Letter by Jong et al Regarding Article, “Dietary Fish and \( \omega-3 \) Fatty Acid Consumption and Heart Rate Variability in US Adults”

To the Editor:

We read with interest the recent report from Mozaffarian et al\(^1\) that consumption of \( \omega-3 \) fatty acid containing fish is associated with increased heart rate variability (HRV) markers of vagal heart rate modulation. Importantly, in their analysis, higher HRV was accompanied by a lower risk of subsequent cardiac death. Their findings, which demonstrate the potential use of HRV indices as surrogates for secondary measures of treatment efficacy when evaluating preventive strategies for cardiovascular disease, raise 2 important questions for research on the HRV response to interventions such as diet. First, how would one characterize the magnitude of treatment effects such as those reported in this study? Second, how might these observations inform future study design?

Mozaffarian et al\(^1\) reported changes in HRV from differences in dietary fish consumption that were low to moderate in magnitude. For example, among the 4263 subjects who were assessed by 12-Lead ECG, increasing fish consumption from the lowest to the highest quintile was associated with an increase in SDNN (standard deviation of N-N intervals) and rMSSD (root mean square of successive differences of N-N intervals) of 9.7% and 12.3% respectively. In their subset of 1177 subjects who underwent 24-hour Holter monitoring, normalized high-frequency power increased by 10.8%.

We were struck by the similar magnitude of these treatment effects\(^1\) and the overall pooled effect of interventions derived from our meta-analysis\(^2\) of 33 clinical trials that used HRV markers of vagal-heart rate modulation as surrogates for clinical outcome. Among subjects with coronary heart disease, randomization to 1 or more of conventional drug therapy, exercise, and biobehavioral interventions such as biofeedback and relaxation training resulted in a significant improvement in pooled HRV indices that was moderate in magnitude (standardized mean difference = 0.40). This outcome was equivalent to a relative increase in SDNN of 15.9%. We further estimated that a sample of 1232 subjects would be required in order to reliably detect a treatment effect of this magnitude. Thus, the report by Mozaffarian et al\(^1\) validates our predictive model.\(^2\) Indeed, their sample size may have been critical to their detection of a statistically significant dietary effect on HRV, in that this was low to moderate in magnitude.

By suggesting that a sample of \( \approx \)1200 subjects may be a minimal criterion to achieve adequate statistical power in future studies designed to evaluate the effect of diet or other preventive cardiovascular disease strategies on HRV, these 2 publications\(^1,2\) establish a framework for a second generation of HRV-based outcome research. To date, prognostic information derived from HRV assessment has been based almost exclusively on baseline measurements. Findings such as those reported by Mozaffarian et al\(^1\) underscore the need for clinical trials to evaluate whether change in HRV after preventive strategies independently predicts clinical events. Until this issue is resolved, it is not possible to determine whether provocative findings such as those of Mozaffarian et al\(^1\) indicate added prognostic benefit. Meanwhile, we share these authors’ caution that current HRV indices provide limited information on the specific autonomic regulatory mechanisms by which interventions such as diet modify the risk for cardiovascular events.

Disclosures

None.

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