Statistical analysis plan (SAP)

Official study title: Effects of exercise in prostate cancer patients initiating androgen deprivation therapy: A randomised controlled trial

NCT number: Not yet assigned

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1. Objective

The main objective of this study was to evaluate whether exercise can reduce treatment-related adverse effects in prostate cancer patients initiating androgen deprivation therapy (ADT).

2. Primary outcome

The primary outcome was whole-body fat mass at 3-month endpoint, as measured with Bioelectrical Impedance Analysis and concurrent Bioelectrical Impedance Vector Analysis using a single-frequency, phase-sensitive 50 kHz analyser (BIA-101, RJL/Akern Systems, Firenze, Italy). This method is highly valid for measuring changes in body composition (1). Fat mass was chosen as the primary outcome because adiposity has shown a high propensity to increase during the initial phases of ADT (2), more so than other measures (3), which highlights the importance of targeting body fat at this stage of treatment.

3. Secondary outcomes

The secondary outcomes were as following:

- Feasibility (recruitment rates, attrition, acceptability of the outcome measures, exercise adherence, adverse events)
- Body mass
- Body composition (fat-free mass, skinfold thickness at suprailiac and subscapular sites)
- Anthropometry (waist, hip, mid-upper arm, forearm, mid-thigh and calf circumferences)
- Cardiorespiratory fitness (peak oxygen consumption, ventilatory anaerobic threshold, ventilatory equivalents for oxygen and carbon dioxide at the anaerobic threshold, oxygen pulse, oxygen uptake efficiency slope)
- Hand grip strength

- Biomarkers (total cholesterol, LDL-C, HDL-C, triglycerides, prostate specific antigen, testosterone, sex hormone binding globulin).
- Gleason score
- Risk of cardiovascular disease (QRISK®2-2017)
- Patient reported outcomes (The Functional Assessment of Cancer Therapy-Prostate questionnaire, Functional Assessment of Chronic Illness Therapy-Fatigue questionnaire, Godin Leisure-Time Exercise questionnaire).

4. Sample size

To our knowledge, Cormie et al. (4) is the only previous study to have investigated the effects of exercise in prostate cancer patients initiating ADT on whole-body fat mass, reporting an adjusted MD between experimental and control groups of −1.4 kg ($p = 0.001$) at 3-months. A standard deviation (SD) of 1.6 kg was obtained from the MD and *p*-value using established guidelines (5). Therefore, 44 participants (22 per group) were required to detect a between-group difference of 1.4 kg assuming SD = 1.6 kg, numerator df = 1, $\alpha = 0.05$ and $1\text{-}\beta = 0.8$, which was calculated using G*Power version 3.1 (6). An attrition rate of 20% was also considered.

5. Statistical analysis

Analyses will be performed by intention to treat using SPSS (IBM SPSS, version 24.0, Chicago, IL). Descriptive statistics (mean ± SD) will be presented at baseline to characterise participants. Feasibility outcomes will also be presented with descriptive statistics (i.e. recruitment rates, attrition, adherence and adverse events). Between-group differences in outcomes at 3-month and 6-month endpoints will be assessed by analysis of covariance (ANCOVA) with baseline values as covariates. The adjusted mean differences with 95%

confidence intervals (CIs) from the model will be presented. Statistical significance will be set at a two-tailed $p < 0.05$.

6. Missing data

To increase precision of estimates and comply with intention to treat, missing data at 3-month and 6-month endpoints will be multiply imputed using the Markov chain Monte Carlo (MCMC) algorithm with 20 iterations. At the end of the 20 iterations, one imputed data set is created and the process was repeated to generate 20 imputed data sets, which will then be pooled according to Rubin's rules (Rubin, 2004). For participants who have missing data at 3-months, baseline values and other covariates (treatment group, age, Godin score) will be entered into the imputation model. When data are missing at 6-months, baseline and 3-month endpoint values with covariates will be used to impute missing values. Outcomes with missing data at baseline will not be included in the analysis.

References

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