

# Kappa Free Light Chain Index predicts long-term Disease Activity and Disability Accrual in Multiple Sclerosis

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## Introduction

Kappa free light chains ( $\kappa$ -FLC) in the cerebrospinal fluid (CSF) are recognized as a biomarker in neurology, reflecting intrathecal immunoglobulin synthesis. They are produced by plasma cells in excess compared to heavy chains and are secreted alongside intact immunoglobulins. Similar to immunoglobulins,  $\kappa$ -FLC accumulate in the CSF in various inflammatory neurological disorders.

As such, the  $\kappa$ -FLC index has been proposed as a diagnostic marker for MS.

While its diagnostic relevance is increasingly established, the prognostic value of the  $\kappa$ -FLC index over the long-term remains unclear.

## Methods

64 patients with a median age at onset of 32 years [25th-75th percentile: 27-39] and a female predominance of 75% were followed over median of 113 [90-129] months. Forty-six (72%) patients experienced relapse and 30 (47%) showed disability accrual. Multivariable Cox regression analysis adjusted for age, sex, disease duration, T2L, CEL and DMT revealed that  $\kappa$ -FLC index independently predicts time to relapse (Hazard ratio (HR) per increase of 10: 1.04, LL-CI: 1.0002,  $p=0.049$ ) and disability accrual (HR: 1.06, LL-CI: 1.02,  $p=0.008$ ).

## Objectives

To investigate whether  $\kappa$ -FLC index determined at disease onset predicts relapse activity and disability accrual during long-term follow-up.

## Results

Patients with a first demyelinating event of the central nervous system who had cerebrospinal fluid (CSF) and serum sampling were eligible for inclusion. At baseline, demographics, clinical data, number of T2 hyperintense (T2L) and contrast-enhancing lesions (CEL) were assessed. During follow-up occurrence of relapses, Expanded Disability Status Scale (EDSS) and disease-modifying treatments (DMT) were registered.  $\kappa$ -FLC were measured by nephelometry and  $\kappa$ -FLC index calculated as (CSF  $\kappa$ -FLC/serum  $\kappa$ -FLC)/albumin quotient.

## Conclusion

$\kappa$ -FLC index predicts long-term disease activity independently of other risk factors.

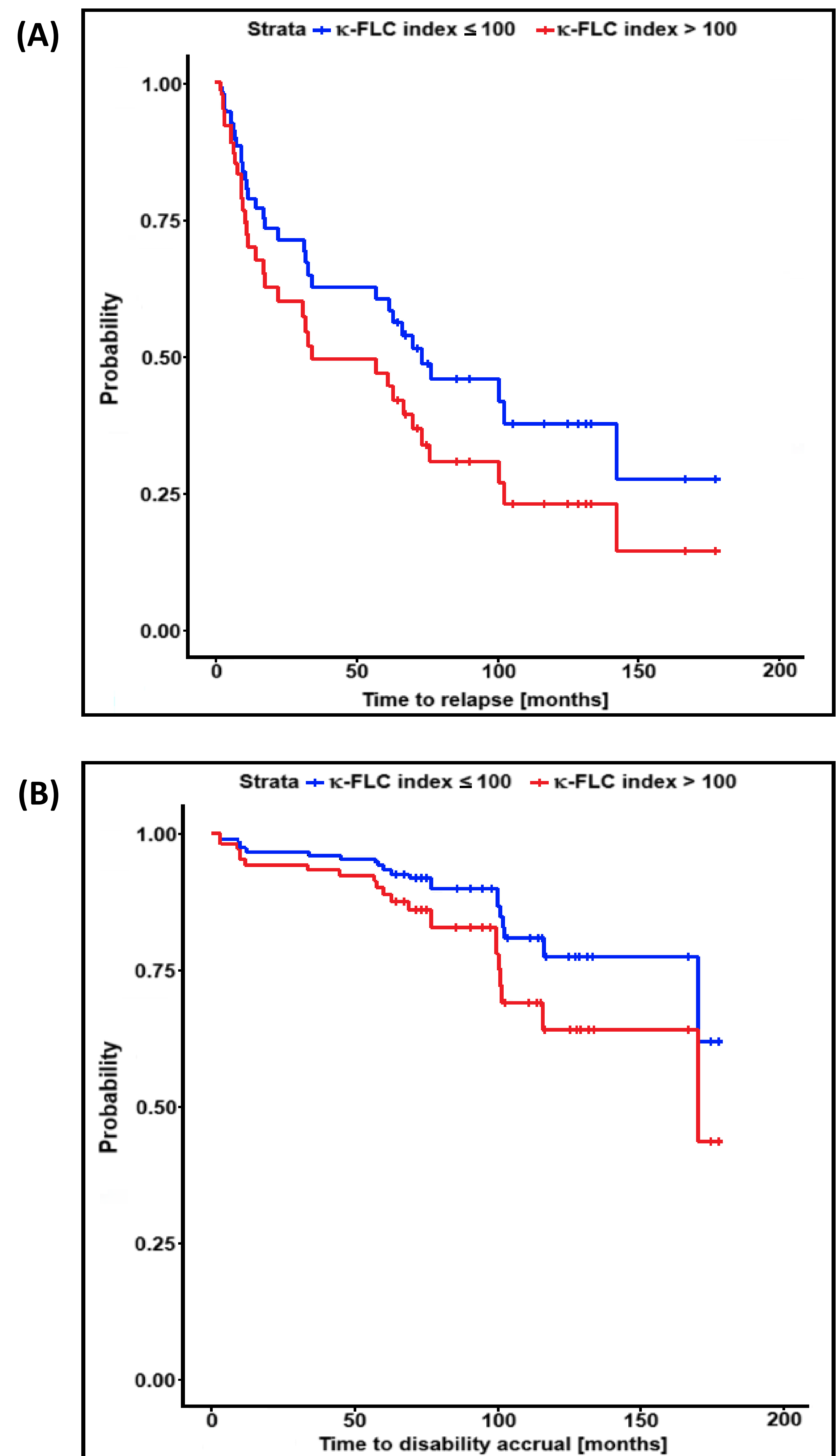


Figure 1: Probability of (A) relapse and (B) disability accrual depending on baseline  $\kappa$ -FLC index. The probability of developing (A) relapse or (B) disability worsening during 10-year follow-up was higher in the high  $\kappa$ -FLC index (>100) group ( $n = 17$ ) than in the low  $\kappa$ -FLC index ( $\leq 100$ ) group ( $n = 47$ ;  $p = 0.049$  and  $0.008$ ).