FACULDADE DE MEDICINA DE RIBEIRÃO PRETO-USP
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LAFAP

LABORATÓRIO DE AVALIAÇÃO FUNCIONAL DOS MÚSCULOS DO ASSOALHO PÉLVICO

PHD PROJECT

Physiotherapeutic protocol compared to usual care in the treatment of postpartum primiparas after perineal trauma: a type 1 hybrid effectiveness-implementation randomized controlled trial with economic evaluation

Ribeirão Preto – SP

July 11, 2025

Statistical analysis plan

The data will initially be analyzed using descriptive statistics, making it possible to characterize the sample at baseline according to the variables collected in the electronic medical record, the patient's assessment and the implementation outcomes. They will then be presented using frequency tables and descriptive averages. Analysis of variance (ANOVA) will be used to confirm homogeneity between the groups of quantitative variables (i.e. age and PFD symptoms). Initially, an exploratory analysis of the data will be carried out, considering the measures of central position and dispersion in each group and study at each time point evaluated. Boxplots and histograms will be produced to verify the distribution of the data. The qualitative variables will be summarized considering absolute and relative frequencies. The chi-square test or Fisher's exact test will be used to check for statistical differences in the qualitative variables assessed only at baseline in relation to the groups. For the quantitative variables, Student's t-test or Wilcoxon's non-parametric test for independent samples will be used.

Mixed-effects regression models will be built to verify the effect of the groups and times in relation to the quantitative results. These models capture the variability between individuals within each time period and between individuals. Residual analysis will be carried out to check the fit of the models. A per-protocol analysis and an intention-to-treat analysis will be carried out. In order to include all variables that may affect the population or the result in the analysis, the directed acyclic graph (DAG) will be used, in which all variables will be entered and visualized before being analyzed. The statistical analyses will be implemented in the SAS program version 9.4.

The economic evaluation will be carried out according to the intention-to-treat principle. Multiple imputation by chained equations will be carried out to deal with missing data. An imputation model will be created, considering baseline variables that differ between groups/patients with and without missing data and variables that are predictive of patients with missing data on cost and/or effect items. Ten complete datasets will be created considering a loss of efficiency of less than 5%, and pooled estimates will be calculated according to Rubin's rules (Miyamoto et al., 2021; Ben et al.,

2023; Sterne et al., 2009). Average differences between groups for cost data will be calculated for societal and disaggregated costs. Seemingly unrelated regression analyses will be conducted to estimate the mean differences between effect and cost groups. These analyses correct costs and effects for baseline values and consider the possible correlation between costs and effects (Miyamoto et al., 2021; Ben et al., 2023; Willan et al., 2004). Incremental cost-effectiveness ratios will be estimated by dividing the corrected difference between the costs of the interventions by the corrected difference between the effects of the interventions. Accelerated and bias-corrected bootstrapping techniques with 5,000 replications will be conducted to deal with the uncertainty surrounding cost differences and incremental cost-effectiveness ratios. The cost-effectiveness pairs of the replications will be presented graphically in cost-effectiveness plots (Miyamoto et al., 2021; Black, 1990). Cost-effectiveness acceptability curves will be plotted to indicate the likelihood of IG being cost-effective compared to CG at different willingness-to-pay thresholds (Miyamoto et al., 2021; Fenwick et al., 2004). The willingness-to-pay threshold for implementing health technologies in Brazil is R$40,000 per QALY gained. If the incremental cost-effectiveness ratio is lower than this value, the intervention will be considered cost-effective and can be recommended for implementation in the SUS.

Sensitivity analyses will also be carried out to assess the robustness of the economic evaluation results. The first sensitivity analysis will be carried out for the health system perspective (considering only the costs of interventions and health care costs covered by the SUS and the total health care costs separately); the second sensitivity analysis will be carried out considering only complete cases, if possible; the third sensitivity analysis will be carried out considering per-protocol analysis (patients with less than 75% adherence will be excluded from the analysis); and the last sensitivity analysis will be carried out considering equity determinants, such as self-identified ethnicity, family income (number of minimum wages), level of education (illiterate, incomplete primary education, complete primary education, incomplete secondary education, complete secondary education, incomplete higher education, complete higher education, postgraduate degree), location of residence, occupation and gender violence (O'Neill et al., 2014), which will be questioned at the time

of the anamnesis, shortly after randomization. The economic evaluation was carried out using STATA (v.14, StataCorp, College Station, Texas, USA).