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# Parkinsonian gait in elderly people: significativity of the threshold value of two and more falls per year

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## ABSTRACT

**Objectives:** Parkinsonism in the elderly presents a major risk factor for recurrent falls (2 and more falls per year) which is associated with increased morbidity. The main objective was to investigate explanatory variables relating to the risk of being recurrent fallers (RF) in persons with parkinsonian gait.

**Methods:** Seventy-nine among 172 eligible persons were enrolled in this prospective study, the findings of which were analyzed at 12 months. Motor and non-motor features, as well as follow-up interviews to identify falls, loss of ability to walk, fluctuating cognition, traumatic falls, all-cause hospitalizations and deaths were collated and results compared between non RF (zero and one fall per year) and RF. Bayesian model averaging was used to predict the probability of patients being RF from their medical history as well as from cognitive assessment, gait velocity, vision and posture.

**Results:** N=79, 0.58 men, 50% had Parkinson's disease, 14% other neurodegenerative parkinsonian syndrome, 23% vascular parkinsonism and 13% Lewy body disease, 58% were RF. Median age 81.2 years and median MMSE 25/30. A history of falls and of hallucinations, median odds ratio respectively 9.06 (CI 2.34-38.22), 4.21(CI 1.04-18.67) were associated with the highest odds ratios along with fluctuating cognition and abnormal posture. Two or more falls a year was a relevant threshold to distinguish a population with a high risk of comorbidity.

**Conclusion:** The whole history of falls, hallucinations and fluctuating cognition can be considered predictive of recurrent falls in elderly people with parkinsonian gait and provide a tracking tool for patient management.

**Key Words:** gait disorder, Parkinson's disease, elderly persons, fluctuating cognition, falls

## 1. INTRODUCTION

The risk of falling increases with age. Seventy percent of people aged 80 and above fall once a year. Of these patients, 30% are recurrent fallers who will fall more than once a year [1].

Risk factors for recurrent falls (two and more falls per year) in the elderly are cognitive impairment, gait disorders, balance disorders, fear of falling, sarcopenia, visual disorders, female sex, orthostatic hypotension, abnormal heart rhythm, heart failure and polypharmacy [2]. Walking is the most common activity at the time of the fall, and walking disorders increase with age, affecting 46% of persons aged 85 and above [3].

Parkinsonian gait is diagnosed in persons exhibiting at least three of the following symptoms: small shuffling steps, flexed posture, absent arm swing, one-piece U-turn, and festination [3].

The walking pattern is slow and combines several risk factors for falls: there is therefore a major risk of recurrent falls and of increased morbidity and mortality. Sixty percent of patients with idiopathic Parkinson's disease (PD) fall at least once a year, of whom 39% are subject to recurrent falls [4]. A link has been established between parkinsonian syndrome, neurocognitive disorders of executive functions and falls [5]. Postural instability is also a risk factor for recurrent falls in PD [6].

This aim of this study was to explore the link between an array of motor and neurocognitive variables and the risk of recurrent falls in an elderly population with parkinsonian gait. This open prospective single-center study was carried out under standard conditions of medical

care in community dwelling people and focused not only on individuals with PD but with other non-drug-induced parkinsonian syndromes.

## 2. MATERIALS AND METHODS

### 2.1 DESIGN

The primary endpoint of this prospective, non-interventional and observational study, in which cumulative data were analyzed at 12 months, was to describe the role of an array of explanatory variables in the risk of recurrent falls. We analyzed in the present study, the intermediary findings at 12 months of a two-year study named EVAMAR-AGEX (EVALuation de la MARche du sujet AGé et des fonctions EXécutives). According to the literature the term “fallers”, is based on the number of annual falls, so we decided to separate the population into two groups: non-recurrent fallers (NRF) who had zero or one fall per year and recurrent fallers (RF) who had at least two falls per year [4,7]. Secondary endpoints were loss of ability to walk, fluctuating cognition (FC), delirium, traumatic falls, all-cause hospitalization and death. All patients were recruited from March 2015 to September 2017 in the geriatric department of Strasbourg University Hospitals. The study was completed in September 2019.

### 2.2 CRITERIA

To be enrolled, patients had to be aged over 65, exhibit a parkinsonian gait but able to walk without assistance for at least 10 meters. Parkinsonian gait etiology was confirmed by a

neurologist. Criteria for parkinsonism (bradykinesia combined with a resting tremor, rigidity or both) were verified [8]. When it had been established that the patient had parkinsonism, Movement Disorders Society–Parkinson’s Disease criteria were applied to determine whether the patient met the criteria for PD as the cause of his or her parkinsonism [9]. If the criteria were positive, PD was retained as a presumptive diagnosis provided the patient showed an excellent response to L-dopa [8]. For other etiologies: McKeith criteria [10] were applied for Lewy body disease, Movement Disorders criteria for other neurodegenerative pathologies causing parkinsonism [8], and Zijlmans’ criteria for vascular parkinsonism [11].

Participants were excluded if they had non-recovered delirium, a traumatic fall during rehabilitation preventing walking alone on 10 meters (inclusion criteria), unstabilized acute or psychiatric pathology, uncontrolled symptomatic orthostatic hypotension, untreated severe depressive syndrome, non-remitting cancer, heart failure, or respiratory failure. Subjects with a neurological deficit (except for parkinsonian gait) or a rheumatological or orthopedic disorder which could explain their falls, subjects with induced parkinsonism or normal-pressure hydrocephalus, and subjects scoring less than 18/30 on mini-mental state examination (MMSE) were also excluded. Patients on psychotropic medication could be enrolled provided they were on no more than 2 psychotropic drugs, e.g. benzodiazepine equivalent to alprazolam 1.5 mg/day or clozapine 25 mg/day, and provided that the parkinsonian gait was present before prescription. Subjects under legal protection or unable to understand information were excluded.

## 2.3 ASSESSMENT

Initial data were collected during two close visits. “No history of falls” participants were those with a history of no falls or who had fallen no more than once within the last 6 months, and who had no recollection of another fall or having narrowly avoided a fall in the year prior to inclusion (zero or one fall per year). Patients with more than one falls in the year prior to inclusion were considered as RF. Subjects were required to have had standard laboratory tests performed within the previous 6 months, and brain imaging within the previous year.

Full patient evaluation was carried out during the initial visits. Patients were asked about visual and auditory hallucinations. A motor-oriented neurological assessment was conducted based on the MDS-Unified Parkinson’s Disease Rating Scale revision [9] and the Functional Gait Assessment (FGA) scale [12]. The MDS-UPDRS scale used to establish parkinsonism was partially selected (and rated out of 56) to evaluate: speech (item 3.1), facial expression (item 3.2), finger tapping (item 3.4), hand movements (item 3.5), quick alternative movements (item 3.6), leg agility (item 3.8), ability to get up out of a chair (item 3.9), postural stability (item 3.12), posture (item 3.13) and body bradykinesia (item 3.14). Ten-item FGA were rated out of 30, the lower the score, the worse it was. All components are evaluated while the participant was walking. Items performed by the participant include walking on a walkway forward and backward walking as well as walking while turning the head, changing walking speeds, stepping over obstacles, climbing and descending stairs, and walking in tandem. Free gait velocity in meters per second was a subtest from FGA.

A Dual Task event or walking while talking task was carried out without assistance over a 10-meter walkway. Participants while walking were required to demonstrate verbal fluency: the number of stops and time taken to complete the walk were noted [13]. Neurocognitive evaluation comprised a Montgomery-Asberg Depression Rating Scale (MADRS) scored out of 60 points and a French version of the 16-item Free and Cued Selective Reminding Test with immediate recall (FCSRT-IR) [14] to assess information storage and recovery capacity rated out of 48, one-minute literal verbal fluency test for the ability to generate words in a given category and a Frontal Assessment Battery scored out of 18 points [15]. A Behavior Rating Inventory of executive dysfunction based on an apathy scale was completed with the caregiver in order to assess the loss of initiative (and scored out of 12). An Instrumental Activities of Daily Living (IADL) appraisal was also performed: the score of 16 marked the highest level of dependency. Following these examinations, a neurologist and geriatrician jointly decided whether to categorize the neurocognitive diagnosis as: absence of disorder, mild or major neurocognitive disorder [15,16]. Cognitive fluctuations prior to the initial visit were assessed and scored out of 16 using the Clinician Assessment of Fluctuation questionnaire [17]. Participants' comorbidities were calculated using Charlson's score on a scale of 10 based on aspects of the patient's history, age and neurocognitive status.

Visual testing was performed by an ophthalmologist and scheduled oculography was interpreted by a neurologist.



## 2.4 FOLLOW-UP

Follow up included telephoning participants and their caregivers every two months and a 12-month visit. The number of falls, whether or not traumatic, hospitalizations and deaths were registered. The Confusion Assessment Method (CAM) questionnaire [18] used to establish the diagnosis of delirium and Fluctuating cognition (FC) assessment were both recorded in the two-month period prior to the telephone call. The follow-up visit at 1 year included vital parameters, orthostatic hypotension, MMSE, recapitulation of falls, traumatic falls, hospitalizations, FC, delirium and mobility. The results were compared between NRF (zero or one fall) and RF (two and more).

## 2.5 STATISTICAL ANALYSIS

### 2.5.1 DESCRIPTIVE STEP

Explanatory variables collected are displayed as mean  $\pm$  SD for continuous variables and as number and percent for categorical variables. To verify that the null hypothesis is unlikely, independent *t*-test samples were used to examine mean differences between NRF and RF for continuous variables. For categorical measures,  $\chi^2$  tests were applied. For each tested variable, a probability value of less than 0.05 was regarded as a significant rejection of the null hypothesis. Resulting variables were to be RF or NRF at 12 months of follow up.

### 2.5.2 INFERENTIAL STEP

An inferential step using fully Bayesian techniques (Markov chains and Monte Carlo integrations, Mc MC, with R software) was applied to evaluate aggravating or protective

effects along with odds ratios (OR) expressed in percentiles (2.5%, 50% median and 97.5%). Median interval between the 2.5% and 97.5% percentiles contained the true parameter with a high probability. The posterior interval of credibility was used as confidence interval (CI). Sensitivity analyses were conducted to assess the robustness of the models. Logistic regression was carried out with each of the potential covariates for recurrent falls (yes/no), followed by Bayesian model averaging to select covariates jointly related to recurrent falls. Rather than P values, results depended on the posterior probability that a parameter was higher (or lower) than a given, clinically relevant threshold either with a change of category or a significant variation around a predetermined cut off score. Variable results were explained in terms of OR and probabilities.

## 2.6 STANDARD PROTOCOL APPROVAL AND PATIENT CONSENT

Ethics approval for this study was received from the Strasbourg University Hospitals Research Ethics Committee. All participants gave their informed consent to take part in the study in accordance with the Declaration of Helsinki. The study has been registered with ClinicalTrials.gov under the codename NCT02885493. Eligible patients were included after they had received the study information package, accepted the study conditions, and signed the informed consent form. The analysis presented here covers the first year of follow-up.

### 3. RESULTS

All the descriptive and Bayesian inference analyses provided information on most risk factors for recurrent falls. Cognitive and motor assessment results were highlighted in this context.

#### 3.1 DESCRIPTIVE VALUES

Of 172 eligible patients, 79 patients were enrolled (Fig. 1). The median age of participants was 81.2 years; the sex ratio was 0.58 in favor of men, and the mean MMSE score 24.72 (SD:  $\pm 3.43$ ) with a median of 25. Parkinsonian gait etiology was PD in 50%, other neurodegenerative parkinsonian syndrome in 14%, vascular parkinsonism in 23% and Lewy body disease in 13%. Fifty-seven percent of participants had a history of falls as defined above, 44% a history of hallucinations, and 13 participants (18%) were treated with clozapine. Forty-one percent of participants had a FC score of two or more, and 24% five or more (out of 16) at the initial visit.

In the first year of follow-up, a total of 536 falls were logged. Two patients with severe phenomena of freezing of gait had a total of 139 falls out of the 536. Twelve percent of falls were traumatic and 80 hospitalizations were recorded. NRF totalized 11 hospitalizations and 4 traumatic falls.

The threshold value of 2 or more falls per year during the 12-months follow-up allowed comparison of two groups, recurrent and NRF (Table 1). Of the 79 participating patients, 58% were recurrent and 42% NRF. Among the NRF, 8% were single fallers and 34% were zero

fallers, there was no significant difference between the two groups except for the MADRS scale. The two groups were significantly very different. RF were older, had more cognitive impairments, more orthostatic hypotension controlled, were more often polymedicated. They were more likely to have a history of hallucination and falls, and had more fluctuating cognition. PD was predominant compare to vascular parkinsonism in RF group. In the FGA free walking task item, walking speed was 0.66 m/sec (SD:  $\pm 0.24$ ) among NRF versus 0.54 m/sec (SD:  $\pm 0.21$ ) among RF. During the Dual Task, there was no statistically significant difference between NRF and RF. Walking speed dropped to 0.36m/sec (SD:  $\pm 0.18$ ) among NRF versus 0.35 m/sec (SD:  $\pm 0.16$ ) among RF (4 patients with non-applicable data). Postural stability (item 3.12) in the MDS-UPDRS displayed a median score of 2, which was identical for both groups. For posture (item 3.13) the median score in the RF group was 1.5 versus 1 in the NRF group.

Seven of 10 patients at the end of life or who died were RF, and 5 of them were diagnosed with PD. Regarding mobility (free walking, use of technical assistance, or loss of ability to walk), 9% of NRF showed a worsening in their functional autonomy compared to 37% of RF between the initial visit and 12-month follow-up analysis.

### 3.2 INFERENTIAL STEP

Univariate analysis was carried out to detect variables that promote falls and, contrariwise, those that appear to protect against falls. More than 25 variables were significant. Among them, hallucinations and a notional history of fall were strongly related to the risk of recurrent

falls: both had particularly high ORs (Table 2). On ophthalmology and on oculography, vertical jerks proved to be significantly different between groups. Compared to PD, vascular Parkinsonism seems to be protected against recurrent falls (probability being RF: OR Median = 0.2345; Pr OR > 1 = 0.0067 or being NRF: 1-Pr = 0.9933): this was not the case for other etiologies of parkinsonian gait (Table 3).

For multivariate analysis, those independent explanatory variables with the most significant OR were selected to establish a pattern of recurrent fall probabilities. Covariates jointly related to recurrent falls were selected. Bayesian model averaging was able to predict the probability of persons being in the RF group from their medical history as well as from their neurocognitive and motor evaluation. Predictors of recurrent falls in participants with Parkinsonian gait were history of falls, history of hallucinations, poor results at the free recall test, FC and posture disorders (Table 4). For example, taking into account the history of fall and hallucination, the probability of belonging to the faller group was 0.9242 (0.8118-0.9771). Conversely, in the absence of a history of fall and hallucination, the probability of belonging to the fall group was 0.1602 (0.0638-0.3134).

#### 4. DISCUSSION

The study involved an average-age population of 81.2 years, older than in previously published studies in the domain of parkinsonism. With the inference of Bayesian method, we try to explain the result with causal variables expressed in terms of probabilities that are easy

to compare. The explanatory variables that have the most impact or the most protective effect on becoming recurrent fallers are developed and discussed. The threshold value of two or more falls per year shows its effectiveness in separating two very different groups of patients both in terms of risk factors for falls and severity of their symptoms. This study confirms prior knowledge about risk factors of falling and brings information about explanatory variables never linked before this study with risk of falling in this population.

#### 4.1 HISTORY OF FALLS, POSTURE AND GAIT VELOCITY

A history of falls is predictive of recurrent falls in PD. This predictor was confirmed in our study for parkinsonian gait (with a high OR): this is most likely due to the fact that a history of falls is defined by at least 2 falls occurring in the previous year, thereby excluding participants who had experienced only one fall. Our population was at high risk of falls, with 58% of patients being RF, which is almost twice that of a general population aged over 80 years. Our result resembled that of a one-year prospective follow-up study in a population with PD and a mean age of 75 that reported 50.5% RF [19]. The prevalence of falls in a population with PD dementia is at 90% compared to 77% in diffuse Lewy body disease, but for a threshold value of one fall or more per year [20]. Analysis of Parkinsonian gait etiologies show that PD is predominant among RF and vascular Parkinsonism among NRF, corroborating the fact that patients with PD fall twice as often as those with other neurological pathologies [21]. In our study, loss of postural control, and posture disorders have an impact

on the risk of recurrent falls according to the MDS-UPDRS scale which assesses the severity of motor impairment in parkinsonism and determines the risk of recurrent falls particularly in the postural instability and gait disability subgroup. FGA scale and walking speed are useful for estimating the potential for falls in PD [22]. The overall mean FGA score of 17.66 (SD:  $\pm$  5.45; range 0-30) obtained in our study for NRF was equivalent to that for RF of 17.62 (SD:  $\pm$  6.66) in a population with PD and mean age of 68.55 years (SD:  $\pm$  9.53) [23]. This is probably due to an older population in our study.

A walking speed of 1.08 m/sec (95% CI: 1.02–1.14) has been observed in a PD population at high risk of falls [23]. In our population, the walking speed was very slow in both groups, especially because of the "slow walk" selection criterion. RF walked even more slowly than NRF. The walking speed coming out of subtest from FGA in our population was 0.59 m/sec (SD:  $\pm$  0.23) and slow down at 0.35m/sec (SD:  $\pm$ 0.17) in a dual task condition (4 patients from RF failed in Dual task test in our study). A walking speed of  $0.83 \pm 0.21$  m/sec has been described in a general population with a mean age of 80 years with difficulties in daily life and in this population the walking speed decreases to  $0.61 \pm 0.26$  m/sec when participants are in a in a dual task situation [24]. The mobilization of attention capacities results in an even more cautious walk and it thus appears that our parkinsonian gait population has a walking speed close to that of a population of the same age performing a double task. Walking speed and Dual Task tests do not appear to be as relevant in predicting the risk of recurrent falls in this elderly population with parkinsonian gait as in younger people.

## 4.2 NEUROCOGNITIVE DECLINE, FLUCTUATING COGNITION, CONFUSIONAL STATE AND HALLUCINATIONS

We scored neurocognitive disorders using different tests which revealed the highest OR in tests reflecting executive dysfunction, i.e. the sum of the three free recall tests in the FRCST-IR and apathy scale. A correlation between impaired executive function including attention and an increased frequency of falls has been established in the elderly. Good performances in these tests appeared protectives in our study.

A correlation has already been described between falls and delirium in a general, non-disaggregated population aged between 75 and 85 years [25]: in our study confusional states collated during the first year were also strongly linked to the RF group. While the utility of assessing cognitive fluctuations in Lewy body disease has been demonstrated, FC is not specific to this pathology. Such FC have hitherto not been considered a risk factor for falls. In our study, it appears that they are strongly linked to the RF group. The prevalence of hallucinations was high in our population: 18% among NRF and 63% among RF. In the study by Riedel *et al.* in 2010, the frequency of hallucinations was lower at 11.5%, although this was a group of patients all of whom had PD: their mean age was 70.7 years, and 14.9% had dementia [26]. The percentage of hallucinations reported in the study by Factor *et al.* was higher at 26%: this study excluded patients with advanced stages of PD dementia and linked hallucinations to executive dysfunction [27]. Psychotropic drugs were used more often in the RF group but it is nevertheless difficult to limit their use owing to the need to control



psychosis in PD and hallucinations in Lewy body disease [2]. If fluctuating cognition and confusional states can regress, we can hope to prevent their appearance.

#### 4.3 TOOLS

Given the major risk that patients with PD will fall, attempts have been made to devise fall prediction tools using multivariate analyses of independent variables. The mini best test was developed following a prospective study of a PD population with a mean age of 63 years. It proved to have 79% sensitivity to predict recurrent falls [28]. Another score was established in a younger population with PD and free of cognitive impairment (mean age 66 years) which was based on the total UPDRS score, freezing-of-gait score, symptomatic orthostatic hypotension, Tinetti score, and loss of postural control in the antero-posterior direction. Sensitivity was 78% and specificity 84% [29]. Another study, focusing on the previous year's history of falling, previous month's gait freezing and a walking speed of 1.1m/sec, showed an AUC at 0.80 [6]. A study with follow-up at 12 months, established a predictive panel for recurrent falls which included a history of two or more falls, the daily living UPDRS score, motor fluctuations, dosage of L-dopa equivalent, and showed an AUC at 0.84, which was further optimized after including the BERG scale score (to 0.86) [7].

The whole, history of falls, hallucinations, abnormal posture, has a strong link with recurrent falling. The presence of FC at 12 months is more linked to recurrent falling than presence of FC at M0, probably due to the necessary learning required for an optimal interview. Preserved executive function and MMSE higher than 25/30 provides protective effects.

Our study provides a new, easily accessible panel to predict the risk of recurrent falls in patients with parkinsonian gait. Age and neurocognitive disorders were not limiting factors since the inclusion criteria were broader than in other studies of this kind [28,30].

## 5. CONCLUSION

The results of our study were consistent with those of similar studies reported in the literature and were original in terms of the study of FC and statistical method. An elderly patient with parkinsonian gait and a history of falls (two and more) and hallucinations, as well as FC and executive dysfunction, can be considered to be a potential RF. By contrast, when cognitive functions are preserved, the elderly patient appears to be protected from complications and should be encouraged to maintain his or her cognitive abilities and physical activity focused on postural stability and posture. It seems essential to manage these patients both therapeutically and functionally by stabilizing posture and balance disorders and walking problems, as well as attempting to prevent or limit confusional states and preserved attention with cognitive rehabilitation.

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#### 7. CONFLICT OF INTEREST AND SOURCES OF FUNDING STATEMENT

None reported

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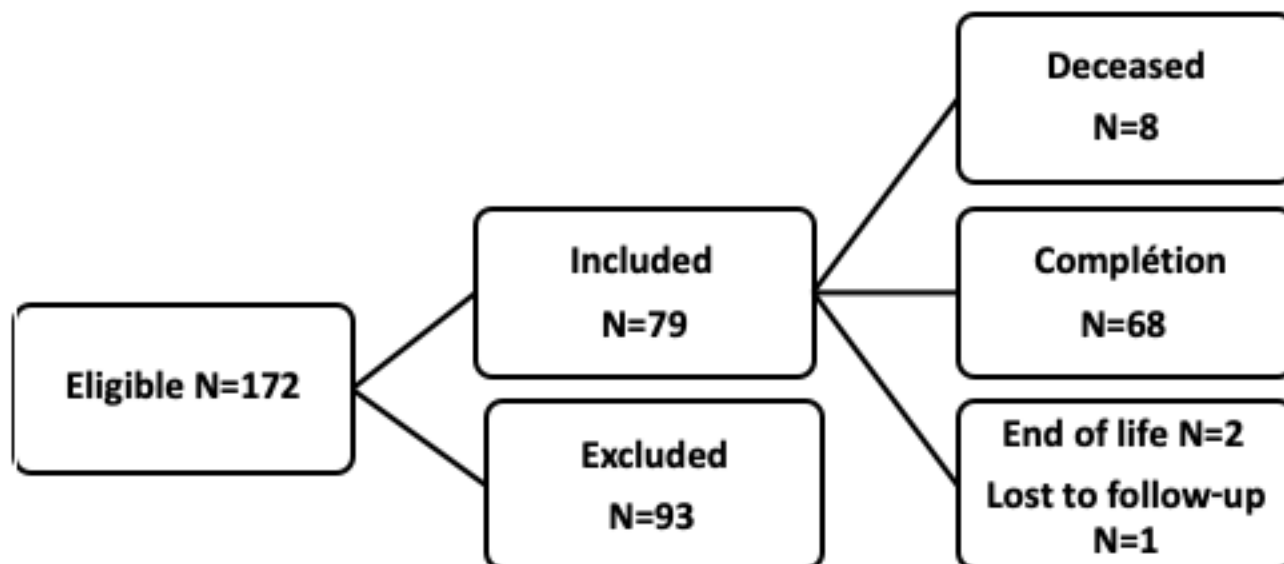
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Fig 1. Flowchart



**Table 1: Baseline patient characteristics.**

|  | NON-RECURRENT FALLERS<br>N=33 |              |        | RECURRENT FALLERS<br>N=46 |             |        | <i>P value</i>   |
|--|-------------------------------|--------------|--------|---------------------------|-------------|--------|------------------|
| Variable score                                   | %                             | Mean (SD)    | Median | %                         | Mean (SD)   | Median | <i>P&lt;0.05</i> |
| Age (y)  | -                             | 79.69 (6.58) | 81     | -                         | 82.34(5.98) | 83     | 0.03             |
| Male, n%   | 66%                           | -            | -      | 51%                       | -           | -      | NS               |
| Age at Parkinsonism diagnosis(y)                 | -                             | 77.21 (7.90) | 77     | -                         | 74.39(10.9) | 76     | 0.035            |
| Mean disease duration (y)                        | -                             | 2.48 (4.00)  | 1      | -                         | 7.95 (7.75) | 5      | <0.0001          |
| Parkinson's disease                              | 36%                           | -            | -      | 60%                       | -           | -      | 0.035            |
| No history of falls                              | 76%                           | -            | -      | 20%                       | -           | -      | <0.0001          |
| Previous hallucinations                          | 18%                           | -            | 0      | 63%                       | -           | 1      | <0.0001          |
| IADL 0-16  | -                             | 7.60 (3.60)  | 6      | -                         | 10.40 (3.2) | 11     | 0.0004           |
| Community dwelling                               | 91%                           | -            | -      | 83%                       | -           | -      | NS               |
| BMI  | -                             | 24.93 (3.86) | 24.9   | -                         | 23.13(4.73) | 22.95  | 0.03             |
| MMSE 0-30  | -                             | 26.51 (2.76) | 27     | -                         | 23.43(3.31) | 23.50  | <0.0001          |
| Major neurocognitive disorders                   | 24%                           | -            | -      | 59%                       | -           | -      | 0.0001           |
| MCI  | 24 %                          | -            | -      | 26%                       | -           | -      | 0.0001           |
| Clozapine  | 9%                            | -            | -      | 24%                       | -           | -      | 0.034            |
| CHARLSON score 0-10                              | -                             | 4.78 (1.65)  | 4      | -                         | 5.43 (1.61) | 5      | 0.043            |
| No cataract history                              | 63%                           | -            | -      | 60%                       | -           | -      | NS               |
| OH controlled                                    | 18%                           | -            | -      | 37%                       | -           | -      | 0.031            |
| Medications <sup>1</sup> except antiparkinsonian | -                             | 2.45 (1.34)  | 2      | -                         | 2.95(1.26)  | 3      | 0.04             |
| L-DOPA equivalent (mg/D)                         | 57%                           | 404(245)     | -      | 87%                       | 729(677)    | -      | 0.0005           |
| FGA 0-30   | -                             | 17.66 (5.45) | 17     | -                         | 11.88(7.09) | 11     | <0.0001          |
| Free Gait velocity (m/sec)                       | -                             | 0.66 (0.24)  | 9      | -                         | 0.54(0.21)  | 12     | 0.02             |
| MDS-UPDRS partial 0-56                           | -                             | 15.36 (6.88) | 15     | -                         | 19.18(8.46) | 19     | 0.016            |
| Optional use of stick                            | 0.09%                         | -            | -      | 0.19%                     | -           | -      | 0.019            |
| MADRS 0-60                                       | -                             | 14.60 (8.45) | 17     | -                         | 16.40(7.09) | 15     | NS               |
| FRCST-IR 3FR 0-48                                | -                             | 19.03 (7.80) | 19     | -                         | 12.90(7.80) | 14     | <0.0001          |
| FRCST-IR 3TR 0-48                                | -                             | 41.00 (6.16) | 43     | -                         | 36.20(9.57) | 38     | 0.005            |
| FAB 0-18   | -                             | 14.24 (3.67) | 15     | -                         | 12.75(3.81) | 14     | 0.043            |
| Apathy scale 0-12                                | -                             | 1.66 (1.42)  | 2      | -                         | 2.76(1.36)  | 3      | 0.0005           |
| Verbal fluency P letter/60sec                    | -                             | 10.03 (4.97) | 10     | -                         | 8.35(4.34)  | 8      | NS               |
| Educational level>6y                             | -                             | 13.00 (4.12) | 11     | -                         | 11.82(3.59) | 10.50  | NS               |
| CAF FC score 0-16                                | -                             | 1.36 (3.07)  | 0      | -                         | 4.22 (4.96) | 2      | 0.001            |

Y, year; N, total number; IADL, Instrumental Activities in Daily Living; BMI, Body Mass Index; MCI, Mild Cognitive Impairment; OH, Orthostatic Hypotension; Medications<sup>1</sup>: hypertensive and hypotensive drugs, psychotropic, anticholinergic and cholinergic drugs; CAF FC score, Clinical Assessment of Fluctuations fluctuating cognition score ; SD, Standard Deviation. FGA, Functional Gait Assessment; MADRS, Montgomery and Asberg Depression Rating Scale; MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale. FAB, Frontal Assessment Battery FRCST-IR 3TR, Free and Cued Selective Reminding Test with Immediate Recall and sum of 3 Total Recall; FRCTS-IR 3FR Free and Cued Selective Reminding Test with Immediate Recall and sum of 3 Free Recalls; VF, Verbal fluency

**Table2. Univariate analysis: Values linked to recurrent fallers**

| Variable                       | N  | OR. 2.5% | OR. Median     | OR. 97.5% | Pr (OR>1)       |
|--------------------------------|----|----------|----------------|-----------|-----------------|
| Educational level              | 79 | 0.4257   | 0.7857         | 1.4328    | 0.2112          |
| History of falls               | 79 | 4.3390   | <b>11.7826</b> | 35.2864   | <b>1.0000</b> ‡ |
| Previous hallucinations        | 79 | 2.7145   | <b>7.3458</b>  | 22.1399   | <b>0.9999</b> ‡ |
| Clozapine medication           | 79 | 0.8913   | <b>3.0611</b>  | 13.2611   | <b>0.9618</b> ‡ |
| Stroke history                 | 79 | 0.4445   | 1.3663         | 4.6625    | 0.7029          |
| Diabetes history               | 79 | 0.1416   | 0.4021         | 1.0412    | <b>0.0299</b> § |
| Atrial fibrillation            | 79 | 0.5849   | 1.7715         | 5.9136    | 0.8393          |
| Pace-Maker                     | 79 | 0.6344   | 2.7274         | 16.2241   | 0.9080          |
| Babinski sign                  | 78 | 0.7114   | 2.0353         | 6.2382    | 0.9067          |
| MDS-UPDRS 3.9 0-4              | 77 | 1.1425   | <b>1.7601</b>  | 2.8881    | <b>0.9964</b> ‡ |
| MDS-UPDRS 3.12 0-4             | 77 | 1.5746   | <b>2.6767</b>  | 5.0443    | <b>0.9998</b> ‡ |
| MDS-UPDRS 3.13 0-4             | 77 | 1.6796   | <b>3.1705</b>  | 6.6934    | <b>0.9999</b> ‡ |
| MDS-UPDRS 3.14 0-4             | 77 | 0.6058   | 1.1805         | 2.3043    | 0.6913          |
| MDS-UPDRS score 0-56           | 77 | 1.0056   | 1.0679         | 1.1402    | 0.9844          |
| FGA1 0-3                       | 77 | 0.1140   | <b>0.3385</b>  | 0.8962    | <b>0.0136</b> § |
| Walks for 6 meters             | 77 | 1.0057   | <b>1.0986</b>  | 1.2182    | <b>0.9816</b> ‡ |
| FGA score 0-30                 | 77 | 0.8019   | <b>0.8733</b>  | 0.9411    | <b>0.0000</b> § |
| Dual Task words                | 75 | 0.7973   | 0.9204         | 1.0522    | 0.1164          |
| Dual Task stop                 | 75 | 0.7542   | 0.9204         | 1.2417    | 0.3959          |
| Dual Task runtime              | 74 | 0.9830   | 1.0055         | 1.0306    | 0.6901          |
| MMSE score 0-30 To             | 79 | 0.7410   | <b>0.8310</b>  | 0.9293    | <b>0.0008</b> § |
| MADRS 0-60                     | 77 | 0.9716   | 1.0320         | 1.0985    | 0.8464          |
| IADL 0-16                      | 79 | 1.0995   | <b>1.2572</b>  | 1.4582    | <b>0.9998</b> ‡ |
| FAB score 0-18                 | 78 | 0.8003   | 0.9072         | 1.0175    | 0.0513          |
| FRCST-IR 3 TR 0-48             | 76 | 0.8868   | <b>0.9403</b>  | 0.9905    | <b>0.0097</b> § |
| FRCST-IR 3 FR 0-48             | 76 | 0.8458   | <b>0.9068</b>  | 0.9648    | <b>0.006</b> §  |
| VF P word                      | 78 | 0.8377   | 0.9266         | 1.0208    | 0.0636          |
| Apathy scale 0-12              | 78 | 1.2378   | <b>1.7306</b>  | 2.5528    | <b>0.9995</b> ‡ |
| Eye R Cornea                   | 55 | 0.0214   | 0.4069         | 5.3724    | 0.2513          |
| Eye L Cornea                   | 54 | 0.6038   | 2.2112         | 14.4125   | 0.8766          |
| Eye R Crystalline              | 65 | 0.6866   | 1.1723         | 2.0034    | 0.7242          |
| Eye L Crystalline              | 64 | 0.7244   | 1.2392         | 2.1699    | 0.7815          |
| Caratact                       | 77 | 0.6180   | 0.8229         | 1.0843    | 0.0842          |
| Glaucoma                       | 76 | 0.1652   | 0.7229         | 3.2223    | 0.3317          |
| Horizontal eye jerks           | 74 | 0.2022   | 1.4555         | 15.5360   | 0.6443          |
| Vertical eye jerks             | 71 | 0.9071   | 1.7456         | 3.7010    | <b>0.9528</b> ‡ |
| Eye chase                      | 74 | 0.3607   | 0.8974         | 2.1879    | 0.4081          |
| CAF FC score M0 0-16           | 78 | 1.0710   | 1.2140         | 1.4582    | <b>0.9995</b> ‡ |
| CAF FC score M12 0-16          | 79 | 1.1136   | 1.2487         | 1.4316    | <b>1.0000</b> ‡ |
| CAF FC M12 levels <sup>1</sup> | 70 | 1.7541   | <b>7.8528</b>  | 67.9837   | <b>0.9982</b> ‡ |
| CAM M12                        | 79 | 1.3520   | <b>4.1082</b>  | 14.9195   | <b>0.9946</b> ‡ |

N, total number; MMSE, Mini Mental State Examination (cut off score >25); MADRS, Montgomery and Asberg Depression Rating Scale; MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale (3.9: arise from chair, 3.12: postural stability, 3.13: posture, 3.14: bradykinesia); FGA, Functional Gait Assessment (cut off score >19); FGA1 gait level surface in 4 levels; IADL, Instrumental Activities in Daily Living (cut off score >6); FAB, Frontal Assessment Battery (cut off score >14); FRCST-IR 3TR, Free and Cued Selective Reminding Test with Immediate Recall and sum of 3 Total Recall (cut off score >40); FRCST-IR 3FR, Free and Cued Selective Reminding Test with Immediate Recall and sum of 3 Free Recalls (cut off score >21); VF, Verbal fluency (cut off score >8); CAF FC score M0 and M12: Clinical Assessment of Fluctuations, fluctuating cognition score at baseline and at 12 months; CAF FC score M12 levels<sup>1</sup>: Clinical Assessment of Fluctuations, fluctuating cognition at 12 months score 3 levels of severity, 0-11 no severe FC, >11 severe FC, = 16 permanent condition; CAM M12, Confusional Assessment Method evaluation at 12 months; OR, Odds ratio of percentiles 2.5%, 50% (median) and 97.5%, Pr: probability OR >1 with *p* value < 0.05; ‡aggravating variable, § protective variable (1- Pr OR).

| <b>Table 3                      Diagnosis of Parkinson's Disease versus:</b> |          |            |          |                 |
|--|----------|------------|----------|-----------------|
|  | OR. 2.5% | OR. Median | OR.97.5% | Pr (OR>1)       |
| <b>Other parkinsonian syndromes</b>  | 0.1499   | 0.5734     | 2.2683   | 0.4015          |
| <b>Vascular Parkinsonism</b>   | 0.0697   | 0.2345     | 0.7095   | <b>0.0067 §</b> |
| <b>Lewy Body disease</b>   | 0.1833   | 0.7225     | 3.0612   | 0.4686          |

OR, Odds Ratio; Pr, Probability; Other parkinsonian syndromes (Multi-system atrophy, Progressive Supranuclear palsy). § protective variable (1-PrOR)

| <b>Table 4 Multivariate analysis: predictive model of recurrent falls</b> |          |         |           |               |
|---|----------|---------|-----------|---------------|
|   | OR. 2.5% | OR. 50% | OR. 97.5% | Pr (OR >1)    |
| <b>History of falls</b>   | 2.3481   | 9.0644  | 38.2245   | <b>0.9994</b> |
| <b>Previous hallucinations</b>  | 1.0479   | 4.2180  | 18.6799   | <b>0.9786</b> |
| <b>FRCTS-IR 3FR</b>   | 0.9738   | 1.0895  | 1.2309    | <b>0.9303</b> |
| <b>MMSE score</b>   | 0.5705   | 0.7534  | 0.9703    | <b>0.0141</b> |
| <b>MDS -UPDRS 3.12</b>  | 0.8355   | 1.9526  | 4.9156    | <b>0.9364</b> |
| <b>MDS-UPDRS 3.13</b>   | 0.7664   | 2.0110  | 5.5577    | <b>0.9215</b> |
| <b>CAF FC score M0</b>  | 0.8882   | 1.0808  | 1.3398    | <b>0.7729</b> |

FRCTS-IR 3FR, Free and Cued Selective Reminding Test with Immediate Recall and sum of 3 Free Recalls cut off score <22); MMSE, Mini Mental State Examination (cut off score >25); MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale (3.12: postural stability, 3.13: posture); OR, Odds Ratio; Pr OR , Probability OR>1 with  $p>0.05$ ; CAF FC score M0, Clinical Assessment of Fluctuations, fluctuating cognition score at baseline (cut off score >1).