Body mass index and severity of parkinsonism in multiple system atrophy

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Abstract

Patients with neurodegenerative disorders lose body weight as their diseases progress. In Parkinson's disease (PD), however, autonomic dysfunction is associated with increased body mass index (BMI). We investigated the correlation between BMI, clinical features, and autonomic dysfunction in patients with multiple system atrophy with predominant parkinsonism (MSA-P). BMI, clinical features, cardiac ^{123}I-metaiodobenzylguanidine scintigraphy (MIBG), Hoehn and Yahr (H-Y) stage, and the coefficient of variation of the R-R interval (CVRR) were analyzed in 50 patients with MSA-P. BMI showed no significant correlation with MIBG parameters or CVRR. On the other hand, the H-Y stage was significantly negatively correlated with BMI. Higher H-Y stage indicates a more severe neuromuscular state in MSA-P and is considered to be related to higher energy expenditure and decrease of BMI. Patients with MSA-P lose weight as the disease progresses. This is the first report indicating a significant correlation between disease severity and BMI decrease in MSA.

Introduction

Patients with neurodegenerative disorders such as amyotrophic lateral sclerosis and progressive supranuclear palsy lose body weight as their diseases progress.[1,2] The relationship between body mass index (BMI) and progression of Parkinson disease (PD) has been reported by several studies. One study indicated a higher BMI before the diagnosis of PD, but another showed the opposite result.[3,4] Since body weight is determined by many factors, including genetic, epigenetic, metabolic, and environmental parameters, disease severity and BMI do not always correlate with each other in patients with slowly progressive neurodegenerative disorders such as PD.[4] In our previous study,[5] we performed cardiac ^{123}I-metaiodobenzylguanidine scintigraphy (MIBG) and assessed the coefficient of variation of the R-R interval (CVRR), and showed that increased BMI was correlated with autonomic dysfunction in PD. Neurodegenerative disorders such as PD and multiple system atrophy (MSA) are associated with α synuclein-related neurodegeneration.[6] Although many studies have investigated the relationship between BMI and clinical features in PD,[4] only a few have focused on this issue in MSA.[7] Here we investigated the correlation between BMI, clinical features, and autonomic dysfunction in patients with MSA with predominant parkinsonism (MSA-P).

Materials and Methods

This was an observational, cross-sectional study.

Subjects

From April 2010 to December 2016, 54 consecutive patients with probable MSA-P were admitted to our hospital for clinical evaluation. Their diagnosis was based on clinical features, MRI findings, and poorly levodopa-responsive parkinsonism.[8,9] Disease stage was defined based on the Hoehn and Yahr (H-Y) scale. No subjects had evidence of left ventricular hypertrophy or heart failure, as determined by at least one of the following: clinical symptoms and electrocardiogram (ECG), chest X ray, and echocardiogram results. None of the patients received droxidopa, anticholinergics, antidepressants, or other sympathomimetic drugs that could potentially interfere with the uptake of ^{123}I-MIBG in organs and target tissues. Written informed consent was obtained from all participants. The study protocol was approved by the local Ethics Committee and was carried out in accordance with the Declaration of Helsinki.

Coefficient of variation of the R-R interval measurement

A standard 12-lead ECG was recorded with an ECG machine (FCP-7541; Fukuda Denshi, Tokyo, Japan) in all subjects between 2 pm and 3 pm after they rested in a supine position for 10 min or longer, and R-R intervals were measured for 3 min. From the recorded R-R intervals, the CVRR was obtained by dividing the standard deviation (SD) by the mean (M). Thus, CVRR (%) = (SD/M) × 100.

^{123}I-metaiodobenzylguanidine myocardial imaging

MIBG scintigraphy was performed as described previously.[5] In brief, following a 20-min rest period, patients received an intravenous injection of 111 MBq ^{123}I-MIBG (Fuji Film RI Pharma, Tokyo, Japan). Planar images of the chest were obtained at two time points after the injection, one at 15 min (early) and the other at 4 h (delayed). Average counts per pixel in the heart and mediastinum were used to calculate the heart-to-mediastinum (H/M) ratio. Cardiac MIBG washout rate (WR) was defined as the percent change in activity from the early image to the delayed image within the left ventricle.

Statistical analysis

Spearman's rank correlation coefficient was used to analyze the relation between clinical features, CVRR, and MIBG scintig-

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Key words: Multiple system atrophy; Body mass index; Cardiac 123I-metaiodobenzylguanidine scintigraphy; Coefficient of variation of the R-R interval.

Conflict of interest: the authors declare no potential conflict of interest.

Ethical approval: all procedures performed in studies involving human participants were in accordance with the ethical standards of the institution and with the 1964 Helsinki declaration and its later amendments.

Informed consent: informed consent was obtained from all individual participants included in the study.

Contributions: AS and YE: interpretation of the data, collection of the material, drafting of the manuscript; HM: design and coordination of the study, drafting of the manuscript; KS and MN: design of the study, analysis and interpretation of the data, drafting of the manuscript.

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raphy parameters. The statistical significance level was set at P=0.05. SPSS version 22 software was used for statistical analyses.

Results

Out of 54 patients with MSA-P, two were excluded from the study due to concomitant diabetes mellitus, and another two were excluded because of atrial fibrillation. The final study population consisted of 50 patients (female 24, male 26). The means and SDs of their BMI, age (year), disease duration (month), and H-Y stage were 21.8±3.3, 68.1±8.0, 23.9±17.2, and 2.6±1.0 (mean±SD), respectively. Based on previously published data,[10,11] the normal BMI of individuals between 60 and 69 years old was about 23–24 in Japan. The mean BMI of our MSA-P patients was slightly lower than that of the general Japanese population. The distribution of our patients' BMI was as follows: higher than 25 in 8 patients, from 20–25 in 24 patients, and lower than 20 in 18 patients. One patient had dysphagia and received tube feeding for 2 months after admission, but the other 49 patients had no signs of dysphagia and no history of aspiration pneumonia.

The means and SDs of the patients' CVRR, early and delayed H/M ratios, and WR (%) of MIBG scintigraphy were 1.95±1.05, 2.68±0.46, 2.68±0.59, and 24.1±10.1, respectively. The average CVRR value was lower than normal (defined as 2.0–2.2 based on a past report[10]), but its degree of reduction was small. In our institution, the normal values for each MIBG index (based on 20 normal subjects, aged 58.8±5.2) are as follows: early H/M ≥ 1.9, delayed H/M ≥ 1.7, and WR ≤ 40%.[12] The MIBG parameters of most MSA-P patients (N = 45) were within normal limits.

Table 1 shows the correlation coefficients between BMI and clinical features in MSA patients. BMI had no significant correlations with MIBG parameters or CVRR. On the other hand, H-Y stage was significantly negatively correlated with BMI. The relationship between H-Y and BMI is shown in the box-and-whisker plot of Figure 1. MSA-P patients with severe symptoms of H-Y stage 4 and 5 tended to have low BMI (mean = 19.6).

Discussion

Our study detected no correlation between BMI on the one hand and early and delayed H/M ratios and CVRR on the other in MSA-P patients. H-Y stage, however, was significantly negatively correlated with BMI. MIBG scintigraphy reflects sympathetic nerve activity, and the CVRR reflects parasympathetic nerve activity. We observed no significant correlation between BMI and either of these parameters of autonomic function. These results differ from those in PD patients in our previous report.[5] This discrepancy may be caused by the almost complete lack of abnormalities in the autonomic parameters (MIBG and CVRR) used in this study.

Daily caloric intake is presumed to influence BMI. In a previous study, however, daily caloric intake was lower in MSA patients with impaired activities of daily living (ADL), but no significant correlation was observed between BMI and ADL

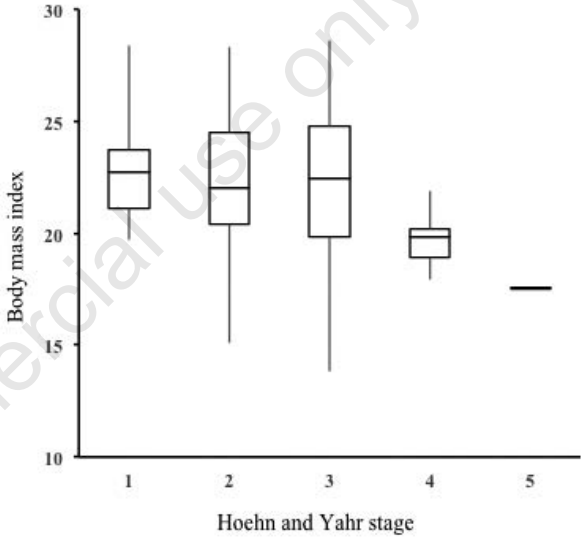

Figure 1. The box-and-whisker plot depicts body mass index (BMI) values in multiple system atrophy with predominant parkinsonism patients. The whiskers show the highest and lowest values, and the three horizontal lines of each box indicate the 25th, 50th, and 75th BMI percentiles. Thus each box represents 50% of the BMI data for each Hoehn and Yahr stage. The numbers of patients in Hoehn and Yahr stages 1 through 5 are 7, 15, 18, 9, and 1, respectively.

Table 1. Correlation coefficients (rho) between clinical features and ^{123}I-metaiodobenzylguanidine scintigraphy.

	BMI	Age	Duration	H-Y	CVRR	Early H/M	Delayed H/M	Washout ratio
BMI	1	-0.520	-0.158	-0.331*	0.042	-0.140	-0.100	-0.190
Age (years)	-0.520	1	-0.041	0.026	0.117	-0.179	-0.265	0.138
Duration (months)	-0.158	-0.041	1	0.639**	-0.252	-0.253	-0.203	0.193
H-Y	-0.331*	0.026	0.639**	1	-0.177	0.016	0.013	0.129
CVRR	0.042	0.117	-0.252	-0.177	1	0.285	0.194	-0.485
MIBG scintigraphy								
Early H/M	-0.140	-0.179	-0.253	0.016	0.285	1	0.780	-0.149
Delayed H/M	-0.100	-0.265	-0.203	0.013	0.194	0.780	1	-0.587
Washout ratio	-0.190	0.138	0.193	0.129	-0.485	-0.149	-0.587	1

BMI, body mass index; H-Y, Hoehn and Yahr stage; CVRR, coefficient of variation of the electrocardiographic R-R interval; H/M, heart-to-mediastinum uptake ratio; MIBG, metaiodobenzylguanidine. The results of Spearman's rank correlation coefficient. Each coefficient (rho) is indicated. *P<0.05; **P<0.01.

level.[7] Another study showed that resting energy expenditure was higher in patients with PD due to their abnormal neuromuscular state, rigidity, or resting tremor.[13] Our results demonstrated a negative correlation between H-Y stage and BMI. Higher H-Y stage indicates a more compromised neuromuscular state in MSA-P and is likely to be related to higher energy expenditure and lower BMI.

In our previous study of patients with PD,[5] no significant correlation was detected between H-Y stage and BMI, which is inconsistent with the findings in MSA-P in the current study. The reason for this discrepancy is unclear, but we speculate that it may be due in part to the different rates of disease progression between PD and MSA-P. The faster progression of parkinsonism in MSA-P might contribute to the greater decrease of BMI in this condition.

Conclusions

This study showed no significant correlation between BMI and autonomic dysfunction in MSA-P. Patients with MSA-P lose body weight as their disease progresses. To our knowledge, this is the first report indicating a significant correlation between disease severity and decreased BMI in MSA.

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