Accuracy of central vein sign in multiple sclerosis diagnosis: a systematic review and Bayesian meta-analysis

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Introduction: In recent years, the need to improve sensitivity and specificity of multiple sclerosis (MS) diagnosis has led the search for new imaging and laboratory markers. Among them, the central vein sign (CVS), i.e. the visualization of a vein at the center of an MS plaque on magnetic resonance imaging, has been one of the most studied. The CVS, a radiological counterpart of the perivenular distribution of MS lesions in pathological specimens, is planned to be included in the forthcoming revision of MS diagnostic criteria. Considering these recent developments, we performed a systematic review and meta-analysis to provide a comprehensive summary of available knowledge.

Methods: We searched Pubmed, Scopus and Embase for studies evaluating the power of CVS to discriminate MS cases from other conditions. Different diagnostic rules involving CVS were considered separately. Risk of bias was assessed through QUADAS-2 tool. To pool collected evidence, we used a Bayesian model allowing to take into account multiple estimates of sensitivity and specificity at different positivity thresholds in the same study.

Results: We screened 767 abstracts and included 28 studies. Two main diagnostic rules based on CVS were found: the first one was based on the percentage of CVS+ lesions (relative threshold method); the second one on a minimum number of CVS+ lesions in gradient echo imaging (select-n* method). For the relative threshold method, the best positivity threshold was 37.5% (sensitivity 97% CI 91-100%, specificity 91% CI 83-96%, Youden index 0.89); for the select-n* method, the best threshold was 4 (sensitivity 87% CI 67-97%, specificity 88% CI 65-98%, Youden index 0.75).

Discussion and conclusion: Our results for the relative threshold method are similar to the 40% positivity threshold often adopted in literature; this confirmation could be useful in the future, when automated detection of CVS will make the calculation of CVS+ lesion percentage more feasible. Conversely, findings regarding select-n* are quite different from the threshold to be adopted in McDonald criteria (4 vs 6). Probably, the choice of the number of six lesions as a threshold is linked to the fact that most published studies adopt a select-3* or select-6* approach; our use of a multiple threshold model allowed us to get more information also on intermediate values, which appear to be more accurate considering available evidence. When McDonald 2024 criteria will come into use, real world data will be useful to assess the impact of positivity threshold on CVS accuracy.

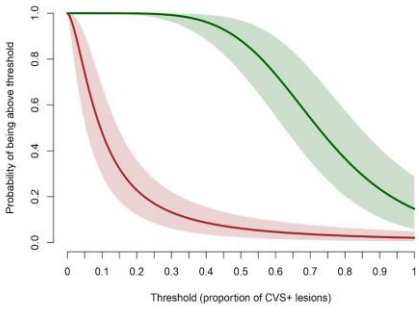

Figure 1. Plot of true positive rate (TPR, green line) and false positive rate (FPR, red line) across different values of positivity threshold for relative-threshold method.

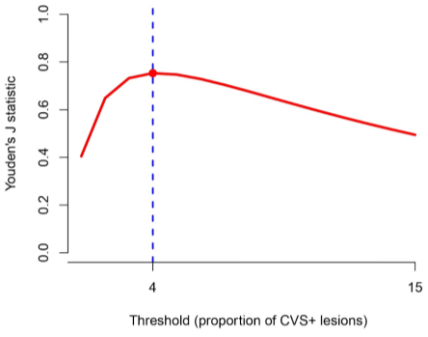

Figure 2. Plot of Youden index across different values of positivity threshold for select-n* method.

References

Jones HE, Gatsonsis CA, Trikalinos TA, Welton NJ, Ades AE. Quantifying how diagnostic test accuracy depends on threshold in a meta-analysis. Statistics in Medicine. 2019; 38: 4789-4803

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