The 5-year risk of MS after optic neuritis Experience of the Optic Neuritis Treatment Trial

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The landmark Optic Neuritis Treatment Trial (ONTT) from 1992 (see Week 13, 52 in 52) showed that treatment with IV methylprednisolone in acute isolated optic neuritis accelerates visual recovery. However, a secondary objective to the trial was an analysis of the risk of MS development within 2 years after an episode of optic neuritis. Results from the ONTT trial suggested that fewer patients in the IV methylprednisolone group had a new diagnosis of MS at follow up as compared to the oral prednisone or placebo groups. As such, this follow-up paper reports the 5-year risk of MS in these same ONTT patient cohorts. This study also analyzed the prognostic factors and degree of neurologic disability among those patients who developed MS.

Experimental design and statistics: The ONTT (1992) was a multicenter randomized controlled trial that enrolled 457 patients aged 18-46 years with acute unilateral optic neuritis (see prior summary from Wk 13 of the original ONTT for details). Because the objective of this follow-up study was to evaluate the risk factors associated with the development of clinically definite MS within the ONTT patient cohort, this study excluded patients who had a diagnosis of either clinically definite MS or probable MS on study entry. Ultimately, the total number of eligible patients for this follow-up study was 388 patients (as compared to the original of 457 patients). The 3 treatment groups were the same as those in the ONTT: (1) IV methylprednisolone group, (2) oral prednisone group, (3) oral placebo. During follow-up visits, each patient's MS status was classified as no, possible, probable, or definite based solely on clinical criteria. MRI brain w/o contrast was also performed at study entry on 351 of the 388 patients (contrast-enhanced MRI was not in widespread use at that time). Out of the 388 eligible patients, only 341 (88%) completed 5+ years of follow-up. Non-completers were more likely to be African American and male, as shown in Table 1. They calculated the cumulative probability of the development of clinically definite MS with Kaplan-Meier estimates.

Results: The 5-year cumulative probability of developing clinically definite MS was 30%. The type of treatment (e.g. whether they were treated with IV steroids or not) did not significantly affect the probability of developing clinically definite MS within 5 years (see Figure 1 Kaplan-Meier curves). The presence of lesions on brain MRIs performed at the time of an episode of optic neuritis was the most important predictor of developing MS. There is an almost "dose-dependent-like" effect, as illustrated in Figure 2: only 16% of patients with no brain lesions developed clinically definite MS but 37% of patients with 1-2 brain lesions, and an even higher 51% of patients with 3+ brain lesions developed clinically definite MS. The presence of prior nonspecific neurologic symptoms was also independently associated with the 5-year development of MS. When brain MRI lesions and prior nonspecific neurologic symptoms were both present, the risk of developing MS was even higher. In patients reporting prior nonspecific neurologic symptoms, the 5-year probability of developing MS was 43% in the 19 patients with 1-2 brain MRI lesions and 66% in the 26 patients with 3+ lesions. When examining patients with no brain MRI lesions or any prior neurologic symptoms, 13% still developed clinically definite MS within 5 years. The clinical features of optic neuritis associated with a particularly low risk of MS development in the patients with no brain MRI lesions included lack of pain, the presence of optic disc swelling, and mild visual acuity loss.

Conclusions: In summary, the authors followed the patients from the original ONTT to identify the risk of MS development within 5 years after an episode of acute optic neuritis. Overall, the 5-year risk was 30%, without any statistical differences in terms of HOW optic neuritis was treated (e.g. with IV steroids or not). The strongest predictor of developing MS was the presence of brain MRI lesions. Therefore, it can be helpful to order an MRI brain in patients with a new episode of acute optic neuritis. Of note, even when patients had no brain MRI lesions or prior history of neurologic symptoms, the risk of developing MS within 5 years was still 13%, so a normal brain MRI does not entirely preclude the development of MS.

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