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A randomized controlled trial testing the immunological impact of high-intensity interval training for patients with metastatic lung cancer in combination with immunotherapy

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Exercise is a potent therapy modality to improve quality of life and physical function in cancer patients, with emerging evidence suggesting benefits for cancer outcomes. Given that the efficacy of cancer immunotherapy relies on sustained antitumor immune responses, high-intensity exercise may enhance its efficacy through immune modulation.

The randomized controlled HI AIM trial (NCT04263467) investigated six weeks of high-intensity interval training (HIIT) in patients with metastatic non-small cell lung cancer (mNSCLC) receiving immune checkpoint inhibitors (ICI) with or without chemotherapy, or under surveillance. Participants in the exercise group completed supervised, group-based HIIT three times weekly. Data on exercise performance, cardiorespiratory fitness, therapy course, psychological distress, and disease outcomes were collected. Peripheral blood samples were obtained before and after acute HIIT sessions and longitudinally for immunological analyses.

Between August 2020 and October 2023, 54 patients (22 males, 32 females) were randomized. Adherence of 83%, resulted in analysis of data from 45 patients (21 exercise, 24 control). Flow cytometry revealed that patients with mNSCLC performed HIIT resulting in mobilization of NK, T cells and catecholamines to the peripheral blood. The primary outcome showed that circulating NK cells from baseline to week 12 was significantly higher in the ex-ercise group compared to control group (log2 ratio week12/bsl -0·012 ±1·057 vs. -0·276 ±0·695; p=0·0247). Secondary outcomes showed feasibility and safety (no severe adverse effect) of the exercise intervention, and a significant increase in power output and VO2peak for the exercise group. Clinical analysis showed that the exercise group experienced less toxicities during active treatment, and reduced anxiety. Notably, in a subgroup analysis, a progression-free survival benefit was observed in the exercise group receiving ICI.

This study shows for the first time, in metastatic cancer patients, that HIIT is not only safe and feasible but elicits immune activation and indicates synergistic clinical activity with immunotherapy.

Keywords

Exercise; lung cancer; immunotherapy; HI AIM

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

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