

A low vitamin D status at diagnosis is associated with an early conversion to secondary progressive multiple sclerosis

Anne-Hilde Muris^{1,2}, Linda Roif^{1,2}, K. Broen³, R. Hupperts^{1,2}, J. Damoiseaux⁴, J. Smolders^{2,5}

¹School for Mental Health and Neuroscience, Maastricht University Medical Center, Maastricht, ²Academic MS Center Limburg, ³Clinical Chemistry, Orbis Medical Center, Sittard, ⁴Central Diagnostic Laboratory, Maastricht University Medical Center, Maastricht, ⁵Department of Neurology, Canisius Wilhelmina Hospital, Nijmegen, The Netherlands

Introduction

- Vitamin D insufficiency is increasingly recognized as a major environmental risk factor for multiple sclerosis (MS).
- Low 25(OH)D levels have been associated with increased disease activity in relapsing remitting MS (RRMS).
- Interestingly, lower 25(OH)D levels were observed in patients with SPMS when compared to patients with RRMS. This could indicate an increased vulnerability to develop SPMS in RRMS patients with a poor vitamin D status.
- We assessed whether the vitamin D status in RRMS patients is associated with the time to conversion to SPMS.

Results

- 25(OH)D levels in RRMS do not predict the 3-year risk of conversion to SPMS.
 - We longitudinally analyzed 338 RRMS patients. During the 3-year follow-up, 51 (15%) patients converted to SPMS.
 - The deseasonalized vitamin D status was not a significant predictor of risk of conversion to SPMS.
- Diagnostic 25(OH)D levels are lower in SPMS patients with a short RRMS duration than in matched RRMS patients.
 - 19 SPMS index patients with a relatively short RRMS duration were matched with 38 RRMS control patients who had not (yet) converted to SPMS. (Patient characteristics in table 1).
 - The SPMS patients had significantly lower 25(OH)D levels (38.5 nmol/L; Q1-Q3: 23.9-50.1) than the RRMS patients (55.4 nmol/L; Q1-Q3: 39.7-70.3; p=0.004) (Figure 1).
 - Alternatively expressed, MS patients within the lowest tertile of diagnostic 25(OH)D levels (4.1-35.7 nmol/L) had a 5.9-times (95% CI: 1.3-27.3) increased risk of being in the SPMS cohort, when compared to the highest tertile (57.6-128.5 nmol/L; p=0.022).

Research questions

- Does vitamin D status in established RRMS predict a 3-year risk of conversion to SPMS?
- Is vitamin D status at diagnosis associated with conversion to SPMS?

Methods

- Subjects with RRMS with 25(OH)D levels measured at the start of a 3-year follow-up were retrospectively selected from a longitudinal MS cohort of the Academic MS Center Limburg (The Netherlands). A logistic regression model was used to analyze whether these levels predict the risk of RRMS to SPMS conversion in 3-year follow-up.
- 25(OH)D levels were measured in diagnostic samples of index patients with SPMS and in RRMS control patients. Patients were matched in a 1:2 ratio, based on sex, year of birth and year of MS diagnosis.

Conclusions

- Vitamin D status in RRMS does not predict a 3-year risk of conversion to SPMS.
- SPMS patients with a short RRMS duration have low diagnostic 25(OH)D levels.
- A low vitamin D status at diagnosis is likely to be associated with early conversion to SPMS.
- Time to SPMS conversion can be an interesting clinical measure for long-term follow-up in vitamin D trials.

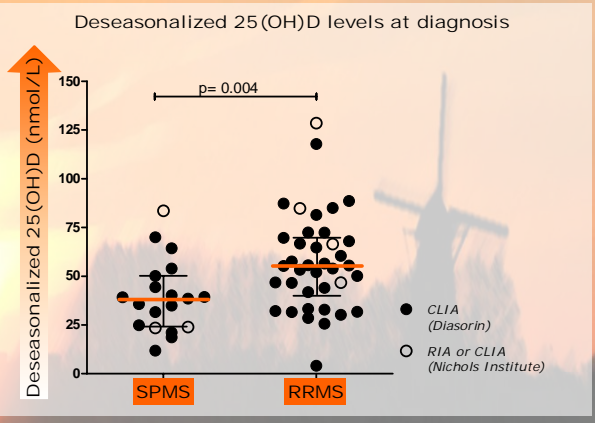


Figure 1. Deseasonalized 25(OH)D levels (median (IQR)) of SPMS and RRMS patients at MS diagnosis.

Table 1. Patient characteristics of the SPMS index patients and the matched RRMS control patients

	SPMS (n=19)	RRMS (n=38)	p-value
M/F ratio (n)	6/13	12/26	1.000
Age (years) Mean (95% CI)	55.1 (51.0-59.1)	53.1 (50.7-55.6)	0.377
Disease duration from diagnosis (years) Median (Q1-Q3)	9.7 (6.6-12.0)	7.7 (6.3-10.0)	0.084
RRMS duration (years) Median (Q1-Q3)	3.5 (1.0-5.7)	7.7 (6.3-10.0)	<0.001
Age at diagnosis (years) Mean (95% CI)	45.4 (41.2-49.6)	45.3 (42.6-48.0)	0.957

SPMS = secondary progressive MS, RRMS = relapsing remitting MS, M = male, F = female, Q1-Q3 = interquartile range.

Correspondence to:
 Anne-Hilde Muris
 a.muris@maastrichtuniversity.nl

School for Mental Health and Neuroscience
 www.maastrichtuniversity.nl/mhens

Postal address:
 Maastricht University Medical Center
 School for Mental Health and Neuroscience
 P.O. box 616
 6200 MD Maastricht
 the Netherlands

T +31 43 3881043
 T +31 6 39410700

Academic MS Center Limburg
 www.mscentrumlimburg.nl