The Modified Rankin Score Compared to EDDS and MRI Measures in the CombiRx Randomized Trial: 3 Year Results

SS Cofield, R Conwit, A Salter, T Gustafson, F Nelson, P Narayana, S Datta, B Gates, GR Cutter, JS Wollinsky and FD Lublin for the CombiRx Investigators

Introduction

The modified Rankin Scale was designed for studies of stroke for grading functional disability on 6 levels (No Symptoms to Death). There is interest in utilizing this scale as a common measure of patient status across other neurological diseases, including multiple sclerosis (MS) where the assessment of clinical severity and time intensive. Historically, common measures of patient status in MS have included the EDSS and more recently the Alternate MS score. The Modified Rankin is a one item scale that can be self-assessed by the patient or completed by clinical personnel with only slight modification and training. Exploring the relationship between the Rankin, EDSS and MRI measures in relapsing remitting MS could lead to understanding of the feasibility of useful measure across multiple neurological diseases.

Background & Objectives

The CombiRx Trial was a three year, double blind, multi-center, randomized clinical trial with 1008 participants diagnosed by Posner or McDonald criteria with RRMS. Fifty percent (50%) of the participants were randomized to the combination of interferon beta 1a (RRN) and glatiramer acetate (GA) and 25% to each single agent arm with matching placebo. The primary endpoint of the clinical trial of the CombiRx trial was the Annualized Relapse Rate (ARR), with relapse being defined, in part, on a change in the EDSS.

The annual time of the EDSS, by a blinded examiner, varies depending upon the condition of the patient and the experience of the examiner. While the completion of the EDSS from the Functional System Scores (FSS) takes only a short time, the 10 page neurological examination that is needed to complete the FSS can take from 15 to 30 minutes and was administered on every participant in CombiRx at screening: baseline for the first year, A 7-sequent MRI was obtained on every participant at screening and Months 6, 12, 24, and 36.

Given that the 7-sequent MRI measures that must be interpreted for the patient to understand them, there is interest in use of a less complicated related measure, the current clinical status, patient status while also accurately assessing progression of the disease.

The primary objective was to compare baseline and annual assessments of the modified Rankin Scale (Figure 1), the EDSS, and number of GD exacerbations and burden of disease (BDQ) from the MRI. BDQ is defined as the total lesion volume (mL) as a sum of the T2 and MacDonald's components. CombiRx expands the use of EDSS by limiting baseline Rankin 5.5, able to walk without assistance.

Materials and Results

Consistency Across Year: Within a Rankin Score of 0, the mean values of EDSS are 1.53, 1.51, 1.49 and 1.51 for BL Year 1, 2, 3 and 4, respectively (Figure 2). The variability about EDSS scores for higher Rankin scores (Rankin 2 & 4) is larger compared to lower Rankin scores (1-2) due to the greater number of participants with the lower Rankin scores.

Predicting EDSS Using Rankin: The modified Rankin Score alone is a statistically significant predictor of the EDSS, accounting for 72.3% of the variability in the EDSS (p<0.0001) regardless of the year of measurement (p<0.05). When both were considered as independent variables, the distance walked and walking with aid are also significant predictors of the EDSS (p<0.0001) only accounting for an additional 2.1% of the variability in the EDSS measures.

Using the EDSS to predict the Rankin accounts for 65.5% of the variability in the Rankin. However, the distance walked and walking with aid are also significant predictors, they account for only 0.4% more variability in the Rankin.

Considering the rankin and distance walked together, for the 12 participants who had an EDSS of 0.33 EDSS of 1.51, 25% an EDSS of 2.25 across all years. Figure 3 Overall 34-32% of Rankin scores exactly matched to applicable EDSS categories, with an additional 40.8% matching to one category above the associated EDSS score and 8.2% matching to one category lower.

Rankin and MRI: Those with higher Rankin scores also had higher BOD (p=0.007), when adjusted for year of follow up (p=0.001). The Rankin was significantly associated with change in Gd lesions (p=0.0265) or cumulative gadolinium lesions over the 3 years (p=0.001).

Discussion

Participants with lower Rankin scores had lower EDDS Scores and lower BOD, regardless of year of follow up. Higher Rankin scores were associated with higher EDSS scores and BOD but not Gd lesions; though changes were not as strongly associated.

There is an association between the modified Rankin Scale and more complex EDSS and MRI measures at baseline and all follow up were in RRMS CombiRx participants, indicating that the modified Rankin may be a suitable less complex measure of patient disease status compared to the EDSS. Additional research is needed to be explored to fully understand the relationship between the modified Rankin and standard RRMS measures.

References
