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Original Article

Association of clinical symptoms and metabolic syndrome-related factors in patients undergoing high tibial osteotomy

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Abstract. [Purpose] This study aimed to investigate the relationship between clinical outcomes after high tibial osteotomy and metabolic syndrome-related factors, such as hypertension, dyslipidemia, diabetes mellitus, and obesity. [Participants and Methods] A total of 73 patients (73 knees) who underwent high tibial osteotomy for knee osteoarthritis between 2018 and 2020 were included. We investigated the correlation between metabolic syndrome-related factors and clinical symptom assessment (Japanese Orthopedic Association Score) and examined knee function and lower alignment. [Results] At three months postoperatively, the Japanese Orthopedic Association score showed no main and synergistic effects on metabolic syndrome-related factors, and the preoperative Japanese Orthopedic Association score only showed a main effect on metabolic syndrome-related factors. At 12 months postoperatively, the Japanese Orthopedic Association score showed main and synergistic effects on diabetes mellitus, obesity, hypertension and dislipidemia. [Conclusion] Metabolic syndrome-related factors are associated with poorer clinical outcomes after high tibial osteotomy.

Key words: Medial opening high tibial osteotomy, Clinical result, Metabolic syndrome-related factors

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INTRODUCTION

Patients with knee osteoarthritis (KOA) have limitations in activities of daily living due to severe knee pain, joint contracture, and knee muscle weakness[1)]. KOA symptoms are associated with mechanical factors such as varus knee alignment[2)] and lateral thrust during gait[3)]. Recently, KOA symptoms have been reported to be associated with metabolic syndrome- (MS-) related factors such as hypertension (HT), dyslipidemia (DL), diabetes mellitus (DM), and obesity (OB)[4)]. Previous studies also examined the impact of MS-related factors on patients with KOA[4–11)]. Subchondral bone loss is common among patients with KOA with HT and DM[6, 11)]. In patients with DL, histological abnormalities of cartilage are associated with pain because they cause abnormal cartilage metabolism[8)]. In patients with OB, increased body weight is associated with worsening symptoms as it increases load on the knee joint during gait[9, 10)]. Finally, patients with DM have been reported to have decreased joint range of motion due to reduced soft tissue flexibility and skeletal muscle atrophy[11)]. Additionally, patients with MS have weight gain and lower limb muscle weakness due to lifestyle disruption and cartilage loss.

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Conservative therapies such as weight loss and exercise therapy reduce KOA symptoms[12]. In cases that do not respond to conservative treatment, high tibial osteotomy (HTO) as a surgical treatment can reduce symptoms[13]. Young patients who hope to return to sports and recreational activities have been selected for HTO instead of arthroplasty, and good surgical outcomes have been reported[14]. Clinical outcomes after HTO have been reported to be related to adequate postoperative knee valgus alignment[15], preoperative KOA grade[16], and knee extensor muscle strength[17]. Poor clinical outcomes are attributed to increased loading pain in activities of daily living associated with increased knee varus alignment and decreased knee muscle strength.

Previous studies reported a correlation between postoperative knee symptoms and knee alignment and muscle strength, but the relation to MS-related factors has not been reported. Metabolic syndrome-related factors have attracted attention as exacerbating factors in KOA, but the impact of preoperative metabolic syndrome-related factors on the postoperative course of HTO has not been reported. We hypothesize that MS-related factors are associated with more clinically symptomatic cases after HTO. Thus, this study aimed to clarify the relationship between clinical symptoms and MS-related factors after HTO.

PARTICIPANTS AND METHODS

This was a longitudinal observational study with measurements obtained preoperatively, 3 months postoperatively, and 12 months postoperatively. A total of 140 patients (150 knees) who underwent HTO for KOA between 2018 and 2020 were enrolled. Exclusion criteria included previous cerebrovascular diseases (5 patients, 5 knees), bilateral HTO (5 patients, 10 knees), missing data (38 patients, 38 knees), concomitant surgery for the contralateral meniscus (20 patients, 20 knees), and distal femoral osteotomy (5 patients, 5 knees). After the exclusion criteria were applied, 72 patients (72 knees) were included in this study. The surgical technique was medial opening HTO (MOWHTO)[18]. Radiographic data from the electronic medical record, including the KL grade and %mechanical axis (%MA)[19] by X-ray, were reviewed by an orthopedic surgeon. Physical examination was performed, and knee flexion and extension range of motion were measured using a goniometer. Knee extension muscle strength was determined as the maximum value of isometric knee muscle strength[20]. Knee extension muscle strength was measured twice with an isometric contraction for 3 seconds using a manual muscle tester (Mobie, Sakai Medical Corporation, Japan, Tokyo), and the value obtained by dividing the higher value by the body weight was the muscle strength value. Knee pain during gait was assessed using a visual analog scale. Finally, the 10 m gait time was measured using a stopwatch. The Japanese Orthopaedic Association Score (JOA score), an observational knee scoring system, was used to evaluate symptoms, knee pain, physical impairment, and disability[21]. This evaluation method was considered to have good clinical performance if the score was high.

MS-related factors (OB, HT, DL, and DM) were assessed using the diagnostic criteria of the Metabolic Syndrome Diagnostic Criteria Study Committee, where body mass index (BMI) [weight (kg)/height (m^2)] ≥25 was defined as OB, systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg as HT, HDL <40 mg/dLas DL, blood glucose ≥200 mg/dL at any time as DM, or those prescribed medication for HT, DL and DM were considered to have each of these factors[22, 23]. All study protocols were approved by the Ethics Review Board of Yawata Medical Center (approval number; 2020-2). In addition, informed consent was obtained from all participants.

For statistical analysis, first, the overall prevalence of MS factors was calculated. The prevalence of each MS factor in males and females was then calculated using the χ^2 test. Second, Pearson's correlation analysis was performed to correlate the JOA scores at 3 and 12 months postoperatively with %MA, BMI, and knee joint function factors at each time point. Finally, we defined those with a preoperative JOA score in the lower quartile of the JOA score of <70 as the poor group and those with a score of ≥75 as the good group. A repeated two-way analysis of variance of JOA scores in the good and poor groups with and without MS-related factors and time was performed. When main effects or interactions were found, comparisons between groups within factors were performed with within-response t-tests (corrected for Bonferroni). Similar statistical treatments were also performed for knee joint range of motion, knee extensor muscle strength, knee pain during gait, and 10 m gait time, %MA and BMI. All statistical analyses were performed with EZR version 1.52 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), with a significance level of less than 5%.

RESULTS

The prevalence of preoperative MS-related factors in the study participants was DM (22%), HT (44%), DL (36%), and OB (40%). The male/female ratios (male/female) for each MS factor were DM (37.5/62.5%), HT (34.4/65.6%), DL (26.9/73.1%), and OB (31.0/69.0%) and did not differ significantly. Table 1 shows the demographic data. The correlation analysis showed no significant correlation between the JOA score and %MA at 3 and 12 months postoperatively. However, a significant correlation was observed between the JOA score and knee joint functional factors and gait ability (Table 2). The two-way analysis of variance showed an interaction with the main effect of the obese group in the poor preoperative group, the main and interaction effects of OB and DM in the poor preoperative group, and the main effects of HT and DL in the good preoperative group (Table 3). Furthermore, significant differences in knee extensor muscle strength, knee joint range of motion, knee pain during gait, and 10 m gait speed at 12 months postoperatively were observed between the good

Table 1. Participant characteristics

		Overall (n=73)	No MS factor (n=16)	DM (n=16)	OB (n=29)	DL (n=26)	HT (n=32)
Mean value (standard deviation)							
Age (years)		66.9 ± 14.8	63.4 ± 8.2	67.6 ± 9.1	66.1 ± 21.1	69.4 ± 9.8	69.2 ± 8.5
Height (cm)		157.6 ± 14.1	158.9 ± 7.9	158.6 ± 7.6	156.8 ± 20.6	156.4 ± 8.7	159.0 ± 9.4
Weight (kg)		63.1 ± 11.7	57.2 ± 9.2	61.7 ± 8.3	72.7 ± 8.6	62.9 ± 9.4	63.3 ± 10.2
Body mass index (kg/m²)		26.9 ± 17.4	22.5 ± 2.3	24.6 ± 3.0	33.4 ± 2.6	25.7 ± 2.9	25.0 ± 3.1
Kellgren–Lawrence grade	II	42 (57.5)	10 (62.5)	7 (56.2)	15 (51.7)	15 (57.7)	19 (59.4)
	III	31 (42.5)	6 (37.5)	7 (43.8)	14 (48.3)	11 (42.3)	13 (40.6)
Gender (males/females female %)		14/59 (80.0)	4/12 (75.0)	6/10 (62.0)	9/20 (69.0)	7/19 (73.0)	11/21 (65.0)
Knee functional factors							
Knee extension range of motion (°)	0 M	−3.8 ± 16.5	−4.1 ± 4.2	−6.3 ± 3.9	−1.6 ± 2.5	−6.9 ± 4.9	−2.7 ± 2.4
	3 M	−3.1 ± 3.5	−1.6 ± 2.4	−3.1 ± 3.1	−3.8 ± 3.2	−3.7 ± 3.3	−4.7 ± 3.8
	12 M	−2.5 ± 3.6	−1.3 ± 2.2	−2.2 ± 3.2	−3.1 ± 4.1	−3.7 ± 4.1	−3.8 ± 4.4
Knee flexion range of motion (°)	0 M	130.6 ± 13.0	126.9 ± 16.7	137.5 ± 7.8	129.5 ± 7.7	131.7 ± 11.1	130.8 ± 13.3
	3 M	135.8 ± 8.1	138.4 ± 4.4	138.1 ± 9.5	131.0 ± 9.0	134.0 ± 7.9	136.2 ± 9.1
	12 M	138.2 ± 7.8	140.6 ± 4.8	140.9 ± 8.6	133.8 ± 8.3	136.2 ± 7.5	137.2 ± 8.6
Knee extension strength (N/kg×100)	0 M	2.85 ± 1.34	2.87 ± 1.40	2.78 ± 1.0	2.60 ± 1.40	2.80 ± 1.30	2.89 ± 1.60
	3 M	3.22 ± 1.30	3.91 ± 1.50	2.86 ± 0.80	2.70 ± 0.90	2.83 ± 0.90	2.96 ± 1.30
	12 M	4.01 ± 1.42	4.66 ± 1.40	3.75 ± 1.10	3.50 ± 1.10	3.95 ± 1.50	3.96 ± 1.65
Pain of knee joint during gait (mm)	0 M	31.9 ± 19.1	30.6 ± 20.8	20.0 ± 12.7	34.8 ± 21.0	37.7 ± 21.8	32.2 ± 17.4
	3 M	10.8 ± 14.3	3.8 ± 8.1	11.3 ± 11.5	13.1 ± 14.5	16.9 ± 17.1	15.9 ± 16.0
	12 M	4.04 ± 7.9	1.3 ± 3.4	5.3 ± 9.2	7.4 ± 10.1	7.12 ± 9.4	5.8 ± 9.3
Gait time of 10m walkway (sec)	0 M	8.3 ± 3.7	8.6 ± 3.9	8.8 ± 4.8	8.4 ± 4.4	9.1 ± 4.5	9.2 ± 4.5
	3 M	7.0 ± 1.4	6.4 ± 1.0	7.3 ± 1.4	7.5 ± 1.4	7.5 ± 1.4	7.3 ± 1.4
	12 M	6.0 ± 1.3	4.7 ± 1.4	6.3 ± 1.7	6.4 ± 1.5	6.4 ± 1.6	6.4 ± 1.5
JOA score (points)	0 M	72.1 ± 12.6	69.4 ± 15.3	74.4 ± 9.5	72.4 ± 12.4	68.5 ± 10.2	70.3 ± 12.4
	3 M	82.0 ± 11.7	87.5 ± 8.9	81.2 ± 13.6	78.1 ± 11.9	77.3 ± 11.0	79.4 ± 11.1
	12 M	88.4 ± 10.0	92.8 ± 8.4	85.3 ± 12.8	83.6 ± 11.1	83.5 ± 11.2	85.9 ± 10.0
Lower alingment							
%MA (%)	0M	30.4 ± 11.4	32.0 ± 11.0	31.6 ± 10.0	32.0 ± 11.9	30.5 ± 10.1	33.3 ± 11.5
	3M	62.0 ± 10.1	60.6 ± 11.3	63.0 ± 11.7	62.7 ± 10.2	63.3 ± 10.2	64.5 ± 10.1
	12M	60.6 ± 10.3	60.0 ± 11.5	60.1 ± 12.6	61.7 ± 10.8	62.0 ± 10.6	62.9 ± 9.6
Prevarence of MS factors (n (%))							
Overall		73 (100)	16 (21.9)	16 (21.9)	29 (35.6)	26 (35.6)	32 (43.8)
DM		16 (22.0)	0 (0)	16 (100)	5 (17.2)	6 (23.1)	9 (28.1)
OB		29 (40.0)	0 (0)	5 (31.2)	29 (100)	12 (46.1)	13 (40.6)
DL		26 (36.0)	0 (0)	6 (37.5)	12 (41.4)	26 (100)	21 (65.6)
HT		32 (44.0)	0 (0)	9 (56.2)	13 (44.8)	21 (80.1)	32 (100)

MS: metabolic syndrome; HT: hypertension; DL: dyslipidemia; DM: diabetes mellitus; OB: obesity; %MA: %mechanical axis; JOA: Japanese Orthopaedic Association Knee Joint Score.

preoperative group with DL and HT and the poor preoperative group with DM and OB by unpaired t-tests (corrected for Bonferroni) (Table 4). Additionally, significant differences in the functional factors with HT in terms of decreased knee joint extension range of motion and prolonged 10 m gait time at 12 months; increased knee pain during gait in patients with DL at 12 months; knee joint extension range of motion, prolonged 10 m gait time, decreased knee extension muscle strength, and increased gait pain among functional factors according to the OB at 3 and 12 months; and prolonged 10 m gait time and increased knee pain during gait with DM were observed at 12 months (Table 4).

Table 2. Correlation between at various postoperative JOA score and knee joint functional factors, gait ability, lower alignment, and preoperative JOA score

	Knee extension ROM	Knee flexion ROM	Knee extension strength	Pain	Gait time	%MA	BMI	pre JOA
JOA 3M	0.21	0.33**	0.38**	−0.32**	−0.52**	0.17	−0.33**	0.33**
JOA 12M	0.28*	0.49**	0.40**	−0.71**	−0.46**	0.10	−0.37**	0.32**

*p<0.05, **p<0.01.
Pain: pain of knee joint during in gait; Gait time: gait time of 10 m walkway; ROM: range of motion; %MA: %mechanical axis; BMI: body mass index; JOA: Japanese Orthopaedic Association Knee Joint Score.

Table 3. Longitudinal changes in JOA score in patients with each MS-related factor

	Pre	Post 3 M	Post 12 M	Main effect		Intaraction
				Time	MS factor	
good-HT (n=21)	77.6 ± 6.2	82.8 ± 11.4	87.6 ± 8.5*	† ‡	§	n.s
good-nonHT (n=29)	79.8 ± 7.4	85.7 ± 9.9	92.8 ± 6.1*	† ‡		
bad-HT (n=11)	56.3 ± 6.7	72.7 ± 7.2	82.7 ± 12.3	† ‡	n.s	n.s
bad-nonHT (n=11)	55.9 ± 5.9	79.6 ± 15.4	83.2 ± 13.8	† ‡		
good-DL (n=15)	76.0 ± 4.3	81.3 ± 11.4	86.0 ± 8.5*	† ‡	§§	n.s
good-nonDL (n=35)	80.1 ± 8.0	85.8 ± 10.4	92.6 ± 6.3*	† ‡		
bad-DL (n=11)	58.2 ± 6.0	71.8 ± 8.2	80.0 ± 13.8	† ‡	n.s	n.s
bad-nonDL (n=11)	54.1 ± 5.8	80.5 ± 14.4	85.9 ± 11.6	† ‡		
good-DM (n=14)	76.8 ± 6.7	83.2 ± 13.1	88.9 ± 8.8	† ‡	n.s	n.s
good-nonDM (n=36)	79.7 ± 7.5	85.0 ± 9.6	91.4 ± 7.0	† ‡		
bad-DM (n=2)	57.5 ± 10.6	67.5 ± 10.6	60.0 ± 0*	†	§	‖
bad-nonDM (n=20)	56.0 ± 6.0	77.0 ± 12.3	85.3 ± 10.9*	†		
good-OB (n=20)	79.3 ± 7.5	82.3 ± 9.9	88.0 ± 6.2*	† ‡	n.s	n.s
good-nonOB (n=30)	78.7 ± 7.3	86.0 ± 10.8	92.4 ± 7.4*	† ‡		
bad-OB (n=9)	57.2 ± 5.6	68.9 ± 11.1*	73.9 ± 13.6**	†	§ §	‖ ‖
bad-nonOB (n=13)	55.4 ± 6.6	81.2 ± 10.6*	89.2 ± 7.6**	†		

JOA: Japanese Orthopaedic Association Knee Joint Score; MS: metabolic syndrome; HT: Hypertension; DL: dislipidemia; DM: diabetes mellitus; OB: Obesity.
good: preopelative JOA score is 75 or over; bad: preopelative JOA score under 70.
*: good MS vs. good nonMS or bad MS vs. bad nonMS.
†: pre vs. post 3 M ‡: post3 M vs. post 12 M.
§: Main effects of MS factors in two-way analysis of variance.
‖: Interaction between MS factor and time in two-way analysis of variance.
One symbol indicates p<0.05, two symbols indicate p<0.01.

Table 4. Comparison of knee joint function and walking ability at various postoperative time points with and without MS factors

	Time	Knee extension ROM	Knee flexion ROM	Knee extension strength	Pain	Gait time	%MA	BMI
good-HT (n=21)	12M	−3.8 ± 4.2*	137.9 ± 9.8	4.14 ± 1.55	5.0 ± 7.8	6.3 ± 1.3*	63.8 ± 10.2	24.5 ± 2.4
good-nonHT (n=29)		−1.6 ± 2.4*	139.7 ± 5.7	4.21 ± 1.10	2.4 ± 6.4	5.5 ± 0.8*	59.9 ± 9.3	25.1 ± 3.4
good-DL (n=15)	12M	−3.3 ± 3.6	136.7 ± 8.4	4.16 ± 1.13	6.3 ± 7.7*	6.2 ± 1.3	66.0 ± 6.8*	25.0 ± 2.2
good-nonDL (n=35)		−2.1 ± 3.3	139.9 ± 7.2	4.18 ± 1.38	2.3 ± 6.5*	5.7 ± 1.0	59.7 ± 10.4*	24.7 ± 3.4
bad-OB (n=9)	12M	−4.4 ± 5.3	130.6 ± 8.8**	2.73 ± 0.56*	12.2 ± 12.0**	7.1 ± 1.8	56.2 ± 14.9	29.6 ± 2.8**
bad-nonOB (n=13)		−1.5 ± 2.4	139.6 ± 3.2**	4.16 ± 1.86*	0.8 ± 2.8**	6.0 ± 1.1	59.9 ± 8.1	22.6 ± 1.9**
bad-OB (n=9)	3M	−5.0 ± 4.3*	128.3 ± 9.7**	2.02 ± 0.56*	16.7 ± 17.3	8.6 ± 2.0**	58.0 ± 13.6	27.7 ± 2.2**
bad-nonOB (n=13)		−1.2 ± 3.0*	139.2 ± 4.5**	2.98 ± 1.19*	5.4 ± 9.7	6.6 ± 1.0**	61.2 ± 8.5	22.9 ± 1.8**
bad-DM (n=2)	12M	−2.5 ± 3.5	130.0 ± 7.1	2.76 ± 0.54	20.0 ± 14.1**	9.2 ± 3.8**	46.1 ± 31.1	29.4 ± 3.4
bad-nonDM (n=20)		−2.8 ± 4.1	136.5 ± 7.5	3.65 ± 1.67	4.0 ± 8.2**	6.2 ± 1.0**	59.6 ± 8.4	25.0 ± 4.2

*p<0.05, **p<0.01.
MS: metabolic syndrome; ROM: range of motion; HT: hypertension; DL: dislipidemia; DM: diabetes mellitus; OB: Obesity; %MA: %mechanical axis, BMI: body mass index.
good: preopelative JOA score is 75 or over, bad: preopelative JOA score under 70.
Pain: pain of knee joint during gait, Gait time: gait time of 10 m walkway.
*: good MS vs. good nonMS or bad MS vs. bad nonMS.

DISCUSSION

First, this study showed that JOA scores at 12 months postoperatively were poorer in patients with MS-related factors. Second, the postoperative JOA score correlated with the preoperative JOA score. Third, poor JOA scores were related to knee joint dysfunction and decreased gait ability due to MS-related factors.

JOA scores at 3 months and 12 months postoperatively were related to knee joint functional factors, gait ability, and preoperative JOA score. Few reports have shown a correlation between clinical symptoms and knee joint function after HTO. A previous report on the relationship between knee joint function and clinical symptoms showed that reduced quadriceps muscle strength leads to impaired balance during movement, thereby increasing knee pain[17]. Akizuki et al. reported that the limitation of knee joint extension range of motion, resulting in joint instability, leads to knee pain and activity of daily living (ADL) dysfunction[24]. Increased pain during gait has been reported to result in reduced muscle contraction and balancing disability, thereby limiting activities of daily living[1]. These knee joint function factors have been shown to be associated with the postoperative JOA score.

The JOA score at 12 months postoperatively was lower in patients with MS-related factors, and the JOA score at 12 months postoperatively was associated with knee joint functional factors and gait ability. In general previous studies, clinical symptoms after HTO are related to OB and postoperative varus knee alignment[13, 15, 24]. Patients with HT, DL, and DM have been reported to have OB. Thus, we considered it necessary to consider the impact of OB in this study. This study showed no difference in BMI in the HT, DL, and DM groups, suggesting that OB had little effect. Regarding the lower alignment, only the DL group showed significantly more varus alignment than the non-DL group. However, it is unlikely that lower alignment had a negative effect on the DL group, as the DL group had an alignment with better clinical outcomes[15]. No differences in the prevalence of HT, DL, and DM were observed in the OB group. From these, we infer that MS-related factors such as OB, HT, DL, and DM significantly reduced the postoperative JOA score, even when taking the effects of lower alignment and OB into consideration.

In patients with DM, a significant difference was observed in the prolonged 10 m gait time and increased pain during gait. We consider that subchondral bone loss is common among patients with KOA due to the fact that DM results in increased pain during gait, leading to ADL disorder. Patients with DL reported an increase in inflammatory cytokines and disordered lifestyles[13]. In this study, patients with DL reported increased knee pain during gait and more valgus alignment. Lower alignment in the DL group was an optimal alignment of %MA of 60–65[7], so it is unlikely that the alignment affected the JOA. Additionally, no significant difference in BMI was observed between the DL group and the non-DL group. We speculate that the increase in inflammatory cytokines was associated with knee pain. Patients with HT tend to lack exercise habits[25]. The lack of postoperative stretching may have resulted in a limited range of motion. Patients with OB have decreased knee extensor muscle strength, limited joint range of motion due to lack of exercise habits, and increased pain due to inflammatory cytokines produced by mast cells[5, 8, 9]. Significant differences in knee joint extension range of motion, prolonged 10 m walking time, decreased knee extension muscle strength, and increased pain during gait were observed in patients with OB. We speculate that the exacerbation of these knee joint functional factors may have contributed to the increase in clinical symptoms, considering that the increase in body weight adds to the muscle weakness of the quadriceps muscles, resulting in increased joint load during movement, which increases pain and presents with disability in ADL.

This study has some limitations. Although we analyzed the prevalence of preoperative MS-related factors and their post-operative effects, the improvement rate of each MS-related factor and its effect on clinical symptoms is unknown. Additionally, the continuation of postoperative medical treatment for MS-related factors and the effect of such treatment are unknown and require further longitudinal studies. Due to the sample size, it was not possible to disaggregate the analysis of this study by gender. In the future, sample size should be increased and the analysis should be carried out separately by gender. In this study, the effect of the presence and absence of an MS factor on postoperative JOA score and knee joint function was investigated. Previous studies have also reported that an increase in the cumulative index of MS factors is associated with a decrease in the JOA score of KOA. We too would like to analyze the influence of the cumulative index of MS factors after HTO surgery in the future.

The study results showed that many patients with OB might present with knee dysfunction and impaired walking ability and require medical assessment, patient education on MS-related factors, and dietary assessment, in addition to exercise therapy during hospitalization.

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We have no conflict of interest and funding.

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