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Hypermetabolism: should cancer types, pathological stages and races be considered in assessing metabolism and could elevated resting energy expenditure be the therapeutic target in patients with advanced cancer?

Hypermetabolism, defined as elevated resting energy expenditure (REE), was common in cancer cachectic patients[1] as published before in cancer patients[2] and might result in poor outcomes.

In this study, there was no significant difference in age, cancer type, gender, cancer treatment and inflammation between elevated REE group and normal REE group. As authors indicated, the small sample size, the heterogeneous population and the selection bias could have some impacts on the findings. Regarding the sample size, a moderately large study, including 714 cancer patients, suggested that cancer type, pathological stage and duration of disease are contributors to metabolic activity.[2] To keep the homogeneity of the study population, Wu *et al.* enrolled 56 male patients as newly diagnosed with esophageal cancer and showed that the rate of weight loss positively correlated with the ration of REE to body weight and high-sensitivity C-reactive protein.[3] In addition, it is well known that less than 5% of cancer patients participate in clinical studies and that non-enrollment in cancer research was associated with older age and sex (female),[4] which might facilitate the selection bias.

In this study, hypermetabolism is more common in non-Caucasian patients than in Caucasian patients.[1] Interestingly, non-Caucasian healthy subjects had a lower REE compared with Caucasian healthy subjects,[5] and a similar trend was observed in obese patients.[6] It is still controversial whether racial background influences metabolic response in various pathophysiological conditions such as obesity, diabetes and cancer cachexia. At present, the number of cachexia research is critically lacking compared with that of obesity research, and[7] no other evidence has been published on racial differences in REE among cancer patients, in particular cancer cachectic patients.

It remains unclear whether hypermetabolism could be the therapeutic target in advanced cancer patients; however, recently, Ma *et al*. reported that administration of omega-3 polyunsaturated fatty acids resulted in a significant decrease in REE and a significant increase in overall survival in patients with pancreatic cancer.[8] As sustained hypermetabolism leads to muscle wasting, some drugs such as ghrelin agonists, selective androgen receptor molecules, megestrol acetate, activin receptor antagonists, espindolol, and fast skeletal muscle troponin inhibitors,[9] as well as physical exercise,[10] which are promising for the treatment or the prevention of muscle wasting, could be the candidates as therapeutic options for this condition.

To clarify the pathophysiology of hypermetabolism in cancer patients, validation studies on larger samples, various cancer types, different pathological stages and races are needed. In addition, hypermetabolism could be the therapeutic target at least in a sub-population of cancer patients. To confirm it, further research is needed.

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