Letter to the Editor

[Reply to Notarius]

We thank Dr Notarius for her interest in our recent article,[1] and for bringing her own excellent work[2,3] to our attention. The hypothesis that she puts forth—that lower muscle sympathetic nerve activity (MSNA) explains why we found that dietary nitrate (NO_3^-) increased $\dot{V}O_2$ peak and exercise tolerance in patients with heart failure with reduced ejection fraction (HFrEF) of nonischemic origin,[1] whereas Hirai et al[4] observed no such effect in patients with HFrEF primarily due to ischemia—is clearly quite plausible. It is difficult, however, to draw any firm conclusions in this regard. There is considerable overlap of MSNA in patients with nonischemic and ischemic HFrEF,[2] such that it is uncertain whether the 8 patients in our study[1] in fact would have had lower MSNA than the 10 patients studied by Hirai et al.[4] Our patients were also younger (52 ± 5 vs 63 ± 5 y), had a higher $\dot{V}O_2$ peak (21.4 ± 2.1 vs 15.3 ± 0.7 $mL.min^{-1}.kg^{-1}$), and based on New York Heart Association criteria were generally less severely affected by their HFrEF. We also studied our patients during semirecumbent cycling exercise (to aid interpretation of our measurements of whole-body gross and delta efficiency),[1] whereas Hirai et al[4] studied their patients during upright cycling. Any of these differences (or others) could also have directly or indirectly contributed to the divergent results of our studies. The difference in age may be particularly relevant, as it has been reported that even in healthy individuals, aging reduces the vasodilatory effects of dietary NO_3^-.[5,6] Future studies will be required to test this and other hypotheses, eg, by supplementing a large number of patients with HFrEF with dietary NO_3^- then stratifying them by age, $\dot{V}O_2$ peak, functional status, etiology of disease, etc, to determine which particular subgroups are most likely to benefit from this promising treatment. Furthermore, any such studies should include assessment of muscle contractile properties as well as aerobic exercise capacity, because the former is also an important determinant of physical function and quality of life in patients with HFrEF[7] and appears to improve even more with NO_3^- supplementation.[8]

Disclosures

None.

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