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Fatigue, Quality of Life, and Physical Fitness Following an Exercise Intervention in Survivors of Multiple Myeloma: A Randomised Controlled Trial Using a Zelen Design

Background. The benefit of exercise on fatigue and wellbeing in patients with solid tumours (breast, prostate, colorectal) is supported by some randomised controlled trials (RCT). In multiple myeloma (myeloma), osteolytic bone destruction causes persistent pain and fracture risk, leading to reduced physical functioning, and barriers to exercise. There is a paucity of research in this patient group. We aimed to test the efficacy of a previously piloted exercise intervention in a randomised controlled trial in myeloma survivors.

Methods. MASCOT used a double-consent adapted Zelen design to reduce contamination of control group, often found in RCT. Eligible patients had completed chemotherapy and had at least stable disease for ≥6 weeks. Screening for fracture risk was carried out by multi-disciplinary team. After initial consent to a lifestyle cohort study and completion of baseline tests, subjects were randomised to exercise intervention (re-consented) or control (usual care). Control subjects were not informed of the randomisation, and not re-consented. The 12-week intervention was tailored aerobic and resistance exercises with behavioural support and home exercise. Subjects attended weekly supervised gym sessions in weeks 1-12, and then monthly until 6 months. All subjects were assessed at 3, 6 and 12 months. The primary outcome was between group differences in fatigue (Functional Assessment of Chronic Illness Therapy, FACIT-F) change. Regression models were run with the 3-or 6-month fatigue as the dependent variable, with the baseline values and trial arm allocation as independent variables, with same methodology for secondary endpoints (QOL, physical fitness, muscle strength, body composition).

Results. From June 2014 to November 2016, 138 patients consented to the cohort study, of whom 131 were randomised (control, 42, intervention 89). Time from last treatment was 15 months (median, range: 2-251), median age was 63yrs (35-86), 55% were male and 67% had bone disease. Of 89 participants randomised to the intervention, 51(57%) consented; main reasons for declining were number of visits and/or travel distance. Median attendance at sessions was 75%, and 40 completed the programme at 3 months. 3- and 12-month follow-up was 88%, 95% and 63%, 74% respectively, for exercise and control. Forty participants with complete cases in each arm were included in the analyses (per protocol).

Baseline levels of fatigue were similar in the exercise and control groups (40.8±7.8, 41.7±10.7); with 7(17%) and 10(24%) subjects reporting clinical fatigue (score<34). Groups were matched for all other variables. There was no between group difference in fatigue at 3-months (2.14, 95%CI -0.51,4.79, p=0.1) or 6-months. We found no between-group differences in physical functioning, emotional functioning, anxiety, or depression at 3 or 6 months. VO_{2peak} improved significantly at 3-months(p=0.024) but not at 6-months(p=0.25). Leg muscle strength improved at 6-months(p=0.027), with a trend for improvement at 3 months(p=0.052). Trends to improvement in physical activity self-efficacy(p=0.053) and body fat percentage(p=0.051) at 3 months were not seen at 6 months.

Because the trial included patients who did not have clinical fatigue at baseline, hence limited scope for improvement in this endpoint, we undertook subgroup analysis of patients with clinical fatigue at baseline. Here, patients who completed the exercise intervention reported feeling less tired at 3 months, which was maintained at 6- and 12-months. (Figure). They also had improved leg strength at each time point (Figure), which was not seen in the control arm. A similar pattern was observed for VO_{2peak} .

In interviews, participants voiced a sense of achievement, their confidence to exercise under supervision and were pleased to have the opportunity to improve their physical wellbeing.

Conclusion. Benefits in fatigue appeared limited to subjects with clinical fatigue at baseline, although improvements in muscle strength and fitness were seen in the whole group. Future research should consider modifying the intervention delivery format to reduce barriers to recruitment and attendance and incorporate fatigue screening before enrolment.

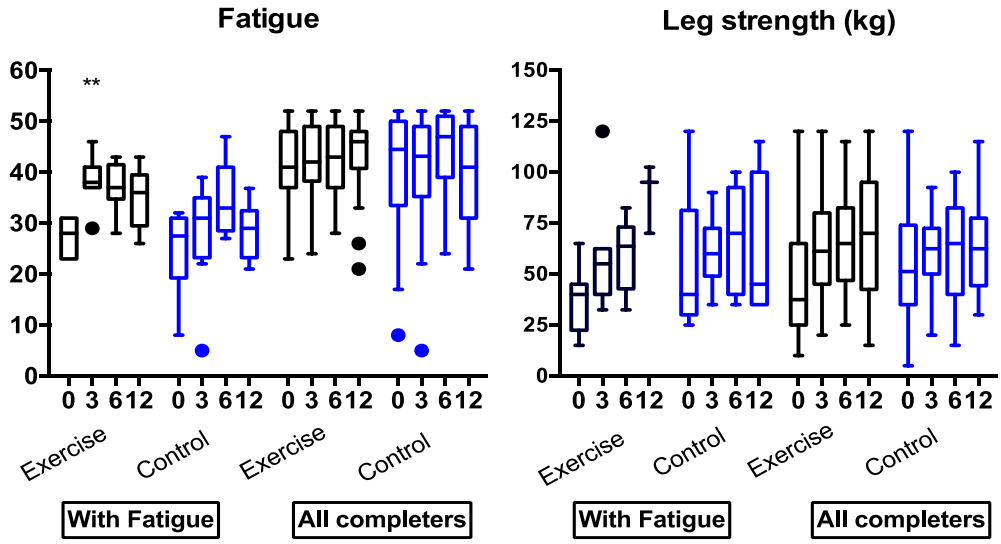

Figure. Effect of exercise intervention on fatigue and leg strength in subjects with clinical fatigue and in all completers (whole cohort). ** p<0.01

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