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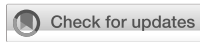
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L-Dopa/Carbidopa intestinal gel infusion in advanced Parkinson's disease: real-life mobility insights from wearable sensors

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Rationale/objectives: In advanced Parkinson's disease (APD), the intermittent dopaminergic delivery of oral L-Dopa contributes to the occurrence of fluctuations and dyskinesia. Continuous dopaminergic delivery through intrajejunal L-Dopa/Carbidopa intestinal gel (LCIG) is an established therapeutic strategy to manage these motor complications, but its impact on real-life motor performances has never been characterised objectively. This cross-sectional pilot study used wearable sensors to quantitatively evaluate the impact of LCIG on patients' motor performance in real-world settings.

Material/methods: Forty-three APD patients, including 15 treated with LCIG infusion (APD_{LCIG}) and 28 on the best oral dopaminergic therapy (APD_{L-Dopa}), were evaluated using standardized clinical scales and sensor-based metrics. A validated waist-worn inertial wearable, positioned on the left side, continuously monitored spatiotemporal gait parameters (step length, stride speed, stride fluidity, and cadence) along with freezing of gait (FOG) occurrence, and time spent with dyskinesia. To quantify intra-day variability in motor performance associated with motor fluctuations, the coefficient of variation of all spatiotemporal gait parameters was calculated. Finally, clinical-behavioural correlations were analysed to examine possible relationships between gait features and clinical outcomes.

Results: Despite comparable clinical and demographic profiles, APD_{LCIG} showed less severe motor fluctuations than APD_{L-Dopa} and exhibited lower intra-day variability in key spatiotemporal gait parameters (step length, stride speed, and stride fluidity). Dyskinesia duration was similar in APD_{LCIG} and APD_{L-Dopa}. Also, mean absolute values of gait parameters and FOG duration did not differ between groups. Stride fluidity, step length, and stride speed were moderately and inversely associated with age and disease severity.

Discussion/conclusion: LCIG provides a more stable gait pattern than optimized oral dopaminergic therapy in appropriately selected APD patients, as captured by wearable sensors in real-world conditions. This likely reflects more consistent motor control throughout the day due to continuous dopaminergic delivery. By detecting fluctuation-related motor impairment through variability metrics,

wearable sensor technology may offer a valuable tool to enhance the clinical management of LCIG, supporting patient selection, medication titration, and the longitudinal monitoring of treatment efficacy and safety.

KEYWORDS

fluctuations, LCIG, motor complications, Parkinson's disease, wearable sensors

1 Introduction

The advanced stage of Parkinson's disease (APD) is characterized by fluctuating symptoms, including motor fluctuations and dyskinesias (i.e., drug-induced involuntary movements), as motor control becomes increasingly reliant on the intermittent intake of oral medications (1). L-Dopa/Carbidopa intestinal gel (LCIG) infusion is a leading therapeutic strategy for managing these motor complications in APD (2). This approach involves the continuous delivery of tailored doses of L-Dopa/Carbidopa directly to the jejunum via an electronic pump and a thin tube inserted through a percutaneous endoscopic gastrostomy with a jejunal extension (PEG-J) (2). Multiple clinical studies have demonstrated that LCIG effectively reduces motor fluctuations and dyskinesias in APD patients while increasing ON time and reducing OFF time (3–6). However, the available evidence mostly derives from regulatory trials and subsequent observational studies that relied on qualitative assessment tools, such as clinical scales and patient diaries (3, 7–9). These instruments are prone to recall bias, suffer from inter- and intra-rater variability, and lack the sensitivity to accurately capture brief or fluctuating motor abnormalities, like fluctuations and dyskinesias (10, 11). Moreover, the in-hospital clinical examination provides only a single snapshot of the patient's condition and cannot capture the full movie of motor performance variability throughout the day. This is particularly relevant in the context of APD, since symptoms fluctuation is one of the primary indications for device-aided therapies. Long-term, quantitative monitoring of motor symptoms through instrumental methods would substantially improve the characterization of intra-day variability in real-world conditions, thereby strengthening all phases of LCIG referral and management.

Recent advances in wearable technology have enabled long-term, real-world monitoring of PD using small inertial measurement units (IMUs) (12, 13). Combined with specialized algorithms, these sensors provide sensitive and objective detection of motor disorders in both controlled and ecological environments (14–17). IMUs have proven effective in quantifying motor disturbances, offering valuable insight into symptom variability and progression (18–20), with high patient adherence and acceptance (21, 22). Several studies have suggested the potential of wearable data to support patient selection for device-aided therapies and to refine treatment strategies (23–29). Among the motor functions measurable with these devices, gait has emerged as a sensitive marker of patients' therapeutic state, showing quantifiable fluctuations in parallel with medication effects throughout the day (30, 31). Accordingly, evaluating the variability of spatiotemporal gait parameters in APD could provide a robust tool to quantify fluctuations and assess the stability of motor performance in real-life conditions (13).

Nevertheless, to date, only a few studies have applied wearable sensors to support clinical decision-making in APD patients

treated with LCIG (APD_{LCIG}). Kilinçalp and colleagues (28) investigated the prognostic value of sensor-based measures for identifying suitable candidates for LCIG, showing that patients with clearly identifiable OFF periods at baseline were more likely to benefit from the therapy. Additionally, Imbalzano and colleagues (32) used wearable sensors in a controlled hospital setting to quantify axial motor symptoms in APD_{LCIG}, demonstrating a positive effect of LCIG on spatiotemporal gait parameters. However, to the best of our knowledge, no studies have assessed gait in APD patients with and without LCIG by using long-term sensor-based monitoring to capture intra-day motor variability in real-world settings.

In this cross-sectional pilot study, we performed and compared long-term gait monitoring in APD_{LCIG} and those receiving the best oral dopaminergic therapy (APD_{L-Dopa}), using a validated wearable sensor in real-world settings. The primary aim was to objectively determine whether LCIG is associated with more stable motor control than oral dopaminergic therapy, as reflected by spatiotemporal gait parameters. We hypothesized that APD_{LCIG} would show lower variability in gait metrics than APD_{L-Dopa}, reflecting the stabilizing effect of continuous dopaminergic delivery. We also took the opportunity to briefly discuss the potential practical applications of wearable sensors in the clinical management of LCIG therapy.

2 Materials and methods

This multicenter, cross-sectional pilot study was conducted following the guidelines outlined in the “Strengthening the Reporting of Observational Studies in Epidemiology” (STROBE) statement. The study protocol was approved by the Institutional Review Board of Sapienza University of Rome, Italy (Prot. 0372/2022). All participants provided written informed consent, in compliance with the principles of the Declaration of Helsinki.

2.1 Subjects and clinical evaluation

We consecutively screened patients with APD undergoing neurological evaluation at the movement disorder outpatient clinics of Sapienza University of Rome and the University of Turin (Italy) between January 2023 and September 2025 for potential enrollment, according to the following inclusion criteria: diagnosis of idiopathic PD based on current consensus criteria and follow-up clinical evaluations (33), advanced disease stage according to the “5–2–1” criteria (including ≥ 5 doses of oral levodopa per day and/or ≥ 2 h of “off” time per day, and/or ≥ 1 h of troublesome dyskinesia per day) (34) or ongoing treatment with LCIG as a device-aided therapy for PD for at least 3 months; ability to walk

independently (Hoehn and Yahr scale – H&Y ≤ 4). We excluded patients with a diagnosis of possible or probable atypical parkinsonism; device-aided therapies other than LCIG infusion (e.g., subcutaneous apomorphine or L-Dopa infusion; deep brain stimulation); previous MRI-guided focused ultrasound or radiofrequency lesioning surgery; inability to walk independently; severe cognitive impairment (Montreal cognitive assessment – MoCA < 18); comorbidities (e.g., neurological conditions other than PD, orthopedic and/or rheumatologic issues, or determining using chronic medications potentially affecting gait). We used standardized protocols to calculate the L-Dopa equivalent daily doses (LEDDs) for each patient (35). No participants were receiving other neuropsychiatric medications possibly affecting gait during the study period.

Before initiating the home-based gait monitoring with wearable sensors, all participants were assessed in the outpatient clinic by a movement disorder specialist. The evaluation included a structured battery of validated clinical scales: H&Y; Movement Disorder Society–Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III; Unified Dyskinesia Rating Scale (UDysRS) parts III–IV; the Wearing-Off Questionnaire-19 (WOQ-19); MoCA; frontal assessment battery (FAB); Beck depression inventory II (BDI-II); and Beck anxiety inventory (BAI). To capture prevalent clinical conditions at home, all clinical assessments were performed in the ON state (i.e., 1 h after the L-Dopa dose in APD_{L-Dopa} and at least 1 h after pump activation in the APD_{LCIG}, once the infusion had achieved a stable therapeutic level).

2.2 Wearable sensor and long-term monitoring

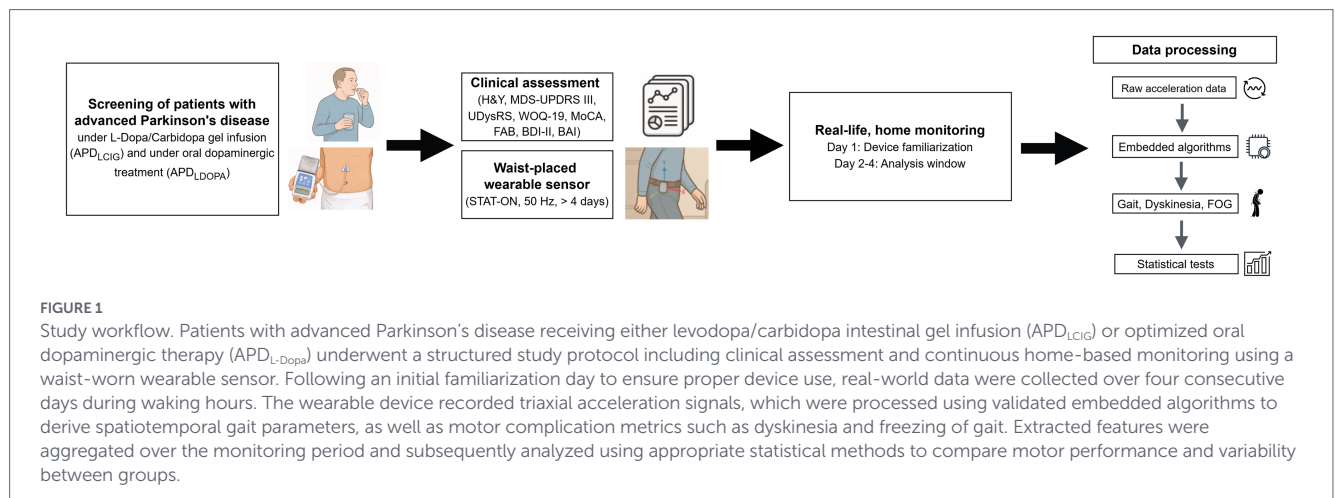
In addition to clinical assessments using standardized scales, patients underwent long-term gait monitoring with a validated wearable sensor (STAT-ON™, Sense4Care, Barcelona, Spain). STAT-ON™ is an inertial medical device developed and licensed for the continuous monitoring of motor symptoms in patients with PD during daily activities (36). The device is compact, measuring 9 × 6.3 × 2.1 cm and weighing 86 g, and features two ultra-low tri-axial nano-accelerometers, two microcontrollers, and a Bluetooth low-energy communication system (37). Its accelerometer operates within a ± 6 g range, offers a resolution of 12 bits, and has a sampling rate of 50 Hz, with a power consumption of 12 μ A and a battery life of up to 7 days under normal operating conditions. STAT-ON™ captures spatiotemporal gait parameters, such as step length, stride speed, stride fluidity and cadence, while utilizing advanced machine learning algorithms to automatically detect dyskinesia and freezing of gait (FOG). Data are stored in internal memory and can be downloaded to mobile devices through a specific application. The device has been certified as a Class IIa Medical Device and has successfully passed comprehensive testing for safe use in home environments (37).

In accordance with previously-validated protocols (37, 38), patients were instructed to wear the sensor on the left side of the waist using an elastic belt for a minimum of 4 days, ensuring at least 8 h of wear each day during waking hours. Caregiver support was encouraged to facilitate proper device use when necessary. The device operated automatically for its entire battery life without the need for manual activation or deactivation. Detailed instructions

were provided for the proper positioning and usage of the wearable sensor. The device was positioned such that the x, y, and z axes of the embedded sensors corresponded to the anterior, vertical (upward), and lateral (left) directions, respectively. Medical staff preconfigured the wearable sensor with the patient's clinical data (e.g., H&Y stage, age, and lower limb length measured from the left anterior-superior iliac spine to the ground). After completing the monitoring period and returning the wearable device, each patient attended a second clinical visit to assess compliance with sensor use and to retrieve the recorded data for later offline analysis.

2.3 Sensor-embedded algorithms and measures

Acceleration data were processed directly by the device using sensor-embedded algorithms. Feature extraction, gait detection, computation of spatiotemporal gait parameters, and motor symptom classification (including dyskinesia and FOG) were automatically performed onboard using previously validated machine learning models. The implemented algorithms, based on support vector machine (SVM) classifiers and both temporal and frequency-domain features, have been described and validated in prior studies (39–42). The device outputs precomputed gait metrics, including number of steps, step length, stride speed, cadence, and stride fluidity, as well as summary measures of dyskinesia and FOG. These outputs were exported and used for subsequent analysis without additional signal-level processing. A brief description of the underlying processing approach is provided below for completeness, while full methodological details are available in the referenced validation studies (39–42). Acceleration data is divided into 3.2-s segments with a 50% overlap, and gait detection is carried out using a SVM classifier with a radial basis function kernel. The SVM model adopts two input features based on energy levels within the frequency bands of [0.1, 3] Hz and [0.1, 10] Hz. Strides are identified by detecting minima in the forward acceleration signal, excluding the first and last strides to ensure greater consistency. Key gait parameters, including number of steps, step length (estimated through the inverse pendulum model) (39), stride speed (forward velocity per stride), cadence (steps per minute), and stride fluidity (computed as the energy content in the 0.1–10 Hz frequency band) (41), are subsequently extracted and provided as average values over one-minute time frames. Dyskinesia detection is triggered when energy levels in the 1–4 Hz frequency band exceed a predetermined threshold while remaining below a threshold in the 0–20 Hz range for a minimum of 6 s, reducing false positives from voluntary movements (40). For FOG detection, the SVM model incorporates both temporal and spectral features (means, integrals, temporal and spectral kurtosis, autoregression coefficients) derived from three-axis accelerometer data (42). The system computes the time spent in dyskinesia every 10 min and records the number and duration of FOG episodes every minute. To optimize the technical reliability of kinematic data, analyses were limited to the three days following the clinical visit, excluding the first day to allow sensor familiarization and minimize behavioural adaptation effects. Moreover, one-minute epochs with an average walking-bout length ≤ 6 steps were excluded from the analysis of gait parameters. This approach allows to minimize estimation variability, thereby



ensuring robust and comparable gait parameter quantification across subjects.

The overall study workflow, including patient selection, data collection, processing, and analysis, is displayed in [Figure 1](#).

2.4 Statistical analysis

Due to the exploratory nature of the study, no formal *a priori* sample size calculation was conducted. As each participant contributed to a single aggregated measure and no temporal changes were analysed, the study was treated as cross-sectional. An iterative matching procedure was applied, selecting subsets of APD_{LCIG} and APD_{L-Dopa} to optimize baseline comparability while preserving the largest feasible sample size. Matching was performed on age, disease duration, and H&Y stage to ensure clinical balance between groups. More in detail, multiple combinations of patients were iteratively evaluated, and subsets were retained when they minimized between-group differences across these variables while maintaining adequate group sizes. The final matched sample was selected based on the best achievable balance across matching variables, as assessed by descriptive comparisons, acknowledging the exploratory nature of this approach.

Descriptive statistics were applied to summarize the demographic and clinical characteristics of APD patients, with continuous variables reported as mean $\pm$ standard deviation. The Shapiro–Wilk test was applied to assess normality of distribution for all continuous variables, revealing non-normal distributions for several key measures. Accordingly, the Mann–Whitney U-test was used to compare demographic and clinical features as well as sensor-based measures between patient subgroups (APD_{L-Dopa} vs. APD_{LCIG}), with statistical significance defined as $p < 0.05$. Categorical variables, when present, were compared using the chi-square test.

To quantify motor fluctuations and assess the stability of patients' motor performances in real-world settings, the coefficient of variation (CV) was calculated and compared for all gait spatiotemporal parameters, including step length, stride speed, cadence, and stride fluidity. The CV was computed as:

$$CV = \frac{SD}{Mean}$$

where *SD* denotes the standard deviation of each parameter and *Mean* represents its average value. For each participant, the CV was calculated using all measurements collected over the full 3-day monitoring period. Lastly, to investigate potential clinical–behavioural correlations between sensor-derived measures and clinical scores, Spearman's correlation analysis was also performed. Adjustment for multiple testing was applied to the outcomes using the Benjamini–Hochberg correction (False Discovery Rate – FDR), and effect sizes were calculated using Cliff's delta (δ) when appropriate.

Statistical analysis was performed using the SPSS package, Version 29.0 (IBM, Armonk, NY, USA). Only datasets meeting predefined quality and wear-time criteria were included, resulting in complete data for all analyzed participants. A thorough pre-analysis review confirmed the absence of missing values. For all statistical tests, the significance level was set at $\alpha < 0.05$ (2-tailed).

3 Results

From the APD cohort screened during routine neurological evaluations, 79 patients underwent clinical evaluations and long-term gait monitoring with the wearable sensor at home. Of these, 21 were receiving LCIG infusion, and 58 were treated exclusively with oral dopaminergic therapy. After the matching procedure to improve baseline comparability between groups, the final analytical sample comprised a total of 43 subjects, including 15 APD_{LCIG} (9 men and 6 women) and 28 APD_{L-Dopa} (22 men and 6 women). All 43 enrolled participants completed the study protocol without deviations or technical issues. All participants adhered to the compliance monitoring requirements and completed the sensor-based gait monitoring as requested. All subjects showed optimal adherence to the wearable device, complying with recording instructions and ensuring at least 8 h of monitoring per day for a minimum of 4 days.

3.1 Clinical features

When comparing baseline demographic and clinical variables, the two subgroups of patients resulted well balanced in terms of demographic features, disease stage and severity, cognitive status,

TABLE 1 Demographic and clinical features of patients with advanced Parkinson's disease.

Variable*	APD _{LCIG} (N = 15)	APD _{L-Dopa} (N = 28)	U-statistic, p-value
Age	77.1 ± 18.6	67.0 ± 11.5	U = 146.0, p = 0.105
Disease duration	12.4 ± 5.7	10.0 ± 3.1	U = 161.0, p = 0.213
Age at onset	58.5 ± 10.3	56.2 ± 11.4	U = 194.5, p = 0.702
Hoehn and Yahr	2.4 ± 0.5	2.2 ± 0.5	U = 181.5, p = 0.406
MDS-UPDRS III	24.4 ± 13.5	23.8 ± 9.4	U = 174.0, p = 0.690
UDysRS III	3.6 ± 4.2	3.6 ± 4.6	U = 193.5, p = 0.676
UDysRS IV	2.8 ± 3.8	2.4 ± 2.8	U = 208.0, p = 0.968
WOQ-19	3.6 ± 2.7	6.4 ± 4.1	U = 122.5, p = 0.026
FOG-Q	6.6 ± 5.2	7.0 ± 6.1	U = 161.5, p = 0.831
MOCA	24.2 ± 3.8	25.1 ± 3.1	U = 177.0, p = 0.405
FAB	13.5 ± 1.6	14.7 ± 2.8	U = 137.0, p = 0.062
BDI-II	6.8 ± 5.1	8.4 ± 7.2	U = 127.0, p = 0.464
BAI	10.2 ± 13.3	10.5 ± 9.9	U = 26.5, p = 0.542
LEDDs	1206.6 ± 492.0	1066.3 ± 478.0	U = 165.0, p = 0.331

APD_{LCIG}, patients with advanced Parkinson's disease treated with L-Dopa/Carbidopa intestinal gel infusion; APD_{L-Dopa}, patients with advanced Parkinson's disease on best medical treatment with oral L-Dopa; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II; FAB, Frontal Assessment Battery; FOG-Q, freezing of gait questionnaire; LEDDs, Levodopa Equivalent Daily Doses; MoCA, Montreal Cognitive Assessment; MDS-UPDRS, Movement Disorder Society–Unified Parkinson's Disease Rating Scale; UDysRS, Unified Dyskinesia Rating Scale; WOQ-19, Wearing-Off Questionnaire-19. *All clinical assessments were performed in the ON state of therapy. Bold values indicate statistically significant results.

anxiety and mood symptoms, and LEDD (all factors that could otherwise influence the interpretation of spatiotemporal gait parameters). While the severity of dyskinesia, assessed through UDysRS parts III and IV, was comparable between groups, APD_{LCIG} reported lower WOQ-19 scores, indicating fewer self-reported symptoms fluctuations compared to APD_{L-Dopa}. All the clinical and demographic variables included in the analysis are summarized in Table 1.

3.2 Sensor-derived measures

Sensor-based analyses revealed some differences in mobility patterns of the two patients' groups. More in detail, during the monitoring period, APD_{LCIG} took a similar number of steps and presented similar average values of step length, stride speed, cadence, and stride fluidity compared with APD_{L-Dopa} (all $p > 0.05$). Also, total time and

percentage of time spent with dyskinesia, as well as time spent with FOG did not differ between groups (all $p > 0.05$). However, variability in spatiotemporal gait parameters was consistently reduced in APD_{LCIG}, with significantly lower CV for stride speed ($p < 0.001$), step length ($p = 0.011$) and stride fluidity ($p = 0.007$). These differences in gait variability parameters remained significant after correction for multiple comparisons (FDR, $p < 0.05$) and were supported by moderate-to-large effect sizes, as indicated by Cliff's delta (δ ranging from -0.48 to -0.71) (Table 2; Figure 2).

Among the spatiotemporal gait parameters, in the final analytical sample ($n = 43$), mean stride fluidity, step length, and stride speed exhibited moderate inverse correlations with age ($r = -0.53$ to -0.58 , all $p < 0.001$), while step length and stride speed were also moderately and negatively associated with disease severity as reflected by H&Y stage ($r = -0.50$ and -0.52 , respectively; both $p < 0.001$) (Figure 3). All these associations remained significant after correction for multiple comparisons (FDR, $p < 0.05$).

4 Discussion

In this observational, cross-sectional pilot study, long-term home monitoring of gait with a wearable sensor enabled an objective comparison of real-life mobility between two clinically matched cohorts of APD patients treated with either LCIG infusion or optimized oral dopaminergic therapy. Despite comparable disease duration and severity, APD_{LCIG} showed less severe motor fluctuations, as clinically shown by lower WOQ-19 scores and objectively indicated by reduced intra-day variability of spatiotemporal gait parameters, compared with APD_{L-Dopa}. Overall, these findings suggest that LCIG therapy is associated with superior quality and stability of real-life movement compared with optimized oral dopaminergic treatment. From a clinical perspective, these results support the use of LCIG to reduce subjective motor fluctuations and improve the stability of motor performance in daily life.

To minimize potential confounding, we implemented strict inclusion criteria and several methodological precautions, with particular attention to clinical variables known to affect spatiotemporal gait parameters, including age, disease severity, orthopedic comorbidities, anxiety and mood disorders, and cognitive status. Although recruiting a clinically homogeneous cohort of patients with APD is inherently challenging, the two subgroups (APD_{LCIG} and APD_{L-Dopa}) were carefully matched for all major demographic and clinical characteristics to ensure a reliable comparison. Participants also received clear, standardized instructions for sensor placement and use during home monitoring, with caregiver support encouraged when needed to further reduce the risk of handling errors.

A first finding of this study concerns the epidemiological distribution of the considered treatment modalities among the APD patients screened for eligibility. Approximately 25% of those meeting the inclusion criteria were receiving LCIG, whereas the remaining ~75% were treated exclusively with best medical oral therapy. This proportion is largely consistent with observations from the literature (43–45). Although the exact percentage of APD patients treated with LCIG is not well established and varies

TABLE 2 Gait parameters of patients with advanced Parkinson's disease.

Variable	APD _{LCIG} (N = 15)	APD _{L-Dopa} (N = 28)	p-value (adjusted)	Cliff's δ
Total number of steps	32500.5 $\pm$ 18905.1	26994.1 $\pm$ 18420.3	U = 166, p = 0.268 (0.344)	−0.21
Average cadence	38.1 $\pm$ 3.2	38.8 $\pm$ 3.1	U = 175, p = 0.379 (0.426)	−0.17
CV cadence	0.11 $\pm$ 0.02	0.12 $\pm$ 0.02	U = 137, p = 0.065 (0.122)	−0.35
Average step length	0.79 $\pm$ 0.14	0.84 $\pm$ 0.12	U = 156, p = 0.173 (0.260)	−0.26
CV step length	0.16 $\pm$ 0.02	0.20 $\pm$ 0.05	U = 110, p = 0.011 (0.033)	−0.48
Average stride speed	0.50 $\pm$ 0.10	0.55 $\pm$ 0.10	U = 138, p = 0.068 (0.122)	−0.34
CV stride speed	0.17 $\pm$ 0.02	0.22 $\pm$ 0.07	U = 61, p < 0.001 (0.009)	−0.71
Average stride fluidity	7.8 $\pm$ 2.3	7.6 $\pm$ 1.4	U = 106, p = 0.929 (0.929)	−0.50
CV stride fluidity	0.25 $\pm$ 0.06	0.31 $\pm$ 0.08	U = 103, p = 0.007 (0.032)	−0.51

APD_{LCIG}, patients with advanced Parkinson's disease treated with L-Dopa/Carbidopa intestinal gel infusion; APD_{L-Dopa}, patients with advanced Parkinson's disease on best medical treatment with oral L-Dopa; CV, coefficient of variation. Bold values indicate statistically significant results.

substantially across health-care systems, real-world evidence consistently indicates that only a minority of APD patients receive any device-aided therapy, with estimates ranging from about 15% to over 40% across studies (43–45). In the present work we did not include APD patients treated with device-aided therapies other than LCIG infusion. Given the specialized expertise of the participating centers in movement disorders management, it is likely that the proportion of APD patients receiving a device-aided therapy would have been higher if patients treated with other device-aided options (such as deep brain stimulation or continuous subcutaneous apomorphine or L-Dopa infusion) had also been included. However, it is well established that, despite their proven value, device-aided therapies remain underused in real-world practice, largely because treatment decisions are often shaped by non-clinical factors rather than consistent guideline-based criteria (45, 46).

4.1 L-Dopa/Carbidopa intestinal gel infusion in advanced Parkinson's disease

Our clinical and demographic matching of the two subgroups ensured that patients entered the comparison with largely similar baseline characteristics. As expected, APD_{LCIG} showed lower WOQ-19 scores than APD_{L-Dopa}, indicating a reduced severity of both motor and non-motor fluctuations. This finding is fully consistent with evidence from clinical trials and real-world observational studies demonstrating that continuous dopaminergic delivery with LCIG substantially reduces OFF time, improves ON time, and significantly attenuates motor symptom variability (3, 47–50). This clinical advantage was objectively supported by long-term wearable sensor monitoring, which revealed markedly lower intra-day variability in key spatiotemporal gait parameters in our LCIG group. Differences in fluctuation-related gait dynamics would have otherwise remained difficult to capture without prolonged and ecologically valid monitoring. This gait pattern suggests that continuous dopaminergic delivery achieved through LCIG infusion not only reduces subjective fluctuation burden but also translates into more stable motor performance under real-life conditions. Clinically, this improved stability may be particularly relevant for activities of daily living, where consistent motor output, rather than peak performance, is required.

From a pathophysiological perspective, LCIG acts by smoothing intra-day motor fluctuations and limiting disabling dyskinesia, thereby leading patients to perceive an overall increase in ON time, an effect traditionally captured by clinical scales and patient diaries (51). This effect is consistent with the therapeutic rationale of LCIG, which aims to stabilize plasma L-Dopa levels and minimize the oscillations associated with intermittent oral dosing. Although not directly assessed in the present study, greater motor stability may plausibly translate into improved functional autonomy. This has potential implications for fall risk reduction and mobility-related disability. In line with this interpretation, increased stride-to-stride variability of spatiotemporal gait parameters is a well-established marker of impaired gait automaticity and instability, and has been consistently associated with reduced mobility and an increased risk of falls in both laboratory and real-life settings in PD (52–55). In general, although APD is often characterized by axial symptoms that are poorly responsive to dopaminergic therapy (56, 57), several spatiotemporal gait parameters remain sensitive to dopaminergic modulation (58, 59). Since changes in gait metrics have been shown to parallel the therapeutic responsiveness of appendicular motor functions (60), gait-based telemonitoring may offer a complementary approach for capturing global motor performance and informing treatment optimization in APD.

While we observed clearly increased gait variability in APD_{L-Dopa} compared with APD_{LCIG}, the absolute values of spatiotemporal metrics as well as FOG occurrence were largely comparable between groups. At first glance, this might suggest that overall gait performance was similar. However, mean values of gait parameters are known to be relatively insensitive to short-term motor fluctuations and are strongly influenced by multiple individual and environmental interfering factors, which may mask between-group differences in APD (61–63). Individual and environmental factors may also contribute to substantial discrepancies in the absolute values of spatiotemporal gait parameters recorded in home-based versus supervised settings (64, 65). Indeed, mobility assessed in real-world, unsupervised conditions reflects complex interactions between physiological, behavioral, cognitive, and environmental influences, leading to potential discrepancies even when average values appear similar. Supervised or aggregated mean measures tend to capture a patient's "best" performance rather than their typical day-to-day motor behavior, thereby reducing sensitivity to

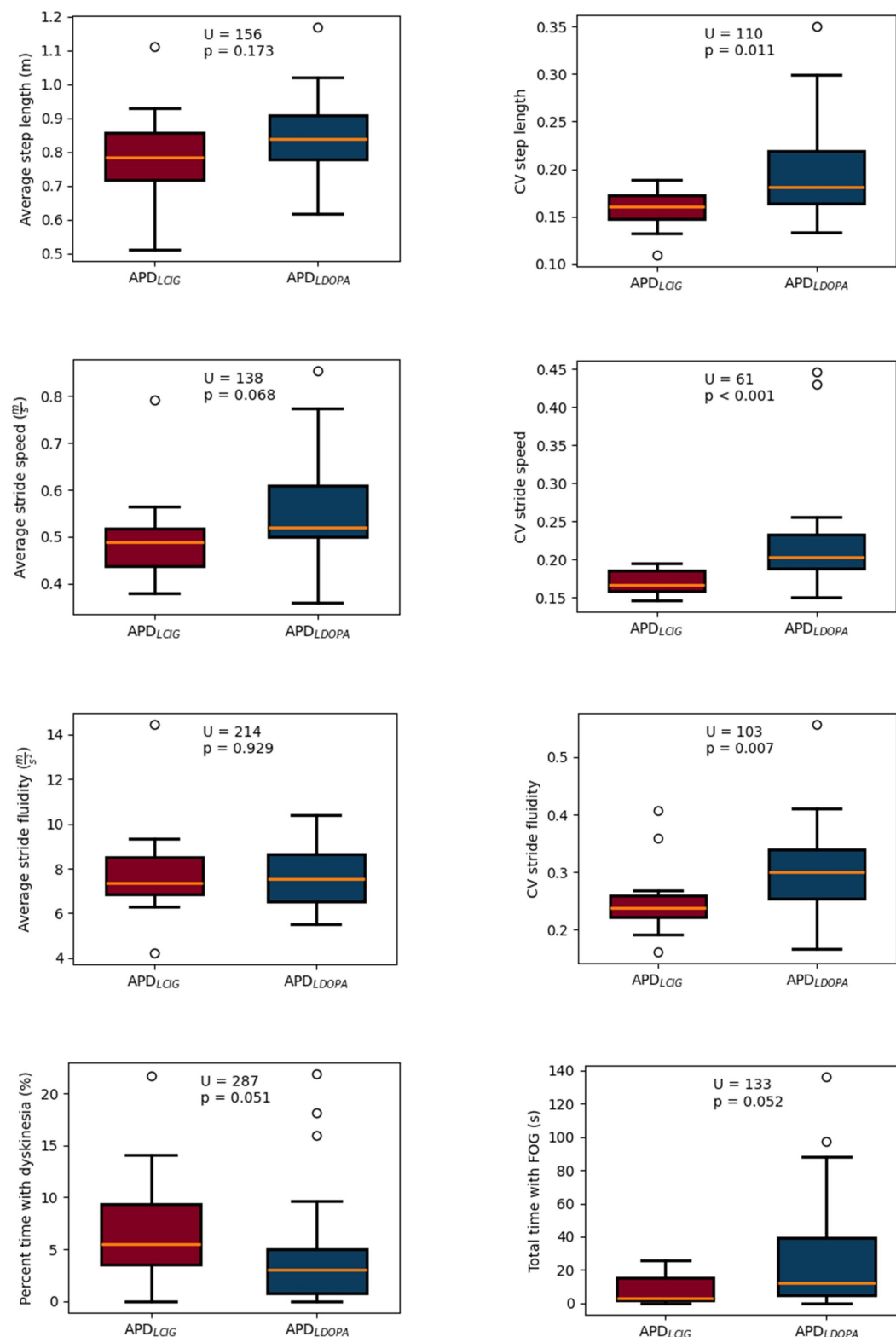
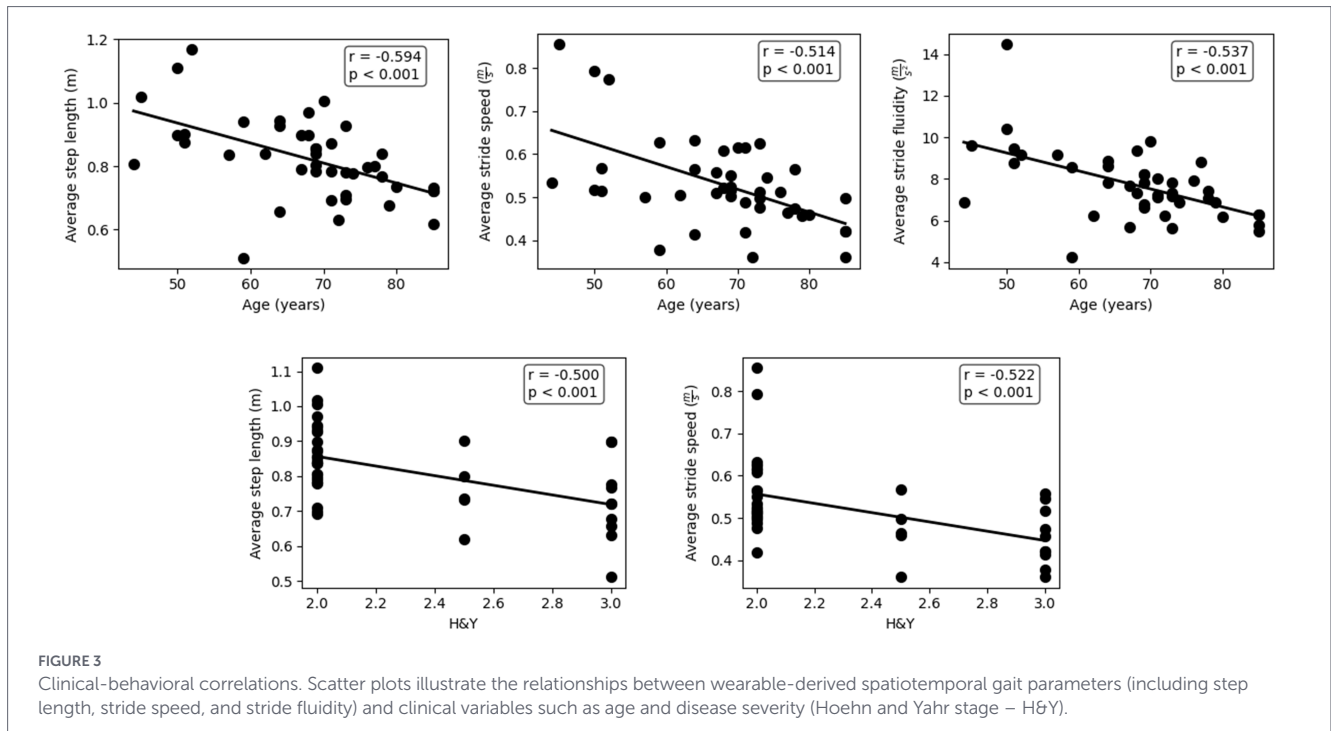


FIGURE 2

Main sensor-based measures. Wearable-derived spatiotemporal gait metrics in patients with Parkinson's disease under L-Dopa/Carbidopa Gel Infusion (LCGI) and those under oral dopaminergic treatment (LDOPA). Boxplots illustrate group distributions of key spatiotemporal gait parameters derived from continuous home-based monitoring using a waist-worn wearable sensor, including total number of steps, cadence, step length, stride speed, and stride fluidity, along with their corresponding coefficients of variation (CV) as measures of gait variability. Central lines indicate medians, boxes represent interquartile ranges, and whiskers denote standard deviations.



fluctuation-related impairment (66). This limitation is particularly relevant in APD, where motor complications are characterized by temporal instability rather than persistent deficits. Accordingly, similar mean values across groups do not exclude meaningful differences in the stability and consistency of motor output. This distinction has important clinical implications, as treatment-related benefits may remain undetected if only average gait performance or brief clinical assessments are considered. Moreover, it should be noted that, given the comparable disease severity between groups, distinct differences in the absolute values of spatiotemporal gait parameters and FOG occurrence would not be expected (67). In contrast, variability measures capture the moment-to-moment stability of motor control and therefore provide a more sensitive index of fluctuation-related impairment (61, 68, 69). From this perspective, the observed increase in gait variability in APD_{L-Dopa} likely reflects less stable motor control across the day, despite comparable average performance, in agreement with previous studies showing that variability-derived metrics better reflect real-world motor fluctuations than absolute spatiotemporal parameters alone (66, 70). Therefore, variability metrics may represent more sensitive and clinically meaningful digital measures for monitoring treatment response in APD. The significant correlations of spatiotemporal gait parameters with demographic and clinical features, including disease severity, further strengthen our observations. Indeed, these associations underscore the close interplay between overall clinical status and gait quality in free-living settings in PD (71, 72).

Further consideration concerns the observation of comparable time spent with dyskinesia in our APD_{LCIG} compared with APD_{L-Dopa}. This result may appear in contrast with previous studies consistently reporting a reduction in troublesome dyskinesia burden following LCIG infusion (73–76). This apparent inconsistency may partially be related to differences in dyskinesia assessment methods across studies. Indeed, while the sensor quantifies the duration of dyskinetic

activity, it does not provide information on dyskinesia severity. It is therefore plausible that APD_{LCIG} may exhibit more prolonged but mild dyskinesia, whereas APD_{L-Dopa} could experience more intense, short-term peak-dose dyskinesia associated with intermittent drug delivery. Such differences in phenomenology and severity would not be distinguished by the sensor but could nevertheless account for the observed similarity in dyskinesia duration. Accordingly, the comparable time spent with dyskinesia observed in APD_{LCIG} and APD_{L-Dopa} may reflect a shift from troublesome to non-troublesome dyskinesia in the APD_{LCIG} group, indicating a reduction in clinical impact despite similar overall duration. Supporting this interpretation, our APD_{LCIG} were clinically stable and did not report troublesome involuntary movements, yet they may have been unaware of subtle, low-amplitude trunk dyskinesia (77, 78). A possible impaired awareness of motor issues in APD further reinforces the need for quantitative, instrumented approaches such as wearable sensors, especially in advanced stages where clinical fluctuations become less reliably captured through patient self-report. Wearable sensors may be therefore particularly valuable in the context of APD, providing objective measures of dyskinesia and motor fluctuations that are not fully captured by clinical tools.

As an alternative hypothesis, despite an overall benefit at the group level, several reports have described a subset of patients who develop new or persistent dyskinesia after LCIG initiation, particularly diphasic or more complex patterns (74, 79–82). This paradoxical response has been attributed to an extremely narrow therapeutic window in some APD patients, maladaptive dopaminergic plasticity resulting from long-standing L-Dopa exposure, and challenges in titrating the optimal LCIG dose in individuals with heightened susceptibility (74). Given that the waist-mounted wearable used in our study captures dyskinesia involving both the trunk and lower limbs, it cannot be excluded that this phenomenon was particularly represented in our LCIG cohort. Lastly, an additional contributing factor may be the uneven sex distribution between groups, with a higher

proportion of women in the APD_{LCIG} subgroup. Women with PD may indeed be more prone than men to developing L-Dopa-induced dyskinesia due to sex-related biological and pharmacokinetic factors (83–85).

4.2 Wearable sensors for the management of LCIG infusion

While our data do not directly address clinical decision-making or medication-titration, hypothetical clinical applications to suggest are promising. The clinical management of LCIG infusion presents several challenges, including patient selection, medication titration, and the longitudinal monitoring of treatment efficacy and safety, that may benefit from the integration of wearable sensor technology (86).

Regarding patient selection, in line with established clinical practice (87, 88), quantifying ≥ 2 h/day of OFF time and ≥ 1 h/day of troublesome dyskinesia is essential to identify APD patients inadequately controlled on optimized oral regimens who may be appropriate candidates for device-aided therapies such as LCIG infusion. These thresholds were originally derived from expert consensus and patient-reported motor diaries (88). High-resolution wearable monitoring may enable a data-driven recalibration of these cut-offs, better aligning them with real-world motor impairment and functional disability. Supporting this observation, our findings showed that long-term, home-based monitoring with a single wearable sensor could reliably quantify dynamic changes in patients' motor status and the occurrence of dyskinesia, identifying distinct mobility patterns in patients treated with different therapeutic strategies. Wearable sensors used in free-living conditions may therefore enhance patient selection by providing objective, ecologically valid metrics that do not rely on patient or caregiver reporting and that may also have prognostic value in predicting treatment response, as previously demonstrated (28). This approach may help identify patients who are most likely to benefit from device-aided therapies, beyond conventional diary-based criteria.

With respect to medication titration, LCIG dose adjustment is not always conducted under prolonged in-hospital supervision. Indeed, in many centres, it is performed in outpatient settings through brief, repeated assessments (89, 90). Even during hospitalization, however, the immediate post-PEG-J initiation period does not fully reflect the patient's home condition due to environmental and activity-level differences, as well as attentional influences (a Hawthorne-like behavioural effect) (91–93). Moreover, LCIG initiation often requires discontinuation of long half-life dopaminergic agents (e.g., dopamine agonists, enzyme inhibitors), which frequently necessitates additional LCIG adjustments after discharge, when continuous supervision is no longer possible (94). Prolonged home-based monitoring with wearable sensors can capture real-world motor performance, including intra-day variability, during this critical phase, thereby supporting a more accurate and individualized titration of LCIG. In clinical practice, this could translate into more efficient dose optimization and reduced need for repeated in-hospital assessments.

Finally, during chronic LCIG infusion, consistent clinical follow-up is required to maintain therapeutic efficacy and adapt infusion parameters to evolving clinical needs, including progression of motor fluctuations or emergence of dyskinesia (94). Wearable sensors provide objective, continuous information on motor status that can reveal subtle deterioration or suboptimal treatment control, allowing

clinicians to modify infusion settings timely and sustain long-term treatment effectiveness.

This study has some limitations to be acknowledged. First, despite multi-day monitoring, the cross-sectional analytical design prevents causal inference, limiting the interpretation of between-group differences. The observed associations should be therefore interpreted as descriptive rather than indicative of treatment effects, as potential confounding factors and selection biases cannot be fully excluded. In particular, the lack of longitudinal data prevents within-patient comparisons over time, which would allow for a more reliable evaluation of treatment effects while minimizing the influence of inter-individual variability. Longitudinal and randomized studies are warranted to confirm our findings and establish causality. Second, the relatively small sample size, particularly in the APD_{LCIG} group, may reduce statistical power and limit the generalizability of the findings. In addition, the sex imbalance between subgroups may have contributed to variability and potential residual confounding. Therefore, the results should be interpreted with caution and confirmed in larger cohorts. Third, despite careful matching for key demographic and clinical variables and for overall physical activity (estimated by daily step count), residual heterogeneity cannot be excluded. Indeed, confounding may derive from unmeasured or incompletely captured factors, such as differences in motor fluctuation patterns, non-motor burden, or environmental influences on patients' daily activity. Fourth, the wearable sensor quantifies dyskinesia duration but cannot distinguish its phenomenology or severity, which may vary across patients and treatment groups. Overall, larger studies with extended, repeated monitoring will be required to validate and generalize our findings.

5 Conclusion

This cross-sectional, observational pilot study provides preliminary objective and quantitative evidence suggesting that LCIG is associated with a more stable gait pattern than optimized oral dopaminergic therapy. Although causal interpretations cannot be established, this effect likely reflects more consistent motor control throughout the day due to continuous dopaminergic delivery, potentially resulting in overall improved physical activity. By capturing fluctuation-related motor impairment through gait variability metrics, wearable sensor technology may represent a valuable tool to enhance the clinical management of LCIG, supporting patient selection, medication titration, and the longitudinal monitoring of treatment efficacy and safety.

Future research should assess whether incorporating wearable sensors into the main phases of LCIG management, including patient selection, medication titration and the longitudinal monitoring of treatment efficacy and safety, results in meaningful clinical advantages. Extending this methodological approach to other device-aided therapies, such as alternative infusion systems (e.g., subcutaneous L-Dopa or apomorphine) or deep brain stimulation, may further clarify the value of continuous real-life motor monitoring in APD. Lastly, the integration of sensor-derived metrics into adaptive or closed-loop therapeutic frameworks could enable more precise and personalized treatment strategies for patients with APD.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the corresponding author upon reasonable request.

Ethics statement

The studies involving humans were approved by the Institutional Review Board of Sapienza University of Rome, Italy (Protocol number: 0372/2022). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

AZ: Conceptualization, Formal analysis, Writing – review & editing, Writing – original draft, Methodology, Investigation, Visualization, Data curation. LB: Writing – review & editing, Software, Formal analysis, Methodology, Writing – original draft, Data curation, Investigation. DR: Writing – review & editing, Conceptualization, Writing – original draft, Visualization, Investigation. GI: Conceptualization, Writing – review & editing, Investigation, Writing – original draft, Visualization. MP: Writing – review & editing, Investigation, Writing – original draft, Visualization, Conceptualization. MF: Writing – review & editing, Writing – original draft, Data curation, Visualization, Investigation. CA: Supervision, Writing – original draft, Writing – review & editing, Data curation, Visualization, Investigation. EB: Writing – original draft, Visualization, Investigation, Writing – review & editing. LL: Visualization, Writing – original draft, Supervision, Writing – review & editing. GO: Writing – review & editing, Supervision, Visualization, Writing – original draft. AS: Visualization, Supervision, Conceptualization, Writing – review & editing, Writing – original draft.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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