CAN MRI BE USED FOR THERAPEUTIC DECISIONS? YES

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Magnetic resonance imaging (MRI) is generally used for the assessment of patients with Multiple Sclerosis (MS) and plays an important role in the management of MS and therapeutic decisions. MRI techniques have improved over the past decade. Conventional MR techniques are very helpful for monitoring patients with relapsing MS in clinical practice providing objective and sensitive measures of disease activity and therefore can be used for therapeutic decisions.

The therapeutic decisions of MS patients depend strongly on disease dissemination in space and time. The particular sensitivity of MRI techniques allows to detect MS lesions and their changes over time. The development of diagnostic criteria for MS which strongly rely on paraclinical measures, especially MRI, has also strengthened the notion of the so-called clinically isolated syndrome (CIS) as a first manifestation (relapse) of the disease. The 2010 revisions to the diagnostic criteria enable a more rapid diagnosis and should be applied when patients have experienced a typical CIS. The relapse-onset of MS is applicable in about 90% of patients and up to 80% of these patients have already lesions in the central nervous system that can be detected by MRI. The detection and description of older and new lesions in the disease course by MRI represents subclinical disease activity which can substitute a clinical relapse. MRI helps to cut down the waiting periode before a patient meets the clinical diagnostic criteria for MS.

I will show in my presentation, that MRI assessment is of great importance to prospectivly predict which patients will be at highest risk for substantial disability. Furthermore, disease activity can be detected in patients with relapsing-remitting and secondary progressive course five to ten times more frequently on MRI scans than with clinical assessment of relapses. CIS studies demonstrated, that about four out of five patients with MS with a pathological MRI of the brain develop clinically definite MS after 20 years, but only one out of five patients will emerge to MS if the MRI was normal at the time of the first clinical event. The diagnostic criteria allow already the diagnosis of (definitive) MS in some patients with a CIS. More T_2 lesions in the brain indicate a higher risk of earlier conversion to MS and clinical progression. The possibility to predict future disease severity influences the decisions to start or to escalate within the disease-modifying drugs for the treatment of relapsing-remitting MS.

We investigated the decision making process regarding immediate or later disease modifying treatment and the impact on CIS patients in Austria (ACISS – study). The decision for initiation of therapy was at the physician's and patient's discretion. In 29% of patients' treatment with disease modifying drugs was started within 3 months and this decision was independently associated with a T_2 lesion number ≥9 on MRI. Treatment has been recommended for CIS patients who have a "high risk" to rapidly develop a second relapse or who will presumably follow a more severe course of MS.

There are only a few possible early predictors of disease severity which mainly rely on MRI findings such as the number of T_2 lesions and the presence of contrast-enhancing lesion. The factor which was most significantly associated with a decision for immediate treatment was the presence of a higher number of (i.e. at least 9 T_2 lesions) on MRI of the brain. Several reasons may account for this. The presence of ≥9 T_2 lesions is one of the criteria for fulfilling dissemination in space. There are several lines of evidence that an increasing number of T_2 lesions is associated with a more active and progressive course of the disease.

There is neither a standard definition for breakthrough disease in MS nor a clear consensus on how to manage such patients. The development of T_2 hyperintensities, Gd + lesions, T_1 hypointensities and brain atrophy while patients are administered interferon-beta or glatiramer acetate therapy are all either associated with or predictive of breakthrough disease as measured by future disability progression or relapse rates. MRI worsening in isolation would only rarely mandate a change in therapy. Breakthrough disease, if defined broadly as any ongoing clinical or MRI activity while on conventional injectable disease modifying treatments is common and a challenge for treatment decisions.

Summary: MRI is the most important paraclinical tool not only in diagnosing MS, but establishing a prognosis even at the onset of the disease. MRI is also used for observing the response to treatment. Though, how and when MRI should be utilized is a matter of debate because the correlation with clinical findings is still limited. In every day practice clinical outcome measures are used primarily to assess the effectiveness of MS treatment, but studies applied MRI for additional information about the effects of the drugs in MS. For instance, a secondary analysis of the pivotal interferon-beta-1a trial has also claimed a greater benefit of immediate immunomodulatory treatment of patients with ≥9 T_2 and ≥1 contrast enhancing lesion(s) at presentation of the CIS.