contamination, about 64% of soybeans are traded globally, which is associated with ~55% of the environmental and health risks associated with ~108 kt of pesticide use [3]. The pesticide footprint of soybeans and the associated environmental and health risks are concentrated in a few hotspot countries such as China, USA, Brazil, and Argentina [3]. About 30 kt of the future increase in pesticide use on soybeans and ~6% of the associated environmental and health risks can be offset if 80% of traded soybeans are shifted from countries with high pesticide use to countries with lower pesticide use [3]. As far as ingredients are concerned, tofu contains water, spices, calcium sulphate, magnesium chloride and delta-glucono-lactone in addition to soybeans [3]. Tofu is marketed either as natural tofu or as smoked tofu. The consistency of tofu can

be firm, extra firm or "silky soft". Tofu can be eaten raw or cooked. Cooked tofu is usually fried, baked or sautéed. Due to this great heterogeneity of tofu products and preparations, it seems extremely difficult to assess the impact of tofu consumption on stroke risk, and the results reported so far are highly questionable.

Second, the amount of tofu consumed per day or week was not included in the analysis. An influence of tofu consumption on stroke risk most likely depends strongly on the "dose" of tofu consumed in a given period. As long as the amount of tofu consumed is not included in the evaluation, the results of Mendelian randomization may be misleading.

Third, we disagree with the statement that there are two types of stroke [1]. The term stroke includes not only ischemic stroke and intracerebral hemorrhage, but also subarachnoid hemorrhage (SAH).

Fourth, studies that show a positive effect in terms of reducing the risk of stroke or hemorrhage must also be evaluated as to whether or not they were sponsored by the tofu industry.

To summarize, this interesting study has limitations that put the results and interpretation into perspective. Removing these limitations could strengthen the conclusions and reinforce the study's message. All unanswered questions need to be clarified before readers can uncritically accept the conclusions of the study. Until all of the above considerations are addressed, no definitive conclusions can be drawn about the relationship between tofu consumption and ischemic stroke, ICB, and SAH.

#### Availability of Data and Materials

All data are available from the corresponding author.

### **Author Contributions**

JF was responsible for the design and conception, discussed available data, wrote the first draft, and gave final approval. JF participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## **Ethics Approval and Consent to Participate**

Not applicable.

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#### **Conflict of Interest**

The author declares no conflict of interest.

#### References

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