Review and Analysis of International Case-Control Studies on CCSVI and Multiple Sclerosis

Abstract: Background: A constellation of neurosonological findings called chronic cerebrospinal venous insufficiency (CCSVI) was introduced as a highly specific and highly sensitive finding in multiple sclerosis (MS) patients. It was postulated that impaired venous cerebral drainage initiates the pathological processes of MS. Several published case-control of studies evaluating the association of CCSVI with MS report inconsistent findings. Methods: Besides an overview of the postulated concept of venous hypothesis, we performed a meta-analysis of the results from published case-control studies evaluating the association of CCSVI with MS using ultrasound criteria. Results: In 25 eligible studies, 2,012 MS patients and 1,425 healthy controls were investigated. The constellation of CCSVI was described in 876 (41.7%) of the patients and in 147 (10.3%) of the controls (OR=3.2; 95% CI=2.5-4.0). However, considerable heterogeneity (I²=82%) across these studies was documented. The analysis of the 3 German studies revealed a very low prevalence of CCSVI of only about 2% in both groups (OR=0.5; 95% CI=0.1-3.1) without heterogeneity (I²=0%). Conclusions: Compared to the first description, no subsequent international case-control study could reproduce the high specificity and sensitivity of CCSVI in MS. There is high heterogeneity across the different studies, so that further comprehensive
meta-analyses with additional sensitivity analyses are required. The studies conducted in Germany have clearly and consistently shown no evidence for the venous multiple sclerosis hypothesis. Interventional procedures should therefore not be performed outside the setting of randomised clinical trials.