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

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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.

Research questions

I. Does vitamin D status in established RRMS predict a 3-year risk of conversion to SPMS?

II. Is vitamin D status at diagnosis associated with conversion to SPMS?

Methods

I. 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.

II. 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.

Results

I. 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.

II. 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).

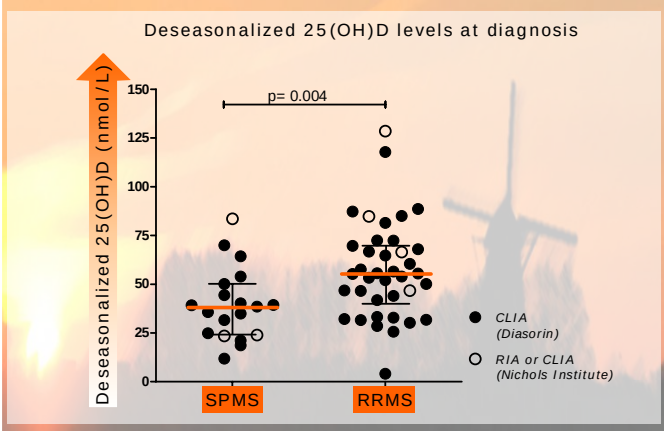

Figure 1. Deseasonalized 25(OH)D levels (median (IQR)) of SPMS and RRMS patients at MS diagnosis.

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.

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.

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