Effect of High Intensity Exercise Rehabilitation on Liver Function and Insulin Sensitivity in Patients With MASLD: CENSORIAL trial

ONZ-2023-0453

Statistical analysis plan

Version January 29, 2024

1. Objective: The objective of this analysis plan is to assess the effectiveness of moderate continuous training combined with strength training versus high-intensity training combined with strength training in improving outcomes in patients with NAFLD over a 14-week intervention period.

2. Study Design:

   a. Randomization: Patients will be randomly assigned to one of two arms:

      Arm A: Moderate continuous training combined with strength training.

      Arm B: High-intensity training combined with strength training.

   b. Intervention: Patients will undergo the assigned exercise regimen for 14 weeks.

   c. Outcome measures:

      Primary outcome: liver function (fibroscan, echografie lever, biomarkers ALT/AST) and insulin sensitivity (glucose, insuline)

      Secundary outcomes: length, weight, body composition (fat mass, fat free mass), exercise capacity (VO2max, strength), blood pressure, blood markers: lipid profile, IL-1beta, IL-6, IL-8 and TNF-α, quality of life

3. Data Collection:

   a. Baseline assessment: We will collect demographic information (age, gender,…) and baseline measurements of outcome variables.

   b. Intervention period: We will monitor adherence and possible adverse events to the exercise regimen

   c. Follow-up: We will assess outcome measurements at the end of the 14-week intervention period.

4. Statistical Methods:

   a. Data will be analyzed by SPSS.
   b. Descriptive statistics: We will present baseline characteristics of participants in each study arm using means and standard deviations (continuous variables) or median (range), frequencies and percentages (categorical variables).
   c. Primary analysis: We will conduct an intention-to-treat (ITT) analysis, including all randomized participants, regardless of adherence or dropout. We will compare the outcomes between the two study arms using mixed linear models
   d. Sensitivity analysis: We will perform a per-protocol analysis, restricted to participants who completed the full 14-week intervention period and adhered to the exercise regimen. We will compare outcomes between study arms using similar statistical methods as in the primary analysis.
   e. Subgroup analysis (if applicable): We will explore potential differences in treatment effects based on participant characteristics (e.g., age, gender, baseline disease severity) by conducting subgroup analyses. This can be

done by linear mixed models or regression analysis but will be determined once the dataset is finished.

f. Missing data: We will assess the extent and pattern of missing data. If applicable, employ appropriate techniques (e.g., multiple imputation) to handle missing data and perform sensitivity analyses to evaluate the impact of missingness on the results.

5. A priori sample size: based on literature:

   Group A: combined aerobic and strength training (primary outcome liver fat content): 30% (10,9%)

   Group B: interval training (primary outcome liver fat content): 37% (12,4%)

   Effect size is 0.5

   Given alfa of 0.05, with a power to achieve of 0.8 we need 40 participants in each group. Accounting for a 15% drop out rate we will recruit 46 patients in each group