Parkinson's Disease Wearable Gait Analysis: Kinematic and Dynamic Markers for Diagnosis

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1. Introduction

Parkinson's disease (PD) diagnosis and symptoms monitoring rely mainly on clinical evaluation of the cardinal motor symptoms (bradykinesia, rest tremor, and rigidity) [1,2]. To date, following the in vivo diagnostic criteria [3], the error rate is about 20% [4]. This is mainly due to the lack of objective biomarkers for the in vivo diagnosis of Parkinson's disease.

Wearable motion sensors are a promising solution to objectively describe PD motor symptoms [5,6], like bradykinesia [7–9], rigidity [9–12], tremor [13–16], and axial symptoms like gait, balance, and postural issues [17–21]. In addition, the symptom identification process through motion sensors [22] could also improve the therapy management process [23]. Generally speaking, body motion can be analyzed from two different points of view: kinetics (dynamics) analysis, which takes into account the forces that generate the motion and their effect on the body. On the other hand, kinematic analysis, defined as the geometry of motion, describes the movement of the body in terms of position, time, velocity, acceleration, or angle of body segments (Figure 1) [21,24,25].

In literature, kinematic analysis in PD patients showed that the stride variability is increased, and the ability to maintain a steady gait rhythm and a stable, steady walking...
pattern with minimal stride-to-stride changes is impaired [26–29]. PD patients show decreased swing time and reduced stride length compared to controls and stride time, i.e., the gait cycle durations is increased with respect to control group but not significantly different, while stride-to-stride variability is increased significantly from the control group [30].

![Gait kinetics (dynamics) features.](image1)

![Gait kinematics features.](image2)

Figure 1. Gait kinetics (upper figure) and kinematics features (lower figure) (modified under the terms and conditions of the Creative Commons Attribution (CC BY) license from [21]).

Increased stride variability has been associated with an increased fall risk in older adults in general, as well as in patients with PD [31–33], suggesting that this aspect of gait may have clinical utility as an aid in fall risk assessment.

On the dynamics analysis side, the features studied are the forces that cause the motion and their effect on gait. During the stance phase, where feet are in contact with the ground, a level of center of pressure (CoP) is applied the ground reaction force (GRF) which represents the results of gravity force and muscular activation forces counterbalanced by the contact with ground [21,24,25]. Gait dynamics studies have highlighted how some features of GRF vary in different phases of PD, while others are preserved. Components of the GRF are the peak-force at the heel-strike and at toe-off. In the novo early PD there is a delayed heel-strike and an earlier forefoot loading. These parameters seems to be altered independently from the stages of the disease or the pharmacotherapy, instead representing an early marker of the disease [34]. GRF measurement could also be useful to determine gait asymmetry. Su et al. [35] demonstrated how VGRF can reveal the asymmetry of gait by comparing the VGRF of both lower limbs between PD patients and healthy controls. Results showed that PD group has a higher degree of gait asymmetry of the GRF wavelet profile compared to healthy subjects [35]. This metric, compared to conventional asymmetry
measures of kinematic features, like step time, stance time, double stance time, or dynamic features like the two peak and the one dep forces of GRF profile, all resulting with higher asymmetry compared to healthy subjects but with lower diagnostic accuracy [35].

The aim of the present study is to evaluate which kind of gait analysis (dynamic or kinematic) can be considered as more informative for discriminating PD and healthy subjects (HS) on the basis of gait features.

2. Materials and Methods

2.1. Subjects

For the present study, gait data were collected for a total of 108 PD patients and 88 HS from four cohorts [36–38] collected in two publicly available datasets [37,38] (Table 1).

For all the four cohorts, inclusion criteria for Parkinson’s disease patients were: idiopathic PD diagnosis, according to the UK Brain Bank criteria [39], and Hoehn and Yahr stage between 2 and 3 [40], a stable antiparkinsonian medication regimen, ability to ambulate independently, and absence of motor fluctuations. Control subjects were included if they did not have Parkinson’s disease or other common exclusion criteria for the Parkinson’s disease group: dementia, clinically significant musculo-skeletal disease, cardio-vascular disease, respiratory disease, other neurological disease, major depression, or uncorrected visual disturbances.

| Ref  | Cohort | Dataset | Data Source | Group | Subjects Number | Gender | Age (m ± SD) | Hoehn and Yahr (m ± SD) | UPDRS (m ± SD) |
|------|--------|---------|-------------|-------|----------------|--------|--------------|------------------------|----------------|
| [36] | 1      | 1       | Movement Disorders Unit at the Tel-Aviv Sourasky Medical Center | PD    | 29             | 69% male | 71 ± 8       | 2.3 ± 0.4              | 33 ± 12         |
|      |        |         |             | HS    | 18             | 56% male | 72 ± 7       |                        |                |
| [37] | 2      | 1       | Movement Disorders Unit at the Tel Aviv Sourasky Medical Center | PD    | 29             | 55% male | 67 ± 9       | 2.4 ± 0.4              | 25 ± 8          |
|      |        |         |             | HS    | 25             | 46% male | 65 ± 7       |                        |                |
| [30] | 3      | 1       | Movement Disorders Unit at the Tel-Aviv Sourasky Medical Center | PD    | 35             | 63% male | 62 ± 9       | 2.1 ± 0.2              | 36 ± 11         |
|      |        |         |             | HS    | 29             | 62% male | 58 ± 7       |                        |                |
| [38] | 4      | 2       | Neurology Outpatient Clinic at Massachusetts General Hospital | PD    | 15             | 67% male | 67 ± 11      | 2.8 ± 0.9              |                |
|      |        |         |             | HS    | 16             | 13% male | 39 ± 19      |                        |                |

Legend: HS: healthy subjects, Hoehn and Yahr scale [41] is a clinical scale that describes the PD stage from 1 (unilateral body involvement) to 5 (confine ment to bed or wheelchair), IQR: interquartile range, med: median, PD: Parkinson’s disease patients, m ± SD: mean ± standard deviation, UPDRS total: Unified Parkinson’s Disease Rating Scale [42] is a clinical scale used to follow Parkinson’s disease symptoms during the disease course.

The first dataset (cohort 1 [36], 2 [37], 3 [30]) was composed of 93 PD patients and 72 HS, while the second dataset (cohort 4) [38] was composed of 15 PD patients and 16 HS. Regarding the demographic analysis cohorts 1, 2, and 3, the 72 HS are age-matched with PD patients. For cohort 4 the 16 HS are younger than PD patients, therefore, although mitigated by the 72 age-matched HS from the other cohorts, we need to take it into account as a possible bias of the study. For all the four cohorts, for both Parkinson’s disease patients and HS, gait-related data were collected through an instrumented force-sensitive insole [43] placed in subjects’ shoes, containing each eight pressure-sensitive sensors (Figure 2), thus allowing the experimenters to record the time series of the GRF while subjects were asked to walk on level ground. In the first and third cohort subjects walked for two minutes, in the second cohort for 100 m (around 80 s), and in the fourth cohort for 5 min. Considering that in each cohort PD and HS walked with the same protocol, and that around 10 m or 10 s
of gait recording are sufficient to catch the gait pattern in PD and HS, the data available in
the four cohorts are sufficient to describe the gait kinematic and dynamic. However, the
inhomogeneity of gait duration protocol across cohorts should be considered as a limit of
the present study.

All patients gave informed consent, and the study was approved by local research
ethics committees in accordance with the Declaration of Helsinki.

Figure 2. Force-sensitive insole. Each insole placed in subjects’ shoes contains eight pressure-sensitive
sensors in order to record the time series of the ground reaction force (GRF), while subjects were
asked to walk on level ground.

2.2. Data Analysis

In the first dataset, only the gait dynamic data were available. Therefore, in order to
analyze kinematic data, the recorded GRF signals were used to segment the single gait
cycle periods for each patient.

According to Figure 3, the segmentation of the gait cycle was implemented using the
differential Ground Reaction Force (GRF) ($\delta$) between total right force and total left force:

$$\delta = R_{foot,tot} - L_{foot,tot}$$ (1)

In (Equation (1)), $R_{foot,tot}$ and $L_{foot,tot}$ denote the sum of the forces (expressed in newton) measured by all the sensors embedded in the insole worn under the right foot and
the left foot, respectively.

On the basis of $\delta$, each gait cycle for each patient was selected between the first double
limb support (DLS) and the left single limb support (SLS-L) (Figure 3).

For each cycle, we computed the following parameters related to the gait:

- Right and Left Stance, expressed both in seconds and as percentage of the stride length;
- Right and Left Swing, expressed both in seconds and as percentage of the stride length;
- Double Limb Supports, expressed both in seconds and as percentage of the stride length;
- Right and Left Single Limb Supports, expressed both in seconds and as percentage
  of the stride length;
- Right and Left Step Duration, expressed both in seconds and as percentage of the
  stride length;
- Gait velocity expressed in m/s
- Time up and go test expressed in seconds

Such parameters were then averaged along all cycles for each subject.

Moreover, in order to remove single cycle outliers, we compared the duration of
each cycle (i.e., stride length) with the average duration ($SL$) computed for each subject.
To this aim, we marked and then discarded all those cycles whose duration was higher
then $SL + 2 \cdot SD(SL)$, denoting with $SD(SL)$ the standard deviation of the stride length of
all cycles.
Figure 3. Segmentation of the gait cycle implemented using the differential ground reaction force (GRF) between total right force and total left force. DLS: double limb support, GRF: ground reaction force, SLS-L: left single limb support, SLS-R: right single limb support.

Considering the second dataset [38,39], two sources of data were available: raw data of the instrumented insoles (containing the whole gait dynamics) and the processed data already containing gait interval parameters (gait kinematics). Therefore, considering the second dataset, no further data manipulation was performed.

For the sake of simplicity, we summarized the main data manipulation steps performed with the two datasets in Table 2.

| First Dataset | Second Dataset |
|---------------|----------------|
| Cohort 1-2-3  | Cohort 4       |
| Type of Data Available | Type of Data Available |
| • raw data of the instrumented insoles (gait dynamics) | • raw data of the instrumented insoles (gait dynamics) |
| • gait interval parameters (gait kinematics) |

Data Manipulation

Table 2. Overview of the main data manipulation steps.

| First Dataset | Second Dataset |
|---------------|----------------|
|                |                |
| Kinematic Analysis: | Kinematic Analysis: |
| 1. Calculation of the differential ground reaction force (δ). | Kinematic parameters were already available; thus no further data manipulation was performed. |
| 2. Extrapolation of the DLS and SLS parameters. | |
| 3. Calculation of the gait cycles and the main kinematic parameters (see Figure 1) | |
| 4. Normalization with respect to gait cycle. | |
| Dynamic Analysis: | Dynamic Analysis: |
| • Dynamic data already available, thus no further data manipulation was performed. | • Dynamic data available but expressed as raw signals of the instrumented insoles (expressed in volt). Thus, a normalization of the raw signals was performed in order with respect the maximal output of the electronic system composing the insole (according to [43]). |
2.3. Dynamic Analysis

In order to estimate the force applied during the gait, we used the raw data of the instrumented insoles from both datasets. However, the data available within the second dataset were not calibrated, i.e., they were expressed in volts. Therefore, in order to compare the data between the two group of subjects, we divided the recorded signals by the maximal output of the electronic system composing the insole, according to [43]. This allowed us to obtain signals expressed in percentage of the maximal detectable force by the insole. For comparing the two groups (PD vs. HS), we computed the following central tendency and dispersion features: (1) mean, (2) standard deviation (SD), (3) median, (4) interquartile range (IQR). We computed such features along the whole trial duration, for each subject and each group, and we used t-test analysis to statistically test the difference between the two groups.

2.4. Kinematic Analysis

The following gait kinematic parameters were included in the analysis:
- Right and Left Stance, expressed both in seconds and as percentage of the stride length;
- Right and Left Swing, expressed both in seconds and as percentage of the stride length;
- Double Limb Supports, expressed both in seconds and as percentage of the stride length;
- Gait velocity expressed in m/s
- Time up and go test expressed in seconds

Similar to the data analysis presented in Section 2.3 from the raw force data, we computed the following central tendency and dispersion features for the gait kinematics parameters: (1) average (ave), (2) standard deviation (SD), (3) median (med), (4) interquartile range (IQR). We computed such features along the whole trial duration for each subject and each group, and we used t-test analysis to statistically test the difference between the two groups.

For both kinematic and dynamic analysis, Bonferroni correction was applied, considering a correction factor of 50, deriving from the number of dynamic and kinematic parameters. Therefore, the statistically significant value (p) threshold is equal to 0.001 (0.05/50).

3. Results

3.1. Kinematic Analysis

Considering the central tendency indices related to Gait Speed and Time Up and Go test, t-tests showed a significant difference between HS and PD (p < 0.001) (Table 3, Figure 4), while all other kinematic central tendency indices t-test showed a non-significant difference in HS and PD (Table 2).

Moreover, t-tests showed a significant difference in HS and PD (p < 0.001) (Table 2, Figure 4) considering the dispersion indices computed for the following parameters:
- Standard deviation (SD) left and right SWING absolute and percentage value
- Standard deviation (SD) left and right STANCE percentage value
- Standard deviation (SD) DOUBLE SUPPORT percentage value
- Interquartile range (IQR) left and right SWING absolute and percentage value
- Interquartile range (IQR) left and right STANCE absolute and percentage value
- Interquartile range (IQR) DOUBLE SUPPORT percentage value

Conversely, for the other kinematic dispersion indices, t-test showed a non-significant difference between HS and PD (Table 2).
Table 3. Kinematic central tendency and dispersion indices.

| Variables                | Group | N  | Average | Standard Deviation | t     | df  | p Value  |
|--------------------------|-------|----|---------|--------------------|-------|-----|----------|
| **Kinematic central tendency indices** |       |    |         |                    |       |     |          |
| Gait Speed (m/s)         | HS    | 88 | 1.260   | 0.166              | 8.278 | 194 | <0.001 * |
|                          | PD    | 108| 1.019   | 0.227              |       |     |          |
| Time Up and Go (s)       | HS    | 62 | 9.300   | 1.604              | −5.187| 150 | <0.001 * |
|                          | PD    | 90 | 12.056  | 3.962              |       |     |          |
| Ave left SWING           | HS    | 88 | 0.442   | 0.040              | 0.361 | 194 | 0.719    |
|                          | PD    | 108| 0.439   | 0.046              |       |     |          |
| Ave right SWING          | HS    | 88 | 0.443   | 0.041              | 1.158 | 194 | 0.248    |
|                          | PD    | 108| 0.435   | 0.047              |       |     |          |
| Ave left SWING %         | HS    | 88 | 41.804  | 3.143              | 1.951 | 194 | 0.053    |
|                          | PD    | 108| 40.781  | 4.018              |       |     |          |
| Ave right SWING %        | HS    | 88 | 41.916  | 3.488              | 2.682 | 194 | 0.008    |
|                          | PD    | 108| 40.395  | 4.284              |       |     |          |
| Ave left STANCE          | HS    | 88 | 0.618   | 0.071              | −2.127| 194 | 0.035    |
|                          | PD    | 108| 0.646   | 0.109              |       |     |          |
| Ave right STANCE         | HS    | 88 | 0.616   | 0.074              | −2.431| 194 | 0.016    |
|                          | PD    | 108| 0.650   | 0.109              |       |     |          |
| Ave left STANCE %        | HS    | 88 | 58.196  | 3.143              | −1.951| 194 | 0.053    |
|                          | PD    | 108| 59.219  | 4.018              |       |     |          |
| Ave right STANCE %       | HS    | 88 | 58.084  | 3.488              | −2.682| 194 | 0.008    |
|                          | PD    | 108| 59.605  | 4.284              |       |     |          |
| Ave DOUBLE SUPPORT       | HS    | 88 | 0.115   | 0.095              | −1.106| 194 | 0.270    |
|                          | PD    | 108| 0.133   | 0.120              |       |     |          |
| Ave DOUBLE SUPPORT %     | HS    | 88 | 10.681  | 8.528              | −0.808| 194 | 0.420    |
|                          | PD    | 108| 11.734  | 9.492              |       |     |          |
| Med left SWING           | HS    | 88 | 0.441   | 0.040              | 0.123 | 194 | 0.902    |
|                          | PD    | 108| 0.440   | 0.048              |       |     |          |
| Med right SWING          | HS    | 88 | 0.442   | 0.041              | 0.963 | 194 | 0.337    |
|                          | PD    | 108| 0.436   | 0.047              |       |     |          |
| Med left SWING %         | HS    | 88 | 41.999  | 3.195              | 1.844 | 194 | 0.067    |
|                          | PD    | 108| 41.029  | 4.003              |       |     |          |
| Med right SWING %        | HS    | 88 | 42.064  | 3.487              | 2.502 | 194 | 0.013    |
|                          | PD    | 108| 40.655  | 4.240              |       |     |          |
| Med left STANCE          | HS    | 88 | 0.611   | 0.069              | −2.043| 194 | 0.042    |
|                          | PD    | 108| 0.638   | 0.106              |       |     |          |
| Med right STANCE         | HS    | 88 | 0.611   | 0.073              | −2.303| 194 | 0.022    |
|                          | PD    | 108| 0.642   | 0.106              |       |     |          |
| Med left STANCE %        | HS    | 88 | 58.001  | 3.195              | −1.844| 194 | 0.067    |
|                          | PD    | 108| 58.971  | 4.003              |       |     |          |
| Med right STANCE %       | HS    | 88 | 57.936  | 3.487              | −2.502| 194 | 0.013    |
|                          | PD    | 108| 59.345  | 4.240              |       |     |          |
| Med DOUBLE SUPPORT       | HS    | 88 | 0.113   | 0.094              | −0.943| 194 | 0.347    |
|                          | PD    | 108| 0.127   | 0.110              |       |     |          |
| Med DOUBLE SUPPORT%      | HS    | 88 | 10.483  | 8.518              | −0.742| 194 | 0.459    |
|                          | PD    | 108| 11.441  | 9.368              |       |     |          |
Table 3. Cont.

| Variables                   | Group      | N  | Average | Standard Deviation | t   | df | p Value |
|-----------------------------|------------|----|---------|--------------------|-----|----|---------|
| SD left SWING               | HS         | 88 | 0.022   | 0.009              | −4.851 | 194 | <0.001 * |
|                             | PD         | 108| 0.032   | 0.017              | −4.357 | 194 | <0.001 * |
| SD right SWING              | HS         | 88 | 0.022   | 0.008              | −4.400 | 194 | <0.001 * |
|                             | PD         | 108| 0.034   | 0.025              | −4.400 | 194 | <0.001 * |
| SD left SWING %             | HS         | 88 | 1.686   | 0.762              | −6.093 | 194 | <0.001 * |
|                             | PD         | 108| 2.357   | 1.254              | −6.093 | 194 | <0.001 * |
| SD right SWING %            | HS         | 88 | 1.568   | 0.613              | −6.093 | 194 | <0.001 * |
|                             | PD         | 108| 2.357   | 1.254              | −6.093 | 194 | <0.001 * |
| SD left STANCE              | HS         | 88 | 0.035   | 0.016              | −1.640 | 194 | 0.103   |
|                             | PD         | 108| 0.065   | 0.170              | −1.736 | 194 | 0.084   |
| SD right STANCE             | HS         | 88 | 1.686   | 0.762              | −4.400 | 194 | <0.001 * |
|                             | PD         | 108| 1.568   | 0.613              | −4.400 | 194 | <0.001 * |
| SD left STANCE %            | HS         | 88 | 0.033   | 0.014              | −1.360 | 194 | 0.103   |
|                             | PD         | 108| 0.058   | 0.135              | −1.360 | 194 | 0.103   |
| SD right STANCE %           | HS         | 88 | 1.686   | 0.762              | −6.093 | 194 | <0.001 * |
|                             | PD         | 108| 2.357   | 1.254              | −6.093 | 194 | <0.001 * |
| SD DOUBLE SUPPORT           | HS         | 88 | 0.019   | 0.015              | −1.441 | 194 | 0.151   |
|                             | PD         | 108| 0.045   | 0.171              | −1.441 | 194 | 0.151   |
| SD DOUBLE SUPPORT %         | HS         | 88 | 1.386   | 0.718              | −3.396 | 194 | <0.001 * |
|                             | PD         | 108| 2.072   | 1.780              | −3.396 | 194 | <0.001 * |
| IQR left SWING              | HS         | 88 | 0.017   | 0.006              | −6.651 | 194 | <0.001 * |
|                             | PD         | 108| 0.027   | 0.014              | −6.651 | 194 | <0.001 * |
| IQR right SWING             | HS         | 88 | 0.017   | 0.006              | −5.821 | 194 | <0.001 * |
|                             | PD         | 108| 0.027   | 0.016              | −5.821 | 194 | <0.001 * |
| IQR left SWING %            | HS         | 88 | 1.326   | 0.323              | −6.279 | 194 | <0.001 * |
|                             | PD         | 108| 1.896   | 0.799              | −6.279 | 194 | <0.001 * |
| IQR right SWING %           | HS         | 88 | 1.229   | 0.337              | −7.009 | 194 | <0.001 * |
|                             | PD         | 108| 1.905   | 0.852              | −7.009 | 194 | <0.001 * |
| IQR left STANCE             | HS         | 88 | 0.026   | 0.009              | −4.577 | 194 | <0.001 * |
|                             | PD         | 108| 0.037   | 0.020              | −4.577 | 194 | <0.001 * |
| IQR right STANCE            | HS         | 88 | 0.026   | 0.009              | −4.902 | 194 | <0.001 * |
|                             | PD         | 108| 0.037   | 0.020              | −4.902 | 194 | <0.001 * |
| IQR left STANCE %           | HS         | 88 | 1.326   | 0.323              | −6.279 | 194 | <0.001 * |
|                             | PD         | 108| 1.896   | 0.799              | −6.279 | 194 | <0.001 * |
| IQR right STANCE %          | HS         | 88 | 1.229   | 0.337              | −7.009 | 194 | <0.001 * |
|                             | PD         | 108| 1.905   | 0.852              | −7.009 | 194 | <0.001 * |
| IQR DOUBLE SUPPORT          | HS         | 88 | 0.013   | 0.008              | −2.875 | 194 | 0.004   |
|                             | PD         | 108| 0.018   | 0.014              | −2.875 | 194 | 0.004   |
| IQR DOUBLE_SUPPORT %        | HS         | 88 | 1.141   | 0.502              | −3.446 | 194 | <0.001 * |
|                             | PD         | 108| 1.613   | 1.203              | −3.446 | 194 | <0.001 * |

Legend: ave: average, HS: healthy subjects, IQR: interquartile range, med: median, PD: Parkinson’s disease patients, SD: standard deviation, *: t-test statistically significant p-value.
Figure 4. Average values of kinematic central tendency indices (gait speed and Time Up and Go) and dispersion indices of PD patients and HS with significant differences on the t-test. IQR = interquartile range. SD = standard deviation.

ROC Analysis

A ROC analysis was performed for all kinematic values which showed a significant t-test difference in HS and PD. It was implemented considering a diagnosis of PD over HS as the target (Figure 5). The value of AUC with upper and lower limits (95% C.I.), the standard error, and the p value are listed in Table 4.

As shown in Figure 5 and Table 4, with the exception of “IQR left STANCE”, and “IQR DOUBLE SUPPORT %”, all the kinematic predictors analysed showed a statistically significant ROC AUC value in the discrimination between diagnosis of PD over HS.
Table 4. ROC analysis of statistically significant kinematic features.

| Variables            | AUC  | Standard Error | p Value | Lower Limit | Upper Limit |
|----------------------|------|----------------|---------|-------------|-------------|
| Gait Speed (m/s)     | 0.200| 0.035          | <0.001 *| 0.130       | 0.269       |
| Time Up and Go (s)   | 0.801| 0.036          | <0.001 *| 0.730       | 0.872       |
| SD left SWING        | 0.682| 0.044          | <0.001 *| 0.595       | 0.768       |
| SD right SWING       | 0.703| 0.043          | <0.001 *| 0.620       | 0.787       |
| SD left SWING %      | 0.674| 0.045          | <0.001 *| 0.585       | 0.763       |
| SD right SWING %     | 0.740| 0.041          | <0.001 *| 0.660       | 0.819       |
| SD left STANCE %     | 0.674| 0.045          | <0.001 *| 0.585       | 0.763       |
| SD right STANCE %    | 0.740| 0.041          | <0.001 *| 0.660       | 0.819       |
| SD DOUBLE SUPPORT %  | 0.643| 0.039          | <0.001 *| 0.566       | 0.720       |
| IQR left SWING       | 0.778| 0.037          | <0.001 *| 0.704       | 0.851       |
| IQR right SWING      | 0.733| 0.041          | <0.001 *| 0.654       | 0.813       |
| IQR left SWING %     | 0.776| 0.037          | <0.001 *| 0.703       | 0.848       |
| IQR right SWING %    | 0.820| 0.034          | <0.001 *| 0.754       | 0.886       |
| IQR left STANCE      | 0.639| 0.045          | 0.0036  | 0.551       | 0.727       |
| IQR right STANCE     | 0.667| 0.044          | <0.001 *| 0.580       | 0.754       |
| IQR left STANCE %    | 0.776| 0.037          | <0.001 *| 0.703       | 0.848       |
| IQR right STANCE %   | 0.820| 0.034          | <0.001 *| 0.754       | 0.886       |
| IQR DOUBLE SUPPORT % | 0.634| 0.040          | 0.0012  | 0.556       | 0.712       |

Legend: IQR: interquartile range, SD: standard deviation, * ROC: statistically significant p-value.

Figure 5. ROC graph of statistically significant kinematic features, considering a diagnosis as a target of PD over HS. IQR: interquartile range, SD: standard deviation.

3.2. Dynamic Analysis

For all the dynamic central and dispersion indices, t-test showed a non-significant difference in HS and PD (p > 0.001) (Table 5).
Table 5. Dynamic central tendency and dispersion indices.

| Variables                  | Group | N  | Average | Standard Deviation | t     | df  | p Value |
|---------------------------|-------|----|---------|--------------------|-------|-----|---------|
| Ave Force left            | HS    | 88 | 372.346 | 181.982            | −0.813| 194 | 0.417   |
|                           | PD    | 108| 392.385 | 162.683            | −1.044| 194 | 0.298   |
| Ave Force right           | HS    | 88 | 369.036 | 181.877            | −1.044| 194 | 0.298   |
|                           | PD    | 108| 394.455 | 158.804            | −0.537| 194 | 0.592   |
| Med Force left            | HS    | 88 | 467.395 | 235.065            | −0.537| 194 | 0.592   |
|                           | PD    | 108| 484.518 | 210.938            | −1.025| 194 | 0.307   |
| Med Force right           | HS    | 88 | 459.291 | 235.530            | −0.537| 194 | 0.592   |
|                           | PD    | 108| 491.887 | 209.364            | −0.537| 194 | 0.592   |
| SD Force left             | HS    | 88 | 324.871 | 160.322            | −0.561| 194 | 0.576   |
|                           | PD    | 108| 336.977 | 141.656            | −0.561| 194 | 0.576   |
| SD Force right            | HS    | 88 | 324.106 | 160.490            | −0.608| 194 | 0.544   |
|                           | PD    | 108| 337.011 | 136.732            | −0.608| 194 | 0.544   |
| IQR Force left            | HS    | 88 | 671.779 | 332.736            | −0.764| 194 | 0.446   |
|                           | PD    | 108| 706.230 | 297.570            | −0.764| 194 | 0.446   |
| IQR Force right           | HS    | 88 | 671.246 | 332.261            | −0.877| 194 | 0.382   |
|                           | PD    | 108| 710.175 | 288.892            | −0.877| 194 | 0.382   |

Legend: ave: average, HS: healthy subjects, IQR: interquartile range, med: median, PD: Parkinson’s disease patients, SD: standard deviation.

In Figures 6 and 7 (and Supplementary Video S1), the average gait cycle dynamic, respectively, in HS and PD groups are summarized, showing no difference in gait cycle dynamic profile in the two groups.

![Healthy Group Average](image)

**Figure 6.** Healthy subjects gait dynamic. Right (R tot) (red line) and Left (L tot) (green line) total force averaged along gait cycles (GC) and subjects over the percentage of completion of the gait cycle (top). The bottom part of the figure represents a graphical visualization of the force measured by the single sensors embedded within the instrumented insole: the larger the circles (right red; left green), the larger the force measured.
4. Discussion

Gait features differ between PD patients and HS under normal conditions. In this article we compared the kinematic and dynamic markers of gait between PD patients and HS. The statistical analyses related to the kinematic parameters showed significant differences among PD patients and HS for gait speed and time Up and Go test, and for selected kinematic dispersion indices, with statistically significant ROC AUC values indicating good discrimination ability between the two groups of these parameters. These results are in line with literature data showing an increased stride-to-stride variability in PD patients compared to HS [26–30]. This may reflect mechanisms that underlie disease pathology, such as reduced automaticity and damaged locomotor synergies. Indeed, different studies showed that stride variability is reduced by levodopa therapy, demonstrating the role of dopaminergic pathways in the gait rhythmicity [27,28,44–46]. Moreover, increased gait variability could be a byproduct of bradykinesia and of a lower gait speed. In literature, no significant increase in stride time variability was observed in healthy elderly subjects, even though they walked significantly slower than young adults [47–49]. Several studies aimed to define the relationship between gait speed and stride time variability. Gait speed seems to be related to stride length, stride time, swing time, and stride time variability, with similar relationships in patients with PD and in controls. A U-shaped relationship between stride length variability and gait speed was described when healthy subjects walked on a treadmill [50]. Other studies observed a linear relationship between gait speed and stride time variability, and the range of walking speeds tested and differences in study populations may explain this apparent contradiction [51]. Indeed, mechanical and energy expenditure optimizations may be affected by aging and disease [52]. Interestingly, in a study of young and older adults, it was reported that gait speed did not affect the variability of walking velocity, stride length, or stride time [53]. The increased swing time variability in PD is apparently independent of gait speed. Furthermore, even when patients with PD walk at the same speed as controls, swing time variability is increased in PD [51].

In our study dynamic features did not show any statistically significant difference between PD patients and HS. The reason for the differences between kinematic and dynamic analysis, from which kinematic parameters seem to be more sensitive to identify PD patient features with respect to HS, could be found in the dynamic analysis technique. For dynamic analysis, GRF has several characteristics that make it suitable for gait study. Above all, the acceleration of the center of gravity of the body (COM) is directly proportional to the GRF,
which implies that many gait features can be extracted from the GRF. GRF is a continuous signal, unlike kinematic parameters such as oscillation time or stride length, which are considered discrete variables. A great advantage of continuous signals is the possibility of being characterized in terms of time and frequency. However, to simplify the cost and complexity of instrumental devices, only the vertical component of the GRF (VGRF) is usually measured. VGRF is the component of the force with the greatest extent that the ground affects the body, and the majority of dynamic studies are focused on different characteristics of VGRF between patients with PD and controls [35,54]. The result of the present study compared to literature data on dynamic studies showed that to catch a difference between PD and HS a more deep dynamic analysis is necessary, like asymmetry between the two sides [35], or analysis not only of the global GRF but of the dynamics of the individual foot sensors sections (e.g., forefoot heel) [34].

The novelty of the present study is in the direct comparison of the two kinds of gait analysis (dynamic and kinematic). Despite kinematics features like acceleration that are directly proportional to dynamic features like ground reaction force, the results of this study showed the so-called force/rhythm dichotomy, since kinematic features were more informative than dynamic ones. In literature, the two kinds of analysis are very well described, with a lack of a direct comparison between the two on the same data. The limits of the present study, which are related to the source of data that comes from available datasets of previous studies, are the inhomogeneity of gait duration protocol across cohorts and the younger age of HS of cohort 4 with respect to other subjects. Therefore, future clinical trials are needed to confirm these results and additional approaches could be devoted to applying machine learning algorithms to more precisely assess and combine kinematics and dynamics parameters, and weigh the impact of single features.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/s22228773/s1, Video S1: Average gait cycle dynamic, in healthy subjects (HS) and Parkinson’s disease (PD) group.

Author Contributions: Conceptualization, L.d.B., L.R. and V.D.L.; Data curation, L.d.B. and L.R.; Formal analysis, L.d.B. and L.R.; Methodology, L.d.B.; Supervision, V.D.L.; Writing—original draft, L.d.B., L.R., M.L.C. and P.M.P.; Writing—review & editing, L.d.B. and V.D.L. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The studies of the dataset were conducted in accordance with the Declaration of Helsinki, and approved by the local Institutional Review Boards.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the original dataset studies.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References
1. Bloem, B.R.; Okun, M.S.; Klein, C. Parkinson’s disease. Lancet 2021, 397, 2284–2303. [CrossRef]
2. Poewe, W.; Seppi, K.; Tanner, C.M.; Halliday, G.M.; Brundin, P.; Volkmann, J.; Schrag, A.E.; Lang, A.E. Parkinson disease. Nat. Rev. Dis. Primers 2017, 3, 17013. [CrossRef] [PubMed]
3. Gibb, W.R.G.; Lees, A.J. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson’s disease. J. Neurol. Neurosurg. Psychiatry 1988, 51, 745–752. [CrossRef] [PubMed]
4. Rizzo, G.; Copetti, M.; Arcuti, S.; Martino, D.; Fontana, A.; Logroscino, G. Accuracy of clinical diagnosis of Parkinson disease A systematic review and meta-analysis. Neurology 2016, 91, e479–e489. [CrossRef]
5. Sanchez-Ferro, A.; Elshehabi, M.; Godinho, C.; Salkovic, D.; Hobert, M.A.; Domingos, J.; van Uem, J.M.; Ferreira, J.J.; Maetzler, W. New methods for the assessment of Parkinson’s disease (2005 to 2015): A systematic review. Mov. Disord. Off. J. Mov. Disord. Soc. 2016, 31, 1283–1292. [CrossRef]
6. Anand, V.; Bilal, E.; Ho, B.; Rice, J.J. Towards motor evaluation of Parkinson’s Disease Patients using wearable inertial sensors. AMIA Annu. Symp. Proc. AMIA Symp. 2020, 2020, 203–212.
7. Stamatikis, J.; Ambrozie, J.; Cremers, J.; Sharei, H.; Delvaux, V.; Macq, B.; Garraux, G. Finger tapping clinimetric score prediction in Parkinson’s disease using low-cost accelerometers. *Comput. Intell. Neurosci.* 2013, 2013, 717853. [CrossRef]
8. Summa, S.; Tosò, J.; Taffoni, F.; Di Blasi, L.; Marano, M.; Rizzo, A.C.; Tombini, M.; Di Pino, G.; Formica, D. Assessing Bradykinesia in Parkinson’s Disease Using Gyroscope Signals. In Proceedings of the 2017 International Conference on Rehabilitation Robotics (ICORR), London, UK, 17–20 July 2017; IEEE: Piscataway, NJ, USA, 2017; pp. 1556–1561.
9. Di Blasi, L.; Summa, S.; Tosò, J.; Taffoni, F.; Marano, M.; Cascio Rizzo, A.; Vecchio, F.; Formica, D.; Di Lazzaro, V.; Di Pino, G.; et al. Quantitative Analysis of Bradykinesia and Rigidity in Parkinson’s Disease. *Front. Neurol.* 2018, 9, 121. [CrossRef]
10. Endo, T.; Okuno, R.; Yokoe, M.; Akazawa, K.; Sakoda, S. A novel method for systematic analysis of rigidity in Parkinson’s disease. *Mov. Disord. Off. J. Mov. Disord. Soc.* 2009, 24, 2218–2224. [CrossRef]
11. Kwon, Y.; Park, S.H.; Kim, J.W.; Ho, Y.; Jeon, H.M.; Bang, M.J.; Koh, S.B.; Kim, J.H.; Eom, G.M. Quantitative evaluation of parkinsonian rigidity during intra-operative deep brain stimulation. *Bio-Med. Mater. Eng.* 2014, 24, 2273–2281. [CrossRef]
12. Raiano, L.; Di Pino, G.; Di Blasi, L.; Tombini, M.; Tagliamonte, N.L.; Formica, D. PDMeter: A Wrist Wearable Device for an at-home Assessment of the Parkinson’s Disease Rigidity. *IEEE Trans. Neural Syst. Rehabil. Eng.* 2020, 28, 1325–1333. [CrossRef] [PubMed]
13. Deuschl, G.; Krack, P.; Lauk, M.; Timmer, J. Clinical neurophysiology of tremor. *J. Clin. Neurophysiol.* 1996, 13, 110–121. [CrossRef] [PubMed]
14. Di Pino, G.; Formica, D.; Melgari, J.-M.; Taffoni, F.; Salomone, G.; di Blasi, L.; Caimo, E.; Vernieri, F.; Guglielmelli, E. Neurophysiological bases of tremors and accelerometric parameters analysis. In Proceedings of the 2012 4th IEEE RAS & EMBS International Conference on Biomedical Robotics and Biomechatronics (BioRob), Rome, Italy, 24–27 June 2012; pp. 1820–1825.
15. Di Blasi, L.; Brittain, J.S.; Shah, S.A.; Pedrosa, D.J.; Cagnan, H.; Mathy, A.; Chen, C.C.; Martin-Rodriguez, J.F.; Mir, P.; Timmerman, L.; et al. Tremor stability index: A new tool for differential diagnosis in tremor syndromes. *Brain J. Neurol.* 2017, 140, 1977–1986. [CrossRef]
16. Di Blasi, L.; Brittain, J.-s.; Peter, B.; Di LAZZARO, V.; Shah, S.A. Methods and System for Characterising Tremors. Patent WO/2018/134579, 26 July 2018.
17. Moore, S.T.; MacDougall, H.G.; Gracies, J.M.; Cohen, H.S.; Ondo, W.G. Long-term monitoring of gait in Parkinson’s disease. *Gait Posture* 2007, 26, 200–207. [CrossRef] [PubMed]
18. Schlachetzki, J.C.M.; Barth, J.; Marxreiter, F.; Gossler, J.; Kohl, Z.; Reinfelder, S.; Gassner, H.; Aminian, K.; Eskofier, B.M.; Winkler, J.; et al. Wearable sensors objectively measure parkinsonian parameters in Parkinson’s disease. *PLoS ONE* 2017, 12, e0183989. [CrossRef]
19. Tosi, J.; Summa, S.; Taffoni, F.; Biase, L.d.; Marano, M.; Rizzo, A.C.; Tombini, M.; Schena, E.; Formica, D.; Pino, G.D. Feature Extraction in Sit-to-Stand Task Using M-IMU Sensors and Evaluation in Parkinson’s Disease. In Proceedings of the 2018 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Rome, Italy, 11–13 June 2018; pp. 1–6.
20. Suppa, A.; Kita, A.; Leodori, G.; Zampogna, A.; Nicolini, E.; Lorenzi, P.; Rao, R.; Irrera, F. L-DOPA and freezing of gait in Parkinson’s disease: Objective assessment through a wearable wireless system. *Front. Neurol.* 2017, 8, 406. [CrossRef] [PubMed]
21. Di Blasi, L.; Di Santo, A.; Caminiti, M.L.; De Liso, A.; Shah, S.A.; Ricci, L.; Di Lazzaro, V. Gait analysis in Parkinson’s disease: An overview of the most accurate markers for diagnosis and symptoms monitoring. *Sensors* 2020, 20, 3529. [CrossRef]
22. Di Blasi, L.; Raiano, L.; Caminiti, M.L.; Pecoraro, P.M.; Di Lazzaro, V. Artificial intelligence in Parkinson’s disease—Symptoms identification and monitoring. In *Augmenting Neurological Disorder Prediction and Rehabilitation Using Artificial Intelligence*; Elsevier: Amsterdam, The Netherlands, 2022; pp. 35–52.
23. Di Blasi, L.; Tinkhauser, G.; Martin Moraud, E.; Caminiti, M.L.; Pecoraro, P.M.; Di Lazzaro, V. Adaptive, personalized closed-loop therapy for Parkinson’s disease: biochemical, neurophysiological, and wearable sensing systems. *Expert Rev. Neurother.* 2021, 21, 1371–1388. [CrossRef]
24. Dicharry, J. Kinematics and kinetics of gait: From lab to clinic. *Clin. Sports Med.* 2010, 29, 347–364. [CrossRef]
25. Webster, J.B.; Darter, B.J. Principles of Normal and Pathologic Gait. In *Atlas of Orthoses and Assistive Devices*; Elsevier: Amsterdam, The Netherlands, 2019; pp. 49–62.e1.
26. Sica, M.; Degos, S.; Crowe, C.; Kenny, L.; Moore, K.; Timmons, S.; Barton, J.; O’Flynn, B.; Komaris, D.-S. Continuous home monitoring of Parkinsonian features using inertial sensors: A systematic review. *PLoS ONE* 2021, 16, e0246528. [CrossRef]
27. Schäafsm, J.D.; Giladi, N.; Balash, Y.; Bartels, A.L.; Gurevich, T.; Hausdorff, J.M. Gait dynamics in Parkinson’s disease: Relationship to parkinsonian features, falls and response to levodopa. *J. Neurol. Sci.* 2003, 212, 47–53. [CrossRef]
28. Blin, O.; Fernandez, A.M.; Pailhous, J.; Serrattiere, G. Dopa-sensitive and dopa-resistant gait parameters in Parkinson’s disease. *J. Neurol. Sci.* 1991, 103, 51–54. [CrossRef]
29. Del Olmo, M.F.; Cudeiro, J. Temporal variability of gait in Parkinson disease: Effects of a rehabilitation programme based on rhythmic sound cues. *Parkinsonism Relat. Disord.* 2005, 11, 25–33. [CrossRef] [PubMed]
30. Frenkel-Toledo, S.; Giladi, N.; Peretz, C.; Herman, T.; Gruendlinger, L.; Hausdorff, J.M. Treadmill walking as an external pacemaker to improve gait rhythm and stability in Parkinson’s disease. *Mov. Disord. Off. J. Mov. Disord. Soc.* 2005, 20, 1109–1114. [CrossRef]
31. Pietrucin-Faria, F.; Montero-Odasso, M.; Hausdorff, J.M. Gait variability and fall risk in older adults: The role of cognitive function. In *Falls and Cognition in Older Persons*; Springer: Berlin/Heidelberg, Germany, 2020; pp. 107–138.
32. Hausdorff, J.M.; Rios, D.A.; Edelberg, H.K. Gait variability and fall risk in community-living older adults: A 1-year prospective study. *Arch. Phys. Med. Rehabil.* 2001, 82, 1050–1056. [CrossRef]
33. Maki, B.E. Gait changes in older adults: Predictors of falls or indicators of fear. *J. Am. Geriatr. Soc.* 1997, 45, 313–320. [CrossRef] [PubMed]

34. Baltadjieva, R.; Giladi, N.; Gruendlinger, L.; Peretz, C.; Hausdorff, J.M. Marked alterations in the gait timing and rhythmicity of patients with de novo Parkinson’s disease. *Eur. J. Neurosci.* 2006, 24, 1815–1820. [CrossRef]

35. Su, B.; Song, R.; Guo, L.; Yen, C.-W. Characterizing gait asymmetry via frequency sub-band components of the ground reaction force. *Biomed. Signal Process. Control* 2015, 18, 56–60. [CrossRef]

36. Yoge, G.; Giladi, N.; Peretz, C.; Springer, S.; Simon, E.S.; Hausdorff, J.M. Dual tasking, gait rhythmicity, and Parkinson’s disease: Which aspects of gait are attention demanding? *Eur. J. Neurosci.* 2005, 22, 1248–1256. [CrossRef]

37. Hausdorff, J.M.; Lowenthal, J.; Herman, T.; Gruendlinger, L.; Peretz, C.; Giladi, N. Rhythmic auditory stimulation modulates gait variability in Parkinson’s disease. *Eur. J. Neurosci.* 2007, 26, 2369–2375. [CrossRef]

38. Hausdorff, J.M.; Lertratanakul, A.; Cudkowicz, M.E.; Peterson, A.L.; Kaliton, D.; Goldberger, A.L. Dynamic markers of altered gait rhythm in amyotrophic lateral sclerosis. *J. Appl. Physiol.* 2000, 88, 2045–2053. [CrossRef] [PubMed]

39. Goldberger, A.L.; Amaral, L.A.; Glass, L.; Hausdorff, J.M.; Ivanov, P.C.; Mark, R.G.; Mietus, J.E.; Moody, G.B.; Peng, C.-K.; Stanley, H.E. PhysioBank, PhysioToolkit, and PhysioNet: Components of a new research resource for complex physiologic signals. *Circulation* 2000, 101, e215–e220. [CrossRef] [PubMed]

40. Gelb, D.J.; Oliver, E.; Gilman, S. Diagnostic criteria for Parkinson disease. *Arch. Neurol.* 1999, 56, 33–39. [CrossRef]

41. Hoehn, M.M.; Yahr, M.D. Parkinsonism onset, progression, and mortality. *Neurology* 1967, 17, 427. [CrossRef]

42. Fahn, S.; Elton, R.; UPDRS Development Committee. *Recent Developments in Parkinson’s Disease*; Macmillan Health Care Information: Folorham Park, NJ, USA, 1987; Volume 2, pp. 153–163, 293–304.

43. Hausdorff, J.M.; Ladin, Z.; Wei, J.Y. Footswitch system for measurement of the temporal parameters of gait. *J. Biomech.* 1995, 28, 347–351. [CrossRef]

44. Son, M.; Han, S.H.; Lyoo, C.H.; Lim, J.; Jeon, J.; Hong, K.-B.; Park, H. The effect of levodopa on bilateral coordination and gait asymmetry in Parkinson’s disease using inertial sensor. *NPJ Parkinson’s Dis.* 2021, 7, 42. [CrossRef] [PubMed]

45. Blin, O.; Ferrandez, A.M.; Serratrice, G. Quantitative analysis of gait in Parkinson patients: Increased variability of stride length. *J. Neurol. Sci.* 1990, 98, 91–97. [CrossRef]

46. Hausdorff, J.M.; Cudkowicz, M.E.; Firtion, R.; Wei, J.Y.; Goldberger, A.L. Gait variability and basal ganglia disorders: Stride-to-stride variations of gait cycle timing in Parkinson’s disease and Huntington’s disease. *Mov. Disord. Off. J. Mov. Disord. Soc.* 1998, 13, 428–437. [CrossRef] [PubMed]

47. Gabell, A.; Nayak, U.S. The effect of age on variability in gait. *J. Gerontol.* 1984, 39, 662–666. [CrossRef]

48. Hausdorff, J.M.; Mitchell, S.L.; Firtion, R.; Peng, C.K.; Cudkowicz, M.E.; Wei, J.Y.; Goldberger, A.L. Altered fractal dynamics of gait: Reduced stride-interval correlations with aging and Huntington’s disease. *J. Appl. Physiol.* 1997, 82, 262–269. [CrossRef]

49. Hollman, J.H.; Von Arb, H.M.; Budreck, A.M.; Muehlemann, A.; Ness, D.K. Treadmill walking alters stride time dynamics in Parkinson’s disease. *Gait Posture* 2020, 77, 195–200. [CrossRef] [PubMed]

50. Yamasaki, M.; Sasaki, T.; Torii, M. Sex difference in the pattern of lower limb movement during treadmill walking. *Eur. J. Appl. Physiol. Occup. Physiol.* 1991, 62, 99–103. [CrossRef] [PubMed]

51. Frenkel-Toledo, S.; Giladi, N.; Peretz, C.; Herman, T.; Gruendlinger, L.; Hausdorff, J.M. Effect of gait speed on gait rhythmicity in Parkinson’s disease: Variability of stride time and swing time respond differently. *J. Neuroeng. Rehabil.* 2005, 2, 23. [CrossRef] [PubMed]

52. Malatesta, D.; Simar, D.; Dauvilliers, Y.; Candau, R.; Borrani, F.; Preaut, C.; Caillaud, C. Energy cost of walking and gait instability in healthy 65- and 80-yr-olds. *J. Appl. Physiol.* 2003, 95, 2248–2256. [CrossRef]

53. Grabner, P.C.; Biswas, S.T.; Grabner, M.D. Age-related changes in spatial and temporal gait variables. *Arch. Phys. Med. Rehabil.* 2001, 82, 31–35. [CrossRef]

54. Alam, M.N.; Garg, A.; Munia, T.T.K.; Fazel-Rezai, R.; Tavakolian, K. Vertical ground reaction force marker for Parkinson’s disease. *PLoS ONE* 2017, 12, e0175951. [CrossRef]