## Abstract

## Effects of exercise prehabilitation on functional capacity and health-related quality of life in head and neck cancer patients: Preliminary results of the FIT4TREAT trial

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Head and neck cancer (HNC) patients submitted to radical chemoradiotherapy (CRT) have to deal with various physical and psychosocial problems related to cancer and its treatment, which negatively affect functional capacity and health-related quality of life (HRQoL). Thus, the aim of this work was to analyse the impact of an exercise prehabilitation (EP) program on the functional capacity and HRQoL in HNC patients. In this randomised-controlled trial (NCT05418842), 30 HNC patients proposed for radical CRT were randomly allocated to EP or usual care (UC) group. The EP group participated in an exercise program composed of a combined aerobic and resistance training program (60 minutes), three sessions/week, from randomisation to the beginning of radiotherapy (RT). Aerobic capacity (6-minute walk test, 6MWT), isometric handgrip muscle strength (dynamometer), lower limb functional capacity (30 seconds chair sit-to-stand test, STS) and HRQoL (EORTC QLQ-C30 and EORTC QLQ-HN43) were assessed at diagnosis (baseline, M0), and 1-3 days before starting RT (M1).

Twenty-six patients completed both pre-treatment assessments, 12 in the EP (61.8±8.4 years, 91.7% men) and 14 in the UC (66.1±9.9 years, 92.9% men) group. The median length of the pre-treatment phase was 28 days (IQR, 24-28 days) and 29 days (IQR, 22-32 days) in EP and UC groups (p=0.786), respectively. Patients adhered on average to 66.3±34.9% of exercise sessions. No differences between groups were observed in any variable at baseline (M0). The 30 seconds STS performance improved with the EP program and remained unchanged in the UC group (EP: Δ4.4±4.6 vs UC: Δ0.1±2.5 repetitions, p=0.007). No differences between groups were observed for the change in the 6MWT (p=0.162); handgrip muscle strength (dominant hand: p=0.819; non-dominant hand, p=0.964); or any domain of HRQoL, except for body image (p=0.020) and dry mouth and sticky saliva (p=0.020) favouring the EP group. In the per-protocol analysis (i.e., adherence ≥80% of planned exercise sessions), changes in 30 seconds STS test remained significant (EP:  $\Delta 7.2\pm 2.9$  vs UC:  $\Delta 0.1\pm 2.5$  repetitions, p=0.009) while the 6MWT improved as compared in EP as compared to the UC group (EP:  $\Delta 44.7\pm 31.5$  vs UC:  $\Delta$ -5.9±36.0 meters, p<0.001). No serious adverse events related to exercise were reported in the EP group.

These preliminary results suggest that EP is safe and improves lower limb functionality, body image, and dry mouth and sticky saliva domains of HRQoL in HNC patients. The benefits of the 6MWT performance appear limited to those with good adherence to the planned exercise sessions.

**Keywords:** Head and neck cancer, exercise, prehabilitation

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