Do spinal cord lesions matter in patients with clinically isolated syndrome and early MS?

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Asymptomatic spinal cord lesions are found in 30-50% of people with a clinically isolated syndrome (CIS).[1-3] Spinal cord MRI can assist in the diagnosis of multiple sclerosis (MS) in CIS patients[4], particularly in the subgroup of patients without evidence of dissemination in space on brain MRI at the time of presentation.[2, 3] Because typical short-segment spinal cord lesions are a relatively specific finding to MS, spinal cord MRI may also assist in differential diagnosis, and may be helpful in avoiding misdiagnosis.[5]

Two recent studies have suggested that spinal cord lesions in CIS patients may not only be helpful in making diagnosis of MS, but may also provide additional prognostic information.[1, 2] In a study involving 131 CIS patients with a non-spinal CIS who had brain and spinal MRI within 3 months of presentation, asymptomatic spinal cord lesions were the strongest MRI predictor of physical disability after 5 years.[1] Similarly, in another study of 207 prospectively recruited CIS patients with brain and spinal imaging with 3 months of disease onset, spinal cord lesions were associated with an increased risk of reaching Expanded Disability Status Scale (EDSS) 3 or more over a follow-up period of almost 3 years, even after adjusting for brain MRI findings and other relevant prognostic markers.[2] The prognostic value of spinal cord lesions was highest in patients with a non-spinal CIS.[2] Collectively these studies suggest that asymptomatic spinal cord lesions seen at the time of presentation with CIS are associated with an increased risk of physical disability, at least in the short to medium term, and may provide much needed prognostic information to help counsel patients about their risk of future disability.[1, 2]

In this issue of *Multiple Sclerosis Journal* Dekker and colleagues investigate the impact of asymptomatic spinal cord lesions in a cohort of patients recruited within 12 months presentation with CIS.[6] More than half of the patients already had a diagnosis of MS using the McDonald 2010 criteria at the time of study entry. MRI scans of the brain and spinal cord were obtained at “baseline” (within 12 months of disease onset) and the patients were followed up prospectively for the development of disability. Over a median follow-up period of 6 years no difference was seen in the time to reaching EDSS 3 and 6, or confirmed worsening in timed 25-foot walk and 9-hole peg test speeds in patients with and without asymptomatic spinal cord lesions. The authors conclude that the prognostic significance of asymptomatic spinal cord lesions in patients with CIS and early MS is uncertain.

The author’s findings do contrast with other recent work[1, 2] and this might reflect differences in the patient population studied, the analytical approach, or both. In the current study over 96% of patients had an abnormal brain MRI at presentation, compared with 65-80% in other studies.[1, 2] The higher proportion of patients with normal brain MRI in previous studies might have accentuated the prognostic value of asymptomatic spinal lesions: this group of patients are at much lower risk for the development of MS and disability[7], and asymptomatic spinal cord lesions are uncommon in patients with a normal brain MRI.[8] The authors approach to the analyses might also potentially account for the negative results. In their main analyses Dekker and colleagues compare the time to disability worsening in patients with asymptomatic spinal cord lesions at study entry to a comparator group without asymptomatic spinal cord lesions. The comparator group was very heterogeneous and included: (1) patients with a non-spinal CIS with normal spinal MRI; (2) patients

with spinal cord syndromes with a normal spinal MRI; and (3) patients with spinal cord syndromes with an abnormal spinal MRI. In total more than three quarters of the patients in the comparator group presented with a spinal cord syndrome, had a spinal cord relapse prior to study entry, or both. Therefore in reality the authors compare the time to disability worsening in patients with CIS or early MS with (predominantly) symptomatic spinal cord lesions to a group with asymptomatic spinal cord lesions. The fact that there was no difference in the time to disability worsening study might suggest that early spinal cord damage in relapse-onset MS, whether symptomatic or asymptomatic, may have similar functional consequences and carry a similar risk of future disability.

Whether routine spinal cord MRI should be done in all patients with CIS and early MS is controversial.[9] Current European and North American guidelines only recommend spinal cord imaging in selected patient groups.[10, 11] The additional diagnostic value of spinal cord MRI is known to be modest[2, 3], at least for providing evidence of dissemination in space in patients with typical clinical presentations suggestive of MS. Although other recent work has suggested a prognostic role for spinal cord imaging in patients with CIS and early MS[1, 2], the findings of Dekker and colleagues will add to the ongoing uncertainty over the diagnostic and prognostic value of spinal cord MRI in this patient group.

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