Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

11.2 (StataCorp, College Station, TX).

The main characteristics of the included studies are presented in the Table. We observed that there was not a significant association between GI symptoms and COVID-19 mortality on the basis of 20 studies with 58,423 patients with COVID-19 reporting adjusted effect estimates (pooled effect size, 0.93; 95% CI, 0.75 to 1.16; P=.535; random effects model) (Figure A). We observed consistent results in the subgroup analyses by effect estimates (pooled odds ratio, 0.97; 95% CI, 0.75 to 1.26 and pooled hazard ratio, 0.78; 95% CI, 0.45 to 1.36), region (Asia: pooled effect size, 1.25; 95% CI, 0.69 to 2.24; Americas: pooled effect size, 0.90; 95% CI, 0.73 to 1.11; Europe: pooled effect size, 0.83; 95% CI, 0.55 to 1.27; and Africa: pooled effect size, 1.17; 95% CI, 0.65 to 2.09), study design (retrospective studies: pooled effect size, 0.92; 95% CI, 0.70 to 1.21; prospective studies: pooled effect size, 0.63; 95% CI, 0.22 to 1.84; and ambispective studies: pooled effect size, 1.06; 95% CI, 0.81 to 1.38), sample size (≤2000 cases: pooled effect size, 0.92; 95% CI, 0.60 to 1.40 and >2000 cases: pooled effect size, 0.98; 95% CI, 0.83 to 1.15), age (≤65 years old: pooled effect size, 1.13; 95% CI, 0.81 to 1.57 and >65 years old: pooled effect size, 0.81; 95% CI, 0.59 to 1.11), and percentage of male patients (≤60%: pooled effect size, 1.04; 95% CI, 0.77 to 1.40 and >60%: pooled effect size, 0.81; 95% CI, 0.58 to 1.15). Sensitivity analysis indicated that our results were reliable and robust (Figure B). Publication bias was not found in the Begg test and Egger test (Figure C and D).

In summary, our findings based on adjusted effect estimates suggested that GI symptoms were not markedly associated with COVID-19 mortality. Further well-designed studies with large sample sizes are needed to confirm our conclusions.

Yang Li, BS
Hongjie Hou, MBBS
Haiyan Yang, MD, PhD
Zhengzhou University
Zhengzhou, China

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ORCID
Haiyan Yang: https://orcid.org/0000-0002-1797-304X

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In reply—Lack of Marked Association Between Gastrointestinal Symptoms and COVID-19 Mortality: An Updated Meta-analysis Based on Adjusted Effect Estimates

We appreciate the interest of Li et al[1] in our systematic review and meta-analysis evaluating the prevalence of gastrointestinal (GI) symptoms and the association with mortality in patients with coronavirus disease 2019 (COVID-19).[2] Li et al performed an updated meta-analysis with a larger sample size to explore the effect of GI symptoms on mortality associated with COVID-19. On the basis of adjusted effect estimates (controlling for potential confounders), they found no association between GI symptoms and mortality (pooled effect 0.93; 95% CI, 0.75 to 1.16; P=.535). The results remain consistent in multiple subgroup analyses. Because of the lack of risk of bias assessment of the included studies, it is hard to ascertain the quality of included evidence. Moreover, different follow-up duration of the included studies could affect mortality estimates.

The results of their pooled meta-analysis are similar to our study with some differences.[2] Because of the lack of reporting of uniform data on confounders and comorbidities, our findings were based on crude estimates. Since then, additional studies have been published, with COVID-19 being a widely researched topic. We completely agree that certain risk factors, including age, sex, and comorbidities could affect the mortality in patients with COVID-19.[3]

Another similar meta-analysis suggested an increased risk of severe COVID-19 with GI symptoms compared with those without GI symptoms (odds ratio, 3.97; 95% CI, 1.49 to 10.62; P=.006).[4] Patients with GI symptoms conceivably had delayed COVID-19 diagnosis, which may have led to severe COVID-19 and worse outcomes. A recent study found that despite the presence of severe acute respiratory syndrome coronavirus 2 antigens in the intestinal tissue, the inflammatory

response observed was mild. The authors also found a significant reduction ($P<.001$) in disease severity and mortality in patients presenting with any GI symptoms compared with those without GI symptoms, independent of age, sex, and comorbid conditions.[5]

Based on the current literature, it can be proposed that patients with COVID-19 and GI symptoms do not have an increased risk of mortality.

Raseen Tariq, MBBS
Mayo Clinic
Rochester, MN

Rochester General Hospital
Rochester, MN

Srishti Saha, MBBS, MD
Mayo Clinic
Rochester, MN

Fateeha Furqan, MBBS
Rochester General Hospital
Rochester, NY

Darrell Pardi, MD, MS
Mayo Clinic
Rochester, MN

Sahil Khanna, MBBS, MS
Mayo Clinic
Rochester, MN

Potential Competing Interests: The authors report no competing interests.

ORCID
Raseen Tariq: https://orcid.org/0000-0001-7586-6691; Srishti Saha: https://orcid.org/0000-0003-1898-3298; Sahil Khanna: https://orcid.org/0000-0002-7619-8338

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The Undulating Life of Omega-3 Fatty Acids: What Have We Overlooked?

To The Editor: The cardiovascular protective effects of omega-3 fatty acids are still under intense debate. Recent results from the Long-Term Outcomes Study to Assess Statin Residual Risk with Epanova in High Cardiovascular Risk Patients with Hypertriglyceridemia (STRENGTH),[1] which enrolled 13,078 patients with high cardiovascular risk and high prevalence of diabetes, showed that 4 g per day of omega-3 carboxylic acids (a final concentration of 75% of eicosapentaenoic acid [EPA] and docosahexaenoic acid) did not reduce cardiovascular events in high-risk patients. Interestingly, in subgroup analysis, Asian populations obtained cardiovascular benefit, but this result may not have been brought to the attention of the authors. However, the results of the previous the Japan EPA Lipid Intervention Study (JELIS), which included 18,645 patients with hypercholesterolemia, revealed that 1.8 g per day of EPA produced cardiovascular benefit.[2] In addition, the results of the Reduction of Cardiovascular Events With Icosapent Ethyl-Intervention Trial (REDUCE-IT), which enrolled 8179 patients with hypertriglyceridemia and high prevalence of diabetes, suggested that, after receiving a large dose of EPA of 4 g per day, there appeared to be more favorable benefits in subgroups of Western populations than in Asian. And most other clinical trials investigating the effect of low doses of EPA in Western populations failed to demonstrate cardiovascular benefit. A recently updated meta-analysis[3] on the potential effect of omega-3 on cardiovascular outcomes suggested that it has a protective cardiovascular effect and that this effect may present in a dose-dependent manner. However, this conclusion does not seem to explain fully the results of large-scale clinical studies. After 1.8 g per day of EPA was administered in JELIS, and 4 g per day of omega-3 carboxylic acids were administered in STRENGTH to all patients with hyperlipidemia, the results were not dose-dependent, or there might be a turning point in this protective effect.

The importance of the omega-6 to omega-3 fatty acid ratio may not have received attention in these studies. Omega-6 fatty acid is thought to have dual effects on the cardiovascular system, especially its excessive intake, which promotes inflammation and thrombosis. There is competition between EPA and the omega-6 family, such as desaturase and cyclooxygenase (Table).[4] A study[5] using UK populations as a sample showed that 3.6 g per day of EPA compared with 1.8 g per day increased bleeding time. The purified high-dose EPA can not only produce cardiovascular protection but also reduce the inflammatory mediators and thrombosis from omega-6.

In the current Western diet, the omega-6 to omega-3 ratio has increased from 1:1 in the late paleolithic period to 15 to 20:1, which is