Iran J Public Health, Vol. 54, No.11, Nov 2025, pp.2541-2542

Letter to the Editor

Gut Microbiota and Recurrence Risk in Acute Ischemic Stroke: Insights from a Competitive Risk Model

Yanmin Gao [1], Yongtao Zheng [2], Bing Xia [3], *Biao Li [4]

1. *Kongjiang Community Health Service Centre of Yangpu District, Shanghai 200093, China*
2. *Xiaoshan District Center for Disease Control and Prevention, Hangzhou 310000, China*
3. *Zhejiang Xiaoshan Hospital, Hangzhou 310000, China*
4. *Hangzhou Center for Disease Control and Prevention, Hangzhou 310000, China*

***Corresponding Author:** Email: mrlibiao@126.com

(Received 08 Apr 2025; accepted 24 Apr 2025)

Dear Editor-in-Chief

The recurrence of acute ischemic stroke (AIS) remains a critical issue in the elderly population, especially among those aged 80 and above. Despite advancements in treatment, recurrence rates are alarmingly high, contributing to substantial morbidity and mortality (1). Our study aimed to explore the relationship between gut microbiota diversity and AIS recurrence using a competitive risk model, providing novel insights into potential preventive strategies.

In a prospective cohort of 217 elderly AIS patients treated at three hospitals in Eastern China, we analyzed fecal microbiota diversity through 16S rRNA sequencing. During a six-year follow-up, 49 patients succumbed to competing events, and 47 experienced AIS recurrence. Our competitive risk analysis (Table 1) revealed that elevated gut microbiota diversity indices (Chao1, Shannon, Simpson) were independently associated with an increased risk of AIS recurrence (e.g., HR for Simpson index: 1.441, 95% CI: 1.116–2.045). Furthermore, increased levels of the gut microbiota metabolite trimethylamine N-oxide (TMAO; HR: 1.230, 95% CI: 1.080–1.411) were significant risk factors.

Table 1: Competitive Risk Model Analysis of Acute Ischemic Stroke Recurrence

Variables	*β*	SE	*z*	*P*	*HR*	95% *CI*
TMAO	0.210	0.069	3.074	0.002	1.230	1.080~1.411
Chao1	0.002	0.001	2.196	0.028	1.003	1.001~1.005
Shannon	0.129	0.049	2.645	0.008	1.138	1.034~1.252
Simpson	0.279	0.041	2.827	0.005	1.441	1.116~2.045

*Model was adjusted for information, including age, gender, BMI, hypertension, diabetes and hyperlipidemia

The role of gut microbiota in AIS recurrence warrants attention (2). Our findings suggest a paradoxical association where greater microbial diversity correlates with worse outcomes. This could reflect the contribution of dysbiosis-induced systemic inflammation and metabolic

perturbations, such as TMAO-mediated atherosclerosis. Prior studies have implicated TMAO in endothelial dysfunction and plaque formation, exacerbating stroke risks. These results underscore the importance of considering gut microbiota as both a biomarker and a therapeutic target for AIS management. Future research should investigate specific microbial taxa and their functional pathways to better understand the microbiota-stroke nexus. Additionally, interventions targeting TMAO production, such as dietary modulation and microbiota-based therapies, may hold promise in reducing AIS recurrence risks (3).

Our study highlights the potential of competitive risk models in uncovering nuanced relationships in geriatric cohorts, accounting for the confounding effects of competing mortality risks. Given the aging population globally, integrating microbiota insights into stroke prevention strategies could offer significant public health benefits.

Funding

This work were financially supported by the Yangpu District Basic Research Capacity Improvement Project and Hangzhou City Biomedicine and Health Industry Development Support Science and Technology Special Project (Grant No. 2024WJC071).

Conflicts of Interest

No conflicts of interest between the authors.

References

1. MaierIL, Bauerle M, Kermer P, Helms HJ, Buettner T (2013). Risk prediction of very early recurrence, death and progression after acute ischaemic stroke.*Eur J Neurol*, 20(4):599-604.
2. Vikramjeet S, Stefan R, Gemma L, et al (2016). Microbiota Dysbiosis Controls the Neuroinflammatory Response after Stroke. *J Neurosci*, 36(28):7428-7440.
3. Koeth A R, Wang Z, Levison S B, et al (2013). Intestinal microbiota metabolism of;-carnitine, a nutrient in red meat, promotes atherosclerosis. *Nature Med*, 19(5):576-585.