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Daily In-Hospital Exercise During Neoadjuvant Chemoradiotherapy Counteracts Immune Suppression in Patients With Esophageal Cancer

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Background: In our previous study, exercise during neoadjuvant chemoradiotherapy (NCRT) showed potential to enhance tumor regression in patients with esophageal cancer, but underlying mechanisms are unclear. As preclinical evidence suggests that exercise decreases tumor growth through mobilization, activation, and tumor infiltration of natural killer (NK) and CD8+ T cells, we explored these pathways in our trial participants.
Methods: Blood samples and tumor tissue were collected from 31 patients with esophageal cancer, randomized to: 1) 30-minute in-hospital moderate-intensity aerobic exercise within one hour before each radiotherapy fraction, five times per week (ExPR); 2) two 60-minute supervised aerobic and resistance exercise sessions per week (AE+RE); or 3) usual care (UC) during NCRT. Blood samples were collected before randomization (T0), after NCRT (T1), and before surgery (T2), as well as before and directly after one ExPR session. Exercise-induced immune mobilization, and exercise training effects on immune profile and peripheral NK and T cell function were examined by flow cytometry. Tumor material is currently analyzed for vascularization, hypoxia, and immune infiltration using multiplex immunofluorescence.
Results: 30-minute aerobic exercise mobilized immune cells into circulation. We observed shifts in peripheral immune profile, particularly trends towards an increase in dendritic cells in ExPR compared to UC and AE+RE at T1 (p=0.07, p=0.06), and in eosinophils compared to UC at T2 (p=0.10). Additionally, NK cell degranulation was preserved in ExPR, but declined in UC and AE+RE resulting in significant between-group differences at T1 (p=0.05, p=0.02). Furthermore, the %IFN-ɣ+CD8+ T cells was maintained in ExPR compared to a decline in UC, causing a significant between-group difference at T2 (p=0.005).
Conclusion: Aerobic exercise before each radiotherapy fraction resulted in a stable NK and CD8+ T cell function, contrasting the deterioration observed with UC. These findings suggest that exercise may counteract treatment-related immune suppression, which could contribute to improved clinical outcomes.

Keywords

Exercise intervention, Neoadjuvant chemoradiation, Esophageal cancer, Immune function

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

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