Subjective Postural Vertical as a Prognosticator of Lateral Trunk Flexion in Patients With Parkinson's Disease.

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Research Article

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Abstract

We conducted a retrospective study to test our hypothesis that the subjective postural vertical (SPV) ratio, i.e., SPV in relation to the lateral flexion axis, is predictive of lateral trunk flexion (LTF) in patients with Parkinson's disease (PD). The study group comprised 25 patients with PD. The SPV angle, i.e., the subjective perception of a vertical position with reference to the vertical axis, and the SPV ratio, i.e., the SPV angle with reference to the axis of lateral flexion, were calculated. The SPV ratio ($r = 0.698$ $p = 0.001$) and LTF angle ($r = -0.601$ $p = 0.001$) were found to correlate with change in the LTF angle calculated at 1 year. The SPV ratio was significantly smaller in the LTF angle-improved group ($n = 12$) than in the non-improved group ($n = 13$) (0.99 ± 0.78 vs 1.66 ± 0.71 , $p = 0.011$). The AUC under the ROC curve of the SPV ratio for discrimination of LTF improvement was 0.795 (95% confidence interval: 0.61–0.98). Our study showed that the SPV ratio is associated with change in the LTF and that the SPV ratio can conceivably be used to predict the likelihood of improvement in patients' LTF.

Introduction

Lateral trunk flexion (LTF), a postural abnormality characterized by lateral deviation of the spine and the corresponding tendency of patients to lean to one side, is common in patients with Parkinson's disease (PD) and is sometimes referred to as the "scoliosis of parkinsonism (1, 2). When first recognized in patients with PD, the LTF is typically mild or moderate (3). LTF affects patients' balance (4), contributes to low back pain (5) and also affects health-related quality of life (QOL) (6, 7), increasing patients' need for treatment. Despite this need, patients have been shown to respond poorly to drug therapy, surgical treatment and spinal orthotics (1), so there is very little evidence that any form of treatment will be effective.

At the onset of LTF, patients tend not to be aware of the postural deviation (1, 8). They are more likely than healthy persons to incorrectly perceive themselves to be standing or sitting upright when they are in fact leaning to one side (9). In addition, as the severity of LTF increases, patients' underestimation of the degree of deviation increases (10). In a previous study of LTF in patients with PD (11), we examined the subjective postural vertical (SPV) angle, defined as the subjective perception of a vertical position with reference to the vertical axis. We also examined the SPV ratio, defined as the SPV angle with reference to the axis of lateral flexion, and we showed that the SPV ratio affects LTF. Although use of the SPV as a predictor of increased severity of postural abnormalities in patients with PD-related forward trunk flexion (FTF) has been verified (12), effects of the SPV on the long-term clinical course of LTF have not been clarified. Long-term follow-up is needed to clarify such effects. We therefore conducted a retrospective study in which we compared the SPV ratio between patients in whom PD-related LTF improved over 1 year and patients in whom PD-related LTF did not improve over 1 year to assess the relation between the SPV and change in LTF and to validate our hypothesis that the SPV can be used to predict the course of LTF in patients with PD.

Methods

Patient selection. Patients included in the study were selected from among patients with PD who visited the outpatient rehabilitation department of Noborito Neurology Clinic regularly for at least 1 year, starting sometime between March 2018 and March 2019. The LTF angle had been measured on initial examination and at 1 year following the initial examination in all patients included in the study. Patients chosen for inclusion also met the following criteria: a definitive diagnosis of PD, based on the Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's disease (21); judgment that the patient will be able to complete a 1-year evaluation; age ≥ 20 years; no change in oral medications within 1 week of the initial or 1-year evaluation; "on" status at the time of initial or 1-year evaluation if the patient was suffering from the "wearing-off" phenomenon; ability to understanding instructions; and ability to stand upright. Exclusion criteria were as follows: diagnosis of a PD-related disorder other than PD itself; presences of any psychiatric symptoms, such as visual or other hallucinations at the time of initial or 1-year evaluation; signs of the wearing-off phenomenon during the drug administration period; restricted range of motion that rendered passive guidance of the patient into a vertical position impossible; dramatic worsening of the PD symptoms within 1 week prior to evaluation; and rapid onset of postural abnormalities, i.e., onset within 1 month prior to evaluation.

Informed consent

was obtained from all patients and/or their family. Patients had been informed that they could decide not to approve use of their clinical data for study purposes and were given directions on how to "opt out" of the study. They were told that they would incur no disadvantages if they did not consent to the use of their data. Furthermore, patient data were anonymized to ensure that no personal identifying information was disclosed. The study was conducted with our university's study guidelines and regulations with the approval of the St. Marianna University School of Medicine ethics committee (approval number: 5004).

Clinical evaluation and data collection. Clinical evaluations included standing posture at rest and determination of the SPV angle. Patients' medical records were accessed for collection of the following information: age, sex, disease duration, PD severity and outcomes of neuropsychological examinations. PD severity had been evaluated on the basis of mH&Y stages (22) and UPDRS (23) scores. The Mini-Mental State Examination (MMSE) (24) and Japanese version of the Montreal Cognitive Assessment (MoCA-J) (25), as well as the Frontal Assessment Battery (FAB) (26), were used for neuropsychological testing. Patients' LEDD and LEDD_{DA} were also obtained (27).

Rehabilitation program. The study patients had undergone 60 min of rehabilitation therapy once a week or more. The rehabilitation program was designed with three objectives in mind (15, 28). The first was to appropriately correct the patient's posture, the second was to enable the patient to perform various physical exercises, including maintaining control of the corrected trunk, and the third was to increase the patient's endurance. Each session was of three separate components: a 20-min period that entailed the patient focusing on somatic sensations while the physical therapist made adjustments to correct for the difference between the patient's actual posture and the vertical axis, a 20-min period designed to help the

patient maintain control of the trunk while adopting various positions and performing various exercises, and a 10-min period of aerobic exercise performed on an ergometer or treadmill.

Postural evaluation. As noted above, patients' LTF had been evaluated at the initial examination and then at 1 year. Patients' SPV had been evaluated at the initial examination. Standing posture at rest and the SPV were taken as the postural endpoints. In accordance with preceding studies (11), the landmark points for postural evaluation were the spinous processes of the seventh cervical (C7) and fifth lumbar (L5) vertebrae, and reflective markers for three-dimensional (3D) motion analysis (Nobbyteck VNS-BL-MC-190) were attached to these sites. Image analysis software Image J (<https://imagej.nih.gov/ij/index.html>) was used to measure the relevant angles. Images were captured at rest using a digital camera (Panasonic DMC-LZ10), after which it was possible to use the software to calculate the angle between the vertical axis and an arbitrary second axis.

Standing evaluation at rest. Patients' LTF and FTF angles had been measured at the time of initial evaluation and at 1 year. The patient's position on opening his/her eyes immediately after standing up was evaluated three times, and the mean value was taken as the patient's standing position. A digital camera was aimed at the center point of Jacoby's line and at the high point of each iliac crest for measurement of the LTF angle and at a point in the sagittal plane for measurement of the FTF angle. Photographs were taken at rest and included both C7 and L5. The standard axis was a vertical line crossing L5 and descending to the floor. The axis of forward flexion was defined as the line connecting C7 and L5 observed along the sagittal plane, while the axis of lateral flexion was defined as a line connecting C7 and L5 observed along the coronal plane (11, 12).

SPV evaluation. SPV was evaluated in the coronal plane, and the SPV angle and SPV ratio were recorded. The SPV angle was defined as the angle between the vertical axis and the axis of lateral flexion. As described previously, the vertical axis was defined as the vertical line passing through L5 and descending to the floor, and was used as the reference, while the axis of lateral flexion was defined as the line connecting C7 and L5 at the point in time when the patient perceived himself/herself to be in a vertical position (Fig. 4) (10). The SPV angle was measured by first establishing the starting position, which entailed the patient closing their eyes in a standing position, and being passively guided into maximum lateral trunk flexion. The investigator then guided the patient towards the vertical axis. The patient then notified the investigator when they perceived their trunk to be a vertical position, and the images at rest were taken in this position at the height of the Jacoby's line and along the posterior midline. This sequence was performed three times each on the left and right, giving a total of six measurements. The mean value of these measurements was used as the SPV angle. The SPV ratio was the SPV measured with reference to the axis of lateral flexion, and in accordance with preceding studies, was calculated by dividing the SPV angle by the LTF angle ($\text{SPV ratio} = \text{SPV angle} / \text{LTF angle}$) (11).

Statistical analysis. Relations between the baseline LTF angle, change in the LTF angle at 1 year and each of the postural evaluation endpoints were analyzed by means of Spearman's rank correlation coefficient. Change in LTF angle was used to divide the patients into two groups: those for whom LTF improved (LTF

improved group) and those for whom LTF did not improve (LTF non-improved group), based on whether or not improvement was observed once or more from the time of initial evaluation to 1 year. The improvement in the LTF angle and items observed to have significant correlation were defined as independent variables and used to create receiver operating characteristic (ROC) curves for performance of significant variables as predictors of improvement, and the areas under the ROC curves (AUCs) were calculated to measure the ability of the variables to predict improvement. Cut off values were derived on the basis of Youden's Index (Youden's J statistic) (29). All statistical analyses were performed with SPSS version 27 (IBM SPSS Statistics for Windows; IBM Corp, Armonk, NY), and $p < 0.05$ was considered significant.

Results

Patient characteristics. The study group comprised 25 patients (13 men and 12 women) with PD and LTF who were evaluated regularly for at least 1 year, with variables assessed at the first evaluation considered baseline variables. As shown in Table 1, patients' baseline age was 72.9 ± 8.3 years, disease duration was 4.9 ± 4.8 years; modified Hoehn & Yahr (mH&Y) stage was 2.7 ± 0.5 , Unified Parkinson's Disease Rating Scale part III (UPDRS III) score was 13.9 ± 7.8 , LTF angle was 5.6 ± 6.4 , SPV angle was 4.6 ± 3.5 , and SPV ratio was 1.4 ± 0.8 . At 1 year, the LTF had improved in 12 patients (improved LTF group) but not in the other 13 patients (non-improved LTF group).

Relation between LTF and change in the LTF angle. Negative correlation was found between patients' baseline LTF angle and baseline SPV ratio ($r = -0.838$, $p = 0.001$) (Fig. 1a), whereas positive correlation was found between patients' baseline LTF angle and baseline SPV angle ($r = 0.506$, $p = 0.010$). Positive correlation was found between change in the LTF angle observed at 1 year (calculated as the difference between the baseline LTF angle and the LTF angle determined at 1 year) and the baseline SPV ratio ($r = 0.698$, $p = 0.001$) (Fig. 1b), and negative correlation was found between change in the LTF angle and the baseline LTF angle ($r = -0.601$, $p = 0.001$). No relation was observed between change in the LTF angle and age, disease duration, the SPV angle, the LTF angle, mH&Y stage, UPDRS III score, UPDRS total score, levodopa equivalent daily dose (LEDD), or LEDD dopamine agonist (LEDD_{DA}).

SPV ratio in the improved LTF group and non-improved LTF group. When we compared the SPV ratios between the improved LTF group and non-improved LTF group, we found significantly smaller values in the former (0.99 ± 0.78 vs. 1.66 ± 0.71 , $p = 0.011$) (Fig. 2).

The AUC for the SPV ratio in the improved LTF group was 0.795 (95% confidence interval [CI]: 0.61–0.98), and that for the LTF angle was 0.272 (95% CI: 0.07–0.47), with the AUC for the SPV ratio being significantly larger ($p = 0.006$, 95% CI: -0.90 – -0.150). The cut-off value for the SPV ratio in the improved LTF group was 1.07, with a sensitivity of 67% and specificity of 85% (Fig. 3).

When we compared baseline daily doses of PD medications and daily doses of the medications 1 year later in the improved LTF group, we found no significant difference in the LEDD ($620.6\text{mg} \pm 220.9$ vs.

463.1mg $\pm$ 172.0) or LEDD_{DA} (209.6mg $\pm$ 210.5 vs. 97.3mg $\pm$ 116.6). The same comparison in the non-improved LTF group revealed no significant difference in the LEDD (577.9 $\pm$ 389.1 vs. 670.8 $\pm$ 269.9) or LEDD_{DA} (217.7 $\pm$ 291.2 vs. 139.1 $\pm$ 157.8).

Discussion

This study of patients with PD and LTF yielded two main findings. The first was positive correlation between patients' baseline SPV ratio, i.e. the SPV with reference to the axis of lateral flexion at the time of the initial evaluation, and the change in patients' LTF angle 1 year later. The second was the significantly lower baseline SPV ratio in the improved LTF group than in the non-improved LTF group, with a cut-off value of 1.07 being predictive of improvement in the LTF angle.

As noted above, positive correlation was observed between the change in LTF at 1 year and the SPV ratio, but no correlation was found between the change in LTF at 1 year and the SPV angle. The SPV ratio is used to evaluate the SPV with reference to the axis of lateral flexion, so an SPV ratio of ≥ 1 means that the SPV angle is larger than the LTF angle. In a previously reported longitudinal study, cases in which the SPV angle was larger than the LTF angle were also observed, suggesting use of the SPV ratio as a predictor of the course of LTF (11). Our study, reported herein, verified a relation between the SPV ratio and change in the LTF angle at 1 year, confirming potential usefulness of the SPV ratio obtained on initial evaluation as a prognosticator of the course of PD-associated LTF. Various sensory inputs are involved in vertical perception, including visual input, vestibular input and somatic input (13), but when we measured the SPV, our study patients were required to close their eyes, which eliminated visual input. In healthy individuals, somatic input is reported to have a greater effect on the SPV than vestibular sensation (14), and the SPV values in patients with PD have been shown to be greater than the SPV values in age-matched healthy individuals (9). In other words, the SPV, which is perceived primarily somatically, tends to increase in patients with PD. In addition, the SPV begins to increase during the early stages of PD, indicating the necessity of evaluating the SPV in patients with early PD. Results of our study suggest that the initially obtained SPV ratio can be used to predict long-term changes in LTF.

The baseline SPV ratio was significantly lower in our improved LTF group than in our non-improved LTF group; thus, it is conceivable that the SPV ratio can be used to predict the likelihood of improvement in patients' LTF. We found the SPV ratio cut-off value for LTF improvement to be 1.07, indicating that it is important to know whether the SPV is identical to the axis of lateral flexion or whether it is closer to the vertical axis than the axis of lateral flexion in patients with PD. There has been a report indicating that musculoskeletal factors, such as trunk flexibility and mobility, are involved in the improvement of LTF in patients with PD (15). However, it appears that the central nervous system is also involved in LTF (2), with reports pointing to asymmetrical basal ganglia output (16); disruption of the sensorimotor system affecting visual input, vestibular input and somatic input (8, 17); and cerebral cortex abnormalities involved in body schema perception and cognition (1, 18). Thus, we presume that the central nervous system is involved in the improvement of LTF in patients with PD and that the SPV ratio may become a useful prognosticator for central nervous system factors involved in the improvement of LTF.

We found no correlation between change in the LTF angle at 1 year and the LEDD and LEDD_{DA} amounts. We also found no significant difference between the baseline LEDD amount or LEDD_{DA} amount and amounts administered at 1 year in the improved LTF group or in the non-improved LTF group. Some investigators have indicated that switching or reducing anti-PD drugs improves LTF (16, 19), whereas others have indicated that most patients with PD-related LTF do not experience improvement in LTF after switching anti-PD drugs (20), so the effects of these drugs on LTF remain unclear. When evaluating patients for inclusion in the present study, we excluded patients who had switched oral medication within 1 week prior to the evaluation, and we also excluded patients who presented with postural abnormalities that had appeared within 1 month prior to the evaluation, so we believe that oral medications had very little effect on the improvement in LTF that we observed in some patients.

Our findings should be interpreted in light of our study limitations. First, all patients included were from a single institution, increasing the likelihood of selection bias and information bias. Second, posture-related study variables were assessed in the coronal plane, but LTF in patients with PD is frequently complicated by FTF (7). Therefore, optimal evaluation is performed on the basis of 3D examination. Third, this study clarified the fact that the SPV ratio is useful for predicting improvement in the LTF angle at 1 year but not improvement in SPV itself.

In summary, our study showed that a patient's initially determined SPV with reference to the axis of lateral flexion (i.e., the SPV ratio) influences LTF evaluated by the time 1 year has passed. Thus, the SPV ratio shows promise for use as a predictor of improvement in LTF in patients with PD.

Declarations

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Author contributions

Kyohei Mikami designed the study, provided clinical information, tabulated and analyzed the data, and wrote the manuscript.

Makoto Shiraishi assisted and advised in the data analysis.

Tsutomu Kamo managed the medical information and supervised the study.

Competing interests

The authors have no conflicts of interest directly relevant to the content of this article.

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Tables

Table 1. Characteristics of the study patients at the time of initial evaluation (n = 25)

Age (years)	72.9 ± 8.3 (72)
Sex ratio (M/F)	13/12
Disease duration (years)	4.9 ± 4.8 (3)
mH&Y score	2.7 ± 0.5 (3)
UPDRS I score	1.4 ± 1.6 (1)
UPDRS II score	6.8 ± 3.9 (8)
UPDRS III score	13.9 ± 7.8 (14)
UPDRS IV score	1.8 ± 2.4 (1)
UPDRS total score	24.0 ± 12.0 (24)
MMSE score	27.8 ± 2.2 (28)
MoCa-J score	23.4 ± 3.5 (24)
FAB score	14.9 ± 1.9 (15)
FTF (°)	12.7 ± 8.0 (12)
LTF (°)	5.6 ± 6.4 (4)
SPV angle (°)	4.6 ± 3.5 (3.3)
SPV ratio	1.4 ± 0.8 (1.2)
LEDD (mg)	598.4 ± 320.3 (530)
LEDD _{DA} (mg)	213.8 ± 255.7 (150)

Mean ± SD (median) values are shown, unless otherwise indicated.

mH&Y; modified Hoehn and Yahr stage, UPDRS; Unified Parkinson's Disease Rating Scale, MMSE; Mini-Mental State Examination, MoCa-J; Japanese version of Montreal Cognitive Assessment, FAB; Frontal Assessment Battery, FTF; forward trunk flexion, LTF; lateral trunk flexion, SPV; subjective postural vertical, LEDD; levodopa equivalent daily dose, LEDD_{DA}; levodopa equivalent daily dose of dopamine agonist

Figures

Figure 1

Scatter plots showing relations between (a) baseline LTF angle and baseline SPV ratio and (b) change in the LTF angle at 1 year and baseline SPV ratio. SPV subjective postural vertical, LTF lateral trunk flexion.

Figure 2

Box and whisker plot showing distribution of the SPV ratios in the improved LTF group and non-improved LTF group.

Figure 3

ROC curves showing performance of the SPV ratio and LTF angle in the improved LTF group.

Figure 4

Evaluation of the SPV angle. SPV subjective postural vertical, C7 seventh cervical vertebra, L5 fifth lumbar vertebra.