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CONVERSION FROM CLINICALLY ISOLATED SYNDROME TO MULTIPLE SCLEROSIS: A LARGE MULTICENTRE STUDY

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Establishing the prognosis for an individual with demyelinating clinically isolated syndrome (CIS) is a major epidemiological goal in MS research. This includes both the risk of conversion to MS and the prognosis for long-term disability. About 45% of CIS patients convert to clinically definite MS (CDMS) within two years. Most people with CIS who convert to MS, do so within the first five year.[1]

A number of risk factors for conversion have been studied, including MRI lesions, CSF oligoclonal bands (OCBs), demographics and more recently, vitamin D levels and Epstein Barr Virus (EBV) serology. The presence of MRI lesions is the strongest predictive risk factor. The prospective cohort of greatest duration reported that 81% of CIS patients who had MRI lesions converted to MS by 20 years.[2] It is also likely that the risk of MS conversion depends upon the number of MRI brain lesions.[3] The additional presence of CSF OCBs increases this risk.[4, 5] Recent studies have also introduced low vitamin D levels and positive EBV serology as potential risk factors worthy of further study.[6, 7] As the number and diversity of risk factors increase, it becomes important to design studies of sufficient power that can help to discriminate their contributions.

In this MSJ issue, Kuhle et al[8] report data from the largest collected CIS cohort (1047 cases), across 33 centres studied retrospectively over at least two years. The authors determined the risk of clinical conversion to MS. Clinical information was available in 87% of cases and showed a cohort with a variety of presentations (31.6% optic neuritis, 20.6% brainstem, 28.2% spinal cord, 19.5% other). During a median follow-up of 4.31 years, 59.5% of CIS patients converted to CDMS. Younger age, the presence of OCBs and a greater number of T2 lesions were all associated with a higher risk of CDMS conversion. People in the lowest vitamin D quartile had a greater risk of converting to CDMS compared with those in the upper three quartiles. However, risk of conversion was not influenced by IgG titres against EBNA1 or CMV, smoking status or type of clinical presentation. With multivariable regression analysis, the vitamin D significance was attenuated, although other variables remained significant. Lower vitamin D levels did not change the estimates of conversion risk in patients with positive OCBs and >9 T2 lesions at 2 (57%) and 5 (86%) years after onset. OCB negative CIS patients with 0-1 T2 lesions still had a conversion risk of 31% at 5 years.

Although this study provides a comprehensive view of the largest CIS cohort to date, there are a few limitations, also recognized by the authors. In order to acquire such a large cohort, a multicentre design was adopted, which provided a heterogeneous sample in terms of patient characteristics, differences in clinical care, MRI protocol and lesion detection. A prospective study would obviously be more desirable than retrospective in which these factors can be controlled. In addition, some other potential confounding factors were not adjusted for e.g. disease modifying treatments,[9, 10] genetic factors,[11] latitude,[12] vitamin D supplementation and seasonal variation in vitamin D levels.[6] The authors used Poser criteria (the occurrence of a

second neurological episode) to define conversion to MS in view of the MRI limitations, but with more contemporary revised diagnostic criteria,[13] the conversion estimates are likely to be higher.

Overall this study adds to our knowledge base in this field. In the future, one would ideally want to perform accurate prognostic risk stratification using relevant factors on an individual basis. This will help to inform treatment decisions for higher risk patients, but this type of knowledge is only likely to be derived from results of very large, well-designed, prospective cohorts.

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