Predictors of time to first confirmed disability progression after CIS: An MSBase Study

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Multiple Sclerosis (MS) is a chronic inflammatory, demyelinating disease that causes neurological disability, typically evolving over many decades. MS usually commences with a distinct syndrome of neurological dysfunction referred to as a first demyelinating event (FDE). The second occurrence of such a syndrome constitutes a relapse and can define the onset of relapsing-remitting multiple sclerosis (RRMS).

Disability in MS and, by extension, disability progression, is typically assessed using the Expanded Disability Status Scale (EDSS). This well-validated metric is widely used in global clinical practice. The EDSS represents an ordinal scale with 19 disease steps from 0 (no neurological symptoms) to 10 (death due to MS). It is derived from a combination of eight individual neurological system scores, the Kurtzke Functional System Scores (KFS). Measurement of EDSS change over time is the gold-standard primary outcome measure in Phase III clinical trials. Clinical trials have defined a measure known as 3-month confirmed EDSS progression, defining a progression event as a 1-point increase in EDSS score above baseline subsequently confirmed at repeat assessment 3 months later.

To assess the relationship of demographic, clinical, CSF, MRI and treatment exposure criteria to time to first confirmed disability progression after CIS in MS-specialist practice.

Methods

• We utilised MSBaseIS, the MSBase seen-from-FDE sub-study cohort. This study commenced in 2004 with patients recruited from 45 centres in 20 countries.
• Data were collected using iMed software and aggregated in MSBase.
• Baseline data collected included patient profile, date of CIS, EDSS and cerebral MRI classification by the neurologist. Other diagnostic tests included cerebrospinal fluid analysis (lumbar puncture, Spinal MRI) was recorded if performed. Follow-up data included relapses, treatments, changes, and EDSS.
• Data were extracted on 7th February 2011.
• All centres with 10 or more cases were included.

Statistical analysis

• Univariable Cox regression was used to identify candidate associations of baseline and time-dependent covariates with time to disability progression.
• Significant predictors identified on univariable analysis were then selected for multivariable analysis.

Results

1. 1,950 CIS patients were followed for a median duration of 2.4 years (OQR 1.4 to 4 years).
2. 501 (26%) CIS patients experienced a first disability progression event. Of these:
   • 402 patients had available baseline brain MRI
   • 379 patients had available spinal MRI
   • 249 had a CSF exam
3. Significant baseline predictors of time to first disability progression on multivariable Cox regression analyses included:
   • Age at CIS (HR 1.02/year, p=0.017) in models 1 & 2.
   • An EDSS of >2 versus EDSS ≤2 (HR 1.26, p=0.031) in model 1, see Figure 1.
   • Two of more abnormal KFS at baseline (HR 1.32, p=0.008) in model 2, see Figure 2.

Conclusions

Using survival analysis, the multicentre, multinational MSBase study has identified a number of independent predictors of first 3-month confirmed disability progression events, including a strong protective effect of beta-interferon 1a SC. We will continue to predict patients of long-term sustained first disability progression events.

Disclosures

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