MSMilan2023
9th Joint ECTRIMS-ACTRIMS Meeting
11–13 October 2023 | Milan, Italy

Abstract Number: [373]

Abstract Title: Incorporation of the central vein sign into the International Panel criteria increases specificity and accuracy for a diagnosis of multiple sclerosis

Abstract Category: Imaging and non-imaging biomarkers - 27 - MRI & PET

Preferred Presentation Type: Oral or poster presentation

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Introduction:
The diagnosis of multiple sclerosis (MS) relies on establishing dissemination in time (DIT) and dissemination in space (DIS) as codified in the 2017 International Panel criteria (IP2017). Although sensitive, the IP2017 has a misdiagnosis rate of 20%, primarily attributed to incorrect application of MRI criteria. The central vein sign (CVS) is a putative diagnostic biomarker for MS that may increase specificity and diagnostic accuracy, but how to optimally incorporate CVS with the IP2017 criteria is not established.
Objectives/Aims:
To evaluate the diagnostic performance of different CVS criteria incorporated into IP2017.
Methods:
This analysis used data from the Central Vein in Multiple Sclerosis Pilot, a cross-sectional, international multi-center study conducted by North American Imaging in MS Cooperative at 10 sites from April 2018 - February 2020. The study collected data on 97 adults referred to an academic MS center for a clinical or radiological suspicion of MS. Participants with unclear final diagnosis and incomplete MRI were excluded. IP2017 was based on clinical documentation and adjudicated by 3 experts. Independent

blinded MRI assessments for IP2017 DIS and DIT were evaluated using T2-weighted, FLAIR, pre and post contrast T1-weighted MPRAGE sequences on the QMENTA platform. CVS was assessed on post-contrast T2*-weighted segmented echoplanar imaging, merged with FLAIR images (FLAIR*). DIS was defined per IP2017 on the study MRI, and DIT was defined as presence of enhancing and non-enhancing lesions. Incorporation of CVS into IP2017 was examined by requiring one of the following criteria in addition to DIS: (a) only CVS+ lesions can be used to meet DIS CVS; (b) ≥1 of the lesions used to meet DIS is CVS+; (c) ≥1 brain lesion with CVS irrespective of location.

Results:

89 participants were included in the analysis, 36 with MS and 53 with other diagnoses. Sensitivity, specificity, and accuracy were, respectively: 92%, 70%, and 79% for DIS alone; 25%, 100%, and 70% for DIT alone; and 25%, 100%, and 70% for DIS plus DIT. Optimal diagnostic performance was seen with requirement of at least one lesion with CVS in any location in addition to DIS with sensitivity, specificity, and accuracy of 92%, 79%, and 84%, respectively. All other combinations of DIS, DIT, and CVS had worse diagnostic performance.

Conclusion:

Addition of CVS to IP2017 increases the specificity for DIS without an impact on sensitivity. Requiring one CVS in addition to DIS could be easily implemented in clinical practice and can be evaluated in future prospective studies.

Disclosures: MA: Received Novartis fellowship award NGC4474.
KN: Received licensing fee from Biogen; received Research Support from Department of Defense, National Institutes of Health, Patient Centered Outcomes Research Institute, and Biogen.
LD: None
CMO: None
QC: None
PR: Employed by and holds stocks in QMENTA
JD: None
CA: Has received grant support from the National Multiple Sclerosis Society and the NIH. Has received consulting fees from Horizon Therapeutics, Genentech, Sanofi Genzyme, TG Therapeutics, and EMD Serono. Has received honoraria for serving on grant review committees for the Department of Defense and the NIH and for participation in unbranded CME activities from the American Academy of Neurology, Efficient LLC, Spire Learning, and Catamount Medical Education
AB: Consulting and/or advisory board fees from Accure, Atara Biotherapeutics, Biogen, BMS/Celgene/Receptos, GlaxoSmithKline, Gossamer, Janssen/Actelion, Medimmune, Merck/EMD Serono, Novartis, Roche/Genentech, Sanofi-Genzyme. Grant support to the University of Pennsylvania from Biogen Idec, Roche/Genentech, Merck/EMD Serono and Novartis. Research funding from the National Institutes of Health (NIH), The National MS Society (NMSS), the Juvenile Diabetes Research Foundation (JDRF), the Canadian Institutes of Health Research, Multiple Sclerosis Society of Canada.
EC: None
PAC: PI on grants to JHU from Genentech. Serves on scientific advisory boards for Lilly and Idorsia.
BACC: Compensation for consulting from: Alexion, Atara, Biogen, EMD Serono, Novartis, Sanofi, and TG Therapeutics
LF: Received fees for consultancy and/or advisory board participation from Genentech, Novartis, Celgene/Bristol Myers Squibb, EMD Serono, and TG Therapeutics; Received fees for educational activities from Medscape, LLC, and the MS Association of America; program sponsorship to UT from EMD Serono; and grant support to UT from NIH/NINDS, PCORI, Genentech, and EMD Serono.
RGH: Research support from Roche, Genentech, Atara, Medday. Consulting for Novartis, Sanofi/Genzyme, Roche/Genentech, QIA, and Neurona.
EEL: Grants: Genentech, Biogen. Consulting: EMD Serono, BMS, Genentech, Genzyme, Bristol Myers Squibb, TG Therapeutics, Janssen, NGM Bio
JO: Research support from Biogen-Idec, Roche, and EMD-Serono; consulting compensation from EMD-Serono, Sanofi-Genzyme, Biogen-Idec, Roche, Celgene, and Novartis

NP: Reports research support from the Race to Erase MS Foundation and from the National Center for Advancing Translational Sciences, National Institutes of Health, through a UCSF-CTSI grant
DP: Consulting compensation from EMD-Serono, Sanofi Genzyme, Roche, and Novartis
VP: Employed by and holds stocks in QMENTA
PR: None
MR: Employed by and holds stock options in QMENTA
RDS: Advisory board participation (Biogen, EMD Serono, Sanofi Genzyme); Consulting (EMD Serono, Biogen)
MKS: None
ESS: Consulting for scientific advisory boards from Viela Bio and Genentech, Speaker honoraria from Viela Bio
NLS: Research support from the National Institutes of Health, National Multiple Sclerosis Society, Patient Centered Outcomes Research Institute, Race to Erase MS Foundation and Biogen-Idec
AJS: Consulting: EMD Serono, Biogen, Alexion, Celgene, Greenwich Biosciences, Octave Bioscience, TG Therapeutics, Sanofi; Non-promotional speaking: EMD Serono; Research Funding: Biogen, Bristol Myers Squibb; Contracted Research: Biogen, Novartis, Actelion, Genentech/Roche
RTS: Supported NIH R01NS112274, R01MH112847, R01MH123550. Consulting income from Octave Bioscience.
DSR: Supported by the Intramural Research Program of NINDS; additional research support from Vertex Pharmaceuticals, Sanofi-Genzyme, and Abata Therapeutics.
PS: Research support from the National Institutes of Health and the National Multiple Sclerosis Society.
DO: Received research support from the National Institutes of Health, National Multiple Sclerosis Society, Patient Centered Outcomes Research Institute, Race to Erase MS Foundation, Genentech, Genzyme, and Novartis. Consulting fees from Biogen Idec, Genentech/Roche, Genzyme, Novartis, and Merck.)

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