

Online only supplementary material

Supplementary Table 1. Demographic data of patients with NMOSD-AQP4 and MS in our cohort.

Variables	NMOSD-AQP4	MS
Number of patients	157	63
Sex, men: women	24:133	27:36
Age at onset, mean (SD), years	41.12 (13.99)	29.78 (9.10)
Follow-up duration, mean (SD), years	7.53 (7.34)	7.73 (6.23)
Cumulative number of attacks, mean (SD)	3.31 (2.19)	3.27 (2.34)
ARR ^a , mean (SD), /year	0.67 (0.55)	0.58 (0.41)
BMI _{naïve} ^b , Mean (SD), kg/m ²	21.67 (2.88)	22.51 (3.46)
BMI _{min-1yr} ^c , Mean (SD), kg/m ²	21.21 (2.93)	22.16 (3.32)
Onset attack type ^d		
Optic nerve, n (%)	63 (40.1)	12 (20.0)
Spinal cord, n (%)	80 (51.0)	19 (31.7)
Brain, n (%)	34 (21.7)	29 (48.3)
CSF study ^e		
White blood cells, mean (SD), /mm ³	21.39 (42.4)	4.15 (5.7)
CSF/serum albumin ratio, mean (SD)	5.75 (5.28)	4.48 (2.5)
CSF/serum IgG ratio, mean (SD)	4.4 (3.3)	6.6 (15.8)

^a 140 NMOSD and 61 MS patients were compared; ^b78 NMOSD and 34 MS patients were compared; ^c103 NMOSD and 41 MS patients were compared; ^d157 NMOSD and 60 MS patients were compared; ^e68 NMOSD and 27 MS patients were compared.

Abbreviations: NMOSD-AQP4, neuromyelitis optica spectrum disorder with aquaporin-4 immunoglobulin G; MS, multiple sclerosis; SD, standard deviation; ARR, annual relapse rate; BMI, body mass index; BMI_{naïve}, BMI measured within 1 month of the first symptom and before intravenous or oral steroid treatment; BMI_{min-1yr} the lowest BMI measured within 1 year of the first symptoms; CSF, cerebrospinal fluid.

Supplementary Table 2. Multivariable logistic regression analysis in matched case-control data

	OR (95% CI)	P-value
Sex (Female)	0.95 (0.45, 1.99)	0.888
Age	1.01 (0.99, 1.03)	0.455
BMI (kg/m²), 1 unit decrease	1.14 (1.05, 1.24)	0.002

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index.

Supplementary Table 3. Demographic data of patients with NMOSD-AQP4 and MS who have available BMI_{naïve} data and diagnosed since 1995.

Variables	NMOSD-AQP4	MS
Number of patients	75	33
Sex, men: women	12:63	11:22
Age at onset, mean (SD), years	40.55 (15.0)	29.48 (9.82)
Follow-up duration, mean (SD), years	5.22 (4.32)	6.13 (4.86)
Cumulative number of attacks, mean (SD)	2.76 (1.97)	3.18 (2.74)
ARR ^a , mean (SD), /year	0.68 (0.51)	0.64 (0.45)
BMI _{naïve} , Mean (SD), kg/m ²	21.69 (2.92)	22.63 (3.42)
Onset attack type ^b		
Optic nerve, n (%)	23 (30.7)	9 (30.0)
Spinal cord, n (%)	46 (61.3)	8 (26.7)
Brain, n (%)	22 (29.3)	13 (43.3)
CSF study ^c		
White blood cells, mean (SD), /mm ³	20.52 (44.0)	4.15 (5.75)
CSF/serum albumin ratio, mean (SD)	5.74 (5.00)	4.48 (2.47)
CSF/serum IgG ratio, mean (SD)	4.1 (2.93)	6.56 (15.8)

^a 64 NMOSD and 31MS patients were compared; ^b75 NMOSD and 30 MS patients were compared; ^c 60 NMOSD and 27 MS patients were compared.

Abbreviations: NMOSD-AQP4, neuromyelitis optica spectrum disorder with aquaporin-4 immunoglobulin G; MS, multiple sclerosis; SD, standard deviation; ARR, annual relapse rate; BMI, body mass index; BMI_{naïve}, BMI measured within 1 month of the first symptom and before intravenous or oral steroid treatment; CSF, cerebrospinal fluid.

Supplementary Table 4. Multivariable linear regression analysis for the influence of BMI_{naïve} on clinical outcomes

	Women			Men		
	Parameter estimates	Standard errors	P-values	Parameter estimates	Standard errors	P-values
Intercept	20.001	1.895	<.0001	22.926	3.625	0.001
EDSS at first attack	-0.463	0.241	0.065	-0.069	0.371	0.858
Age of onset	0.055	0.029	0.074	0.026	0.066	0.706
Nausea/Vomiting at first attack	-0.190	0.923	0.838	_*		
Onset attack type						
Optic neuritis	2.347	1.050	0.034	-3.933	3.690	0.327
Brain lesion	-0.492	0.962	0.613	-0.194	3.237	0.954

* Nausea/vomiting at first attack was not included in a linear regression model for men because there were no patients who experienced nausea or vomiting at diagnosis.

Abbreviation: BMI, body mass index; EDSS, the Kurtzke Expanded Disability Status Scale.

Supplementary Table 5. Demographic data of patients with low BMI_{min-1yr} (< 18.5 kg/m²) and normal BMI_{min-1yr} (≥18.5 kg/m²) groups.

Variables	Low BMI _{min-1yr}	Normal BMI _{min-1yr}	P-value
Number of patients	18	85	
Sex, men: women	1:17	14:71	0.460
Age at onset, mean (SD), years	41.83 (13.64)	40.74 (14.4)	0.821
Follow-up duration, mean (SD), years	4.28 (3.06)	4.83(4.94)	0.876
Cumulative number of attacks, mean (SD)	2.5 (2.04)	2.8 (1.76)	0.277
ARR ^a , mean (SD), /year	0.63 (0.38)	0.78 (0.62)	0.513
BMI _{naïve} ^b , Mean (SD), kg/m ²	18.30 (1.85)	22.27 (2.62)	<0.001
BMI _{min-1yr} , Mean (SD), kg/m ²	17.33 (1.13)	22.03 (2.50)	<0.001
Onset attack type			
Optic nerve, n (%)	3 (16.7)	33 (38.8)	0.103
Spinal cord, n (%)	10 (55.6)	48 (56.8)	>0.999
Brain, n (%)	7 (38.9)	20 (23.5)	0.237
CSF study ^c			
White blood cells, mean (SD), /mm ³	24.00 (36.00)	20.3 (44.5)	0.933
CSF/serum albumin ratio, mean (SD)	5.01 (4.5)	5.8 (5.3)	0.553
CSF/serum IgG ratio, mean (SD)	3.3 (2.1)	4.4 (3.3)	0.535

Categorical variables were analyzed by Chi-square test or Fisher's exact test. Continuous variables were analyzed with the Mann-Whitney U test.

^a 15 patients with low BMI_{min-1yr} and 71 patients with normal BMI_{min-1yr} were compared; ^b 12 patients with low BMI_{min-1yr} and 57 patients with normal BMI_{min-1yr} were compared; ^c 12 patients with low BMI_{min-1yr} and 48 patients with normal BMI_{min-1yr} were compared.

Abbreviations: NMOSD-AQP4, neuromyelitis optica spectrum disorder with aquaporin-4 immunoglobulin G; MS, multiple sclerosis; SD, standard deviation; ARR, annual relapse rate; BMI, body mass index; BMI_{naïve}, BMI measured within 1 month of the first symptom of NMOSD-AQP4 and before intravenous or oral steroid treatment; BMI_{min-1yr} the lowest BMI measured within 1 year of the first symptoms of NMOSD-AQP4; CSF, cerebrospinal fluid.

Supplementary Figure Legend

Supplementary Figure 1. Flow chart of patients' enrollment.

(A) Enrollment of patients with neuromyelitis optic spectrum disorder with aquaporin4 immunoglobulin G from 6 tertiary hospitals. (B) Enrollment of patients with multiple sclerosis from 4 tertiary hospitals.

Abbreviations: NMOSD, neuromyelitis optica spectrum disorder; AQP4, aquaporin-4 immunoglobulin G; MS, multiple sclerosis; BMI_{naïve}, body mass index measured within 1 month of the first symptom of disease and before intravenous or oral steroid treatment

Supplementary Figure 2. The Kaplan–Meier Estimates of the prognosis of women with NMOSD-AQP4 stratified by the BMI parameters (<18.5 kg/m² vs. ≥18.5 kg/m²).

(A) There were no statistical differences in the prognosis between women with NMOSD-AQP4 IgG with BMI_{naïve} <18.5 kg/m² and those with BMI_{naïve} ≥18.5 kg/m². (B) BMI_{min-1yr} <18.5 kg/m² was associated with poor long-term survival of patients with NMOSD-AQP4 IgG. In contrast, BMI_{min-1yr} ≥18.5 kg/m² was not correlated with the poor long-term survival of women with NMOSD-AQP4 IgG (p =0.001 via log-rank test). Moreover, other disability parameters (EDSS6 and VF4) were not different between the two groups

Abbreviations: NMOSD-AQP4, neuromyelitis optica spectrum disorder with aquaporin-4 immunoglobulin G; BMI, body mass index; BMI_{naïve}, body mass index measured within 1 month of the first symptom of disease and before intravenous or oral steroid treatment; BMI_{min-1yr} the lowest BMI measured within 1 year of the first symptoms of NMOSD-AQP4; EDSS, the Kurtzke Expanded Disability Status Scale; VF, visual function.