Supplementary Online Content

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eMethods. Data Analysis Plan

This supplementary material has been provided by the authors to give readers additional information about their work.
Introduction

This is a prospective, randomized, controlled, two groups study, designed to compare the progression of myocardial fibrosis detected by cardiac magnetic resonance (MR) in patients with progressive muscular dystrophy and preserved ventricular ejection fraction, receiving angiotensin-convert enzime (ACE) inhibitors or placebo.

Primary outcome
In the primary outcome myocardial fibrosis progression, the hypothesis being tested for superiority cohort is:

\[ H_0: \bar{m}_T = \mu_C \text{ vs. } H_1: \neq m_T \mu_C \]

where \( m_T \) and \( \mu_C \) are the average myocardial fibrosis for the group with no myocardial disfunction that received treatment (ND-T group or intervention) and the group that received placebo (ND-NT group or control group), respectively. The rejection of the null hypothesis with a 0.05 significance level indicates a significant difference between the two groups.

Secondary outcome:

Screening of specific genetic mutations as predictors of cardiac involvement, defined by the presence of fibrosis by cardiac MR.

Analysis

The descriptive statistics have been obtained using frequencies and percentages for categorical variables and using means and standard deviations for continuous variables. Continuous variables were tested for normality with the skewness-kurtosis test.
The Mann-Whitney test was used to evaluate the differences in continuous variables according to the comparison groups. To verify independent associations between categorical variables, Pearson chi-square test was performed. For comparisons between characteristics of myocardial fibrosis according to different age groups, it was used the Kruskal test, and for multiple comparisons, the Bonferroni method.

To compare proportions and averages obtained at baseline examination RMC and two years-follow-up examination, it was used the McNemar test and Wilcoxon test, respectively (considering that data were collected in a paired manner).

The relationship between continuous variables was performed by Spearman correlation coefficient test. Evaluation of left ventricular ejection fraction predictors and myocardial fibrosis were performed with multivariate logistic and linear regression analyses.

Calculations of sensitivity, specificity, predictive value positive and negative for traditional methods (chest X-ray, electrocardiogram and echocardiogram) in the diagnosis of progressive muscular dystrophy were performed, and compared to cardiac MR. Survival analysis was performed used Kaplan-Meier method.

For comparisons of the baseline CMR variables, the number of observations was equal to 76, and follow-up cardiac MR included 74 observations, considering two patients died before the follow-up CMR.

Statistical analysis was performed with STATA statistics package, version 10.0 (Stata Corp LP, College Station, TX, USA). The results were considered statistically significant at p < 0.05.