

Retinal layer thinning after optic neuritis as a predictor of future relapse remission in relapsing multiple sclerosis

Gabriel Bsteh¹, Nik Krajnc^{1,2}, Katharina Riedl¹, Patrick Altmann¹, Fritz Leutmezer¹, Stefan Macher¹, Christoph Mitsch³, Paulus Rommer¹, Gudrun Zulehner¹, Berthold Pemp³, and Thomas Berger¹ for the VMSD study group

¹Department of Neurology, Medical University of Vienna, Vienna, Austria

²Department of Neurology, University Medical Centre Ljubljana, Ljubljana, Slovenia

³Department of Ophthalmology, Medical University of Vienna, Vienna, Austria

Presenting author:

Prof. Gabriel Bsteh, MD, PhD

Department of Neurology, Medical University of Vienna, Vienna, Austria

Währinger Gürtel 18-20, 1090 Vienna, Austria

Email: gabriel.bsteh@meduniwien.ac.at

[Telephone: 0043 1 40400 31450](tel:+4314040031450)

Keywords: Multiple Sclerosis, biomarker, optical coherence tomography, retina, relapse, remission.

Abstract

Background: Remission of relapses is an important contributor to both short- and long-term prognosis in relapsing multiple sclerosis (RMS) and dependent of the degree of irreversible neuroaxonal damage. In MS-associated acute optic neuritis (ON), retinal layer thinning measured by optical coherence tomography (OCT) is a reliable biomarker of both functional recovery and the degree of neuroaxonal damage. However, prediction of non-ON relapse remission is challenging.

Objective: We aimed to investigate whether retinal thinning after ON could predict relapse remission after subsequent non-ON relapses.

Methods: For this longitudinal observational study from the Vienna MS database (VMSD), we included MS patients with 1) an episode of acute ON, 2) available spectral-domain OCT scans within 1 week after ON onset and 3-6 months after ON, and 3) at least one non-ON relapse after the ON episode. Subsequent non-ON relapses were classified as displaying either complete or incomplete remission based on change in expanded disability status scale (EDSS) assessed 6 months post-relapse. Impact of retinal thinning in peripapillary retinal nerve fiber layer (pRNFL) and macular ganglion-cell-and-inner-plexiform-layer (GCIPL) for prediction of incomplete remission was tested by multivariate logistic regression models adjusting for age, sex, disease duration, baseline EDSS, time to steroid treatment, and DMT status with internal bootstrap cross-validation.

Results: We analyzed 167 MS patients (mean age 36.5 years [SD 12.3], 71.2% female, mean disease duration 5.4 years [SD 6.2]) during a mean observation period of 3.4 years (SD 2.8) after the ON episode. Mean retinal thinning after ON was 43.1 μ m (SD 45.2) in pRNFL and 12.1 μ m (SD 8.2) in GCIPL. In 61 patients (36.5%) at least one relapse showed incomplete remission. In the multivariable models, incomplete remission was predicted by GCIPL thinning after ON (odds ratio [OR] 2.4 per 5 μ m, 95% confidence interval [CI]: 1.4 – 4.1, $p < 0.001$) independently explaining 29% of variance (change in R^2 : 0.29). pRNFL was also associated, although with both less effect size (OR: 1.9 per 10 μ m, 95% confidence interval [CI]: 1.1 – 3.2, $p = 0.041$) and explaining less of variance (change in R^2 : 0.12).

Conclusions: Retinal layer thinning after optic neuritis may be useful as a predictor of future relapse remission in relapsing multiple sclerosis, potentially informing treatment strategy.

Funding

There was no funding to this research.

Acknowledgements

We thank all the VIMSD investigators, clinical research staff, and especially the patients for helping to collect these data. The named individuals were not compensated for their help.

Group information

VMSD investigators in alphabetical order: Altmann, Patrick (Medical University of Vienna, Vienna, Austria); Berger, Thomas (Medical University of Vienna, Vienna, Austria); Bsteh, Gabriel (Medical University of Vienna, Vienna, Austria); Kornek, Barbara (Medical University of Vienna, Vienna, Austria); Leutmezer, Fritz (Medical University of Vienna, Vienna, Austria); Monschein, Tobias (Medical University of Vienna, Vienna, Austria); Rommer, Paulus (Medical University of Vienna, Vienna, Austria); Zebenholzer, Karin (Medical University of Vienna, Vienna, Austria); Zulehner, Gudrun (Medical University of Vienna, Vienna, Austria); Zrzavy, Tobias (Medical University of Vienna, Vienna, Austria).

Disclosure of conflicts of interest

Gabriel Bsteh: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene, Roche and Teva.

Nik Krajnc: has participated in meetings sponsored by, received speaker honoraria or travel funding from Merck, Novartis and Roche.

Katharina Riedl: reports no disclosures.

Patrick Altmann: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Merck, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting from Biogen. He received a research grant from Quanterix International and was awarded a combined sponsorship from Biogen, Merck, Roche, Sanofi-Genzyme and Teva for a clinical study.

Fritz Leutmezer: has participated in meetings sponsored by or received honoraria for acting as an advisor/speaker for Actelion, Alexion, Almirall, Bayer, Biogen, Celgene, MedDay, Merck, Novartis, Octapharma, Pfizer, Roche, Sanofi-Aventis and Teva.

Stefan Macher: reports no disclosures.

Christoph Mitsch: has received honoraria for consultancy/speaking (incl. funds for e-learning modules) from Bayer, Novartis and Takeda.

Paulus Rommer: has received honoraria for consultancy/speaking from AbbVie, Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sandoz, Sanofi-Genzyme, has received research grants from Amicus, Biogen, Merck and Roche.

Gudrun Zulehner: has participated in meetings sponsored by or received travel funding from Biogen, Merck, Novartis, Roche, Sanofi-Genzyme and Teva.

Berthold Pemp: has received honoraria for consulting from Novartis.

Thomas Berger: has participated in meetings sponsored by and received honoraria (lectures, advisory boards, consultations) from pharmaceutical companies marketing treatments for MS: Allergan, Almirall, Bayer, Biogen, Biologix, Bionorica, Celgene, MedDay, Merck, Novartis, Octapharma, Roche, Sanofi-Genzyme, Teva and TG Pharmaceuticals. His institution has received financial support in the past 12 months by unrestricted research grants (Biogen, Merck, Novartis, Sanofi-Genzyme, Teva and for participation in clinical trials in multiple sclerosis sponsored by Alexion, Biogen, Merck, Novartis, Octapharma, Roche, Sanofi-Genzyme, Teva.