Automatic Assessment of Clinical Frailty of Parkinson's Disease Subjects

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Abstract. A wearable actigraph was applied in the functional assessment of subject affected by Parkinson Disease in Day Hospital setting. 24 Parkinson Disease patients participated in this study. A set of standard functional tests (6-Minutes Walking Test, Timed-Up-and-Go test, 10-m and 50-m) were administered to collect data of functioning and physiatrist assigned the score according to the Clinical Frailty Scale. An automatic evaluation of this frailty score is proposed using data from 6-Minutes Walking Test and Timed-Up-and-Go test. The coherence of this automated classification method based on a basic summative linear equation of the 2 functional scores, is 66,7% with respect to the score assigned by skilled physiatrists. The inclusion of the other data is expected to improve reliability and the possibility to have an automatic identification of the frailty level through quantitative data could open the possibility to have a more detailed assessment and even continuous and domiciliary follow ups. Our goal is to have a predictive tool for the patient's state of frailty.

Keywords: Clinical frailty scale · Wearable · Actigraphy · Parkinson's disease · Functional assessment

1 Introduction

Parkinson's disease (PD) is a neurodegenerative disease of the central nervous system (CNS) with reduced levels of dopamine due to the degeneration of neurons in the *substantia nigra* area. It is characterized by a progressive and chronic disorder, mainly concerning the control of movements and balance [1]. PD is characterized clinically by precise distinctive signs:

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- involuntary tremors at rest of some parts of the body (e.g. one hand, one foot)
- muscle stiffness (linked to an involuntary increase in muscle tone) which makes a series of movements, such as getting up from an armchair, difficult or impossible. It can affect the limbs, but also the neck or trunk
- *bradykinesia*, i.e. progressive and important slowing of movements
- *akinesia*, i.e. the difficulty in starting a movement (e.g. starting to walk)
- postural instability with loss of balance (in the late stages of the disease).

Often this disease is associated with the elderly population. Fragility is also related to being elderly. In a frail elderly person, the onset of PD creates an exacerbation of his vulnerability to the various internal and external stimuli to which the subject tries to balance. All these factors strongly affect the ability to stand of the subjects so that falls are one of the most frequent complications in people with PD and are the main cause of morbidity and hospitalization [2]. The prevalence of falls ranges from 11% to 68% in subjects with PD. The development of measures that discriminate "fallers" from "non fallers" in people with PD will allow to steer interventions to prevent the risk of falls.

The state of frailty of the subject is assessed by physiatrists by assigning a proper score or level according to the Clinical Frailty Scale (CFS) [3, 4]: 1 = Very Fit, 2 = Well, 3 = Managing Well, 4 = Vulnerable, 5 = Mildly Frail, 6 = Moderately Frail, 7 = Severely Frail, 8 = Very Severely Frail, 9 = Terminally Ill. The CFS was a signi-ficant predictor of inpatient mortality in idiopathic Parkinson's disease patients admitted to the acute hospital and it may be useful as a marker of risk in this vulnerable population [15]. For every subject, the revision of this index is not frequent because it is related to follow-up visits. Indeed, its continuous update could be relevant for PD patient monitoring. The possibility of monitoring the patient both in hospital and at home opens up the ability to better treat the person by continuously adapting the interventions necessary to safeguard his quality of life. An even priority mission is the possibility to define a personalized therapy program, that is crucial since the early beginning of the pathology so to have a stable functioning and high quality of life. Despite lack of training for medical staff, increasing frailty was correlated with functional decline and mortality supporting the validity of the CFS as a frailty screening tool for clinicians [16].

The recent introduction of wearables systems for monitoring subject's parameters including gait performance and variables and physiological signals offers a unique opportunity to help clinician in assessing the conditions of the patients and tune the therapy accordingly [5]. Automatic evaluation of PD symptoms using wearable sensors has been proposed. This quantitative approach may improve patient-doctor interaction, influence therapeutic decisions, and ultimately ameliorate patients' global health status [19]. The wearable sensor-based gait analysis reaches clinical applicability providing a high-biomechanical resolution for gait impairment in PD [21]. In our previous work [6, 7], a Wearable Actigraph (WA) was developed and validated [8] for collecting biome-chanical parameters of human gait even during the execution of specific functional tests:

6-Minutes Walking Test (6MWT), Timed-Up-and-Go test (TUG), 10-m and 50-m test. This new wearable device for functional evaluation provides a set of parameters that integrate the standard clinical outcome of each test for evaluating the global motor functioning of subjects. When considering an elderly person, his state of health can be more or less compromised depending on the particular state in which he is found after personal life experiences. The biological subsystems that make up the organism have complex correlations that only an expert doctor can evaluate deeply and correctly. The geriatrician who must evaluate the health status of an elderly person is faced with a particularly complex clinical picture because each of these biological systems can be more or less compromised by disease and age and consequently also the relative interaction dynamics of biological systems are more complex to interpret. The frailty of the elderly is a particularly complex and highly dynamic state of equilibrium in the sense that small perturbations can induce large and drastic changes in his health. These dynamics if neglected, can also lead to the death of the elderly. When the fragile situation is acute, death may be inevitable in the three months following its appearance. Among the various tools that the physiatrist has available to assess the patient's frailty, there is the CFS. The complexity and variability of compromise of biological systems requires an expert physician and the patient's evaluation becomes subjective. Quantitative tools can help.

We will focus on the global functional outcome of walking test and the clinical frailty scale classification of the PD patient. The goal of the study here described is the possibility to develop a method and an algorithm for an automatic classification system of the frailty level of PD patients based on the recorded biomechanical outcomes in standard functional tests using 6MWT and TUG test. If this is possible, it means that we can use functional tests as a personalized database to have a predictive tool for the patient's state of fragility. Although for what has been said, the state of frailty of the elderly subject described as CFS can be correctly and specifically assessed by a geriatrician, we propose the use of wearable technologies such as WA to help the geriatrician in a pre-triage by applying a two-steps approach. In the first phase, WA can be used as source of data to score the patient's state of fragility according to predicted CFS by the proposed algorithm. In the second phase, the physiatrist evaluates the patient's state of fragility according to his expert clinical judgement using CFS. This means that beyond the precision of the proposed method (that is, even if good percentages of correct evaluation are demonstrated), it can be seen as an "inexperienced geriatric practitioner". However, it has its own importance in the management of the clinical entry or follow-up routine both in the hospital and at home because the healthy status of a PD subject is not the same within and across days. In fact, the system in phase 1 can be seen as a monitoring of the patient's state of frailty which can generate an alarm to activate actions in a short time. This allows to anticipate an evaluation of the patient by the physiatrist which otherwise would have only taken place in subsequent times depending on the programming carried out in the previous visit and without any information on the evolution of the fragile condition over time.

2 Materials and Methods

2.1 Subjects

As study population, a court of 24 subjects (19 males and 5 females), aged between 68 and 91 years with a PD diagnosis, was recruited at the geriatric institute *Azienda Servizi alla Persona "Piero Redaelli"* in Milan (Italy). All subjects were able to walk alone. The use of walking aids was permitted. The following Table 1 describes the characteristics of the participants to the study. The execution of the tests was limited to those already programmed by the attending physiatrist for the patient. We have limited ourselves only to adding a non-invasive tool for recording the data of interest. Before performing the functional tests, the subject was received in a study by his physiatrist where he was explained how the tests would be performed, with what tools, what they entailed for him and for what purpose. The subject was also introduced to the operators who would perform the tests (some of these were already known to patients). Having received complete information, the subject could decide whether to sign the individual informed consent. All the enlisted subjects chose to participate in the project and signed the individual informed consent. All subjects were able to complete the protocols of test setup.

2.2 Anthropometric Measures and Data Collection

The personal data, age, height and weight are recorded. Anthropometric measures of the lower limbs were measured for each subject as input for biomechanical model. Shoes are included for anthropometric measurement on the initial setup. Anthropometric segments are measured while the subject is standing: lower limb (ground-greater trochanter), ground- malleolus, lateral condyle-greater trochanter, malleolus- lateral condyle, and fifth metatarsal-malleolus. The width of the foot, length of the foot, and outer distance between the feet are acquired to the ground when the subject is resting in natural balance. The physiatrist assesses the subject's state of fragility using the score of CFS. All data are recorded by hand of physiatrist on paper forms defined by protocol.

2.3 System for Data Collection and Protocol Setup

Patients should not perform tests other than those already scheduled. Data were collected while performing the standard programmed clinical assessment during the routine Day Hospital activity and periodical follow up. Each subject must perform four functional walking tests (10-m, 50-m, TUG and 6MWT). All data are recorded by hand of physiatrist on paper forms defined by protocol. The sequence of tests and the pause between tests were chosen to take account of the patient's fatigue and fragility. The functional walking tests were executed in a large corridor of Hospital. Any approaches with other people (both staff and otherwise) were managed in time by the operators asking to clear the passage. A linear path of 10 meters was used for the 10-m test. A linear path of 25 m was used for 50-m test with one turn back around a visible corner. A linear path of 3 m with a corner for turn back and a rigid chair with four legs without wheels and armrests was used for TUG. A linear path of 30 m with two corner for turn back was used for

Table 1. Subjects sample and characteristics.

ID No.	Age (yrs)	Gender	Weight (Kg)	BMI	Stature (cm)	Walking aid
GRP001	80	M	66	28,2	153	None
GRP002	77	M	79	26,4	173	None
GRP003	82	M	72	24,1	173	Stick
GRP004	83	M	96	32,1	173	None
GRP005	91	M	82	32,0	160	Stick
GRP006	81	M	70	22,9	175	None
GRP007	81	M	84	29,8	168	Walker
GRP008	68	M	65	23,6	166	None
GRP009	81	M	80	24,7	180	None
GRP010	78	M	82	32,4	159	Walker
GRP011	77	F	69	29,1	154	Quadripod
GRP012	69	M	56	21,3	162	Stick
GRP013	78	M	49	17,8	166	Quadripod
GRP014	82	F	78	27,3	169	None
GRP015	88	F	75,5	24,7	175	None
GRP016	79	M	82	28,4	170	Stick
GRP017	81	M	70	22,9	175	None
GRP018	75	M	83	27,1	175	Stick
GRP019	78	F	60	28,5	145	None
GRP020	84	M	79	24,4	180	None
GRP021	83	F	50	21,9	151	None
GRP022	74	M	75	27,9	164	None
GRP023	85	M	76	26,6	169	None
GRP024	84	M	54	18,7	170	None
Average	*80,0*		*72,2*	*25,9*	*166,9*	
Std	*5,2*		*11,8*	*3,9*	*9,3*	

6MWT. Along the way of corridor there are signs to define the starting point of the test, the points of turn-back around which to reverse the walking path and the measure of the distance traveled for an easy manual measurement according to the standard protocol. A stopwatch was used for manual measures of time. The subjects walked with their shoes and eventually with their walking aids. The beats per minute (bpm) were registered by oximeter at rest and after the 6MWT was executed. During the tests, measurements were made both automatically by the IMU system (it was turned on and off before and after each test) and manually by a skilled operator registering on a paper report the traveled distance, the number of steps and the time of walking. The step's length and gait speed

were self-selected with the only initial request to walk as fast as possible according to protocol.

Before the subject began the test, he stood still and motionless for 10 s to record the acceleration baseline. At the end of the test a 10-s time of motionless was asked before concluding the data recording. In all tests, this baseline was used during data processing for offset compensation with respect to the action of gravity on IMU output. All tests were executed after a proper recovery period in-between two trials. 3D accelerations of the center of mass (COM) were recorded by a small WA whose main elements are: a 3D IMU, microprocessor for basic data preprocessing, Bluetooth data transmission and memory module supporting a microSD card for the logging of data up to 1 week, a LiPo rechargeable battery. The microSD can be removed. Tri-axial accelerations of the pelvis were collected at a sampling frequency of 64 Hz. The WA can store several consecutive tests in different files and subsequently download them in bulk. The data was downloaded at the end of the tests performed by each subject and the device was reset. Four raw data files (one for each test) were generated for each patient. Every file's name was renamed putting in the format label the execution date, the subject identifier and the type of test. A dedicated software developed in Matlab executed off-line data processing using the biomechanical model and the method presented in [6–8]. Post processing of raw data produced by IMU system in all tests used raw data and manual data from 50-m test to define input parameters so to adapt the biomechanical model to the subject.When the subject is moving, in order to measure the acceleration of his COM, the IMU must be placed near the COM itself. The experimental protocol uses a single IMU for the maximum simplification of the procedure and equipment. IMU with a triaxial accelerometer is placed on the back of the subjects on the pelvis and precisely next to the second sacral vertebra. An elastic belt with a pocket firmly fixes the device to the body. This is done to avoid artifacts in raw data originating from movements of the device with respect to the COM. Concerning the biomechanical approach, the wearable IMU-based system for kinematic gait analysis implements the pendulum and harmonic oscillator models [11–13] with an original approach [6–8]. The biomechanical model introduced simplifies the human anatomical structure into a rigid body with the joints which are connected to the bars that represent the legs. Also, the legs are considered as a rigid body hinged on an axis passing through the COM. The swinging movement of the legs in the execution of the steps is assumed to be an oscillation of an equivalent pendulum, and the natural balance is obtained with the legs aligned along the vertical during standing. The COM is a single point where it can be assumed that the whole mass of the body is concentrated. When a subject is at rest in a standing posture, his/her COM position is about 10 cm lower than the navel, in the sagittal plane and in correspondence of the anterior superior iliac crests (the top of the hipbones). The external forces acting on subject's body are equivalent to the same forces acting on the COM. When the subject is stepping, COM descends from its highest point to the lowest one. In the vertical and mediolateral planes, the COM moves along an oscillating path following a quasi-sinusoidal pattern [9, 10]. The trajectory of COM during walking in the sagittal plane can be assumed to have a sinusoidal pattern is the step length. The use of a harmonic oscillator model allows for exploring the human locomotion and analyzing the correlation between the cycle of COM positions and the

cycle of walking. Each step (either left or right) is carried out following this pattern. The cycle is repeated at every step with its characteristics, (i.e., the pattern is very similar but not exactly the same). The use of a harmonic oscillator model allows us to define a correlation between the cycle of COM positions and the step cycle during walking. One harmonic oscillator is associated with each step cycle; thus, we look at the walking as a set of oscillators describing human kinematics. The oscillation period defines gait frequency and cadence. Spatial-temporal measures during walking can be evaluated.

3 Results and Discussion

3.1 Automatic Classification of Functioning in PD Court

One goal of the study is to use the functional tests to produce a simple but efficient score to provide an overall assessment of the PD patient according to the international scale used in clinical practice for CFS. We propose a simple frailty classification algorithm based on the sum of the scores from 6MWT and TUG. The interpretation of the outcome produced by 6MWT uses normalcy thresholds presented in Table 2 and the score patient classification of Table 3. The interpretation of the TUG result is described in Table 4.

Table 2. Normalcy Thresholds (T) of 6-MWT (i.e. walked distance in meters) for different healthy populations in age and sex (M/F).

Age range (yrs)	60–64	65–69	70–74	75–79	80–84	85–89
M distance (m)	558	512	498	430	407	347
F distance (m)	498	457	439	393	352	311

Table 3. 6MWT outcome evaluation. T = threshold of Table 2. M = outcome measured during the test

6MWT score	> T	< T	100*|M-T|/T > T*0,20 and M < T	<300 m
Patient cslassification	Normal	Frail	Assistance needed	Very frail

Table 4. TUG Normalcy thresholds (time in s).

TUG score (time, s)	0–10 s	10, 1–20 s	20, 1–30 s	>30 s
Patient classification	Normal	Frail	Assistance needed	High risk of falling

The proposed frailty classification algorithm operates using the 6MWT and TUG outcome scores as defined in Table 3 and Table 4, with a first hypothesis of equivalent weight in the classification, and they are the input for the rules in (1) and Table 5. The

Table 5. Algorithm for patient frailty classification. The sum of 6MWT and TUG scores produces the assigned automatic classification.

6MWT score	TUG score	Automatic computation of clinical frailty scale
2	0	2 - Well
2	1	3 - Managing well
2	1	3 - Managing well
2	2	4 - Vulnerable
3	0	3 - Managing well
3	0	3 - Managing well
3	1	4 - Vulnerable
3	2	5 - Mildly frail
4	– 1	3 - Managing well
4	0	4 - Vulnerable
4	1	5 - Mildly frail
4	2	6 - Moderately frail
4	0	4 - Vulnerable
4	0	4 - Vulnerable
4	1	5 - Mildly frail
4	2	6 - Moderately frail

Frailty classification algorithm used is a linear not-weighted sum of the scores reported in Table 5 for the 2 functional tests. Its formula produces the FS (Frailty Score) index as reported in (1):

$$FS = 6MWT + TUG \tag{1}$$

The proposed index was computed and compared with the PD patient classification given by an expert physiatrist. The corresponding coherence is 16 out of 24 corresponding to an overall reliability of 66,7% (Table 6).

Some small evaluation differences between the expert physiatrist and the automatic algorithm, could be related to some other variable to be investigated as the expert physiatrist evaluates the patient in its entirety. We consider the result to be good and promising.

This is just a preliminary method and but it shows interesting and promising outcomes:

1) This study indicates the possibility to have a methodology based on an automated procedure for functional tests executions, analysis and classification, with the computation of the frailty score as with good reliability with respect to the assessment assigned by skilled physiatrists;

Table 6. Automatic algorithm for patient classification: comparison with the standard classification assigned by an expert physiatrist and coherence verification (Yes = 1, No = 0).

ID No.	Clinical frailty scale - Physiatrist	6-MWT score	TUG score	Frailty classification algorithm	Coherence (Y = 1, N = 0)
GRP001	3 - Managing well	383,94	10,63	3 - Managing well	1
GRP002	4 - Vulnerable	217,49	17,86	4 - Vulnerable	1
GRP003	4 - Vulnerable	259,25	18,98	4 - Vulnerable	1
GRP004	4 - Vulnerable	336,25	13,84	3 - Managing well	0
GRP005	4 - Vulnerable	278,51	13,91	4 - Vulnerable	1
GRP006	4 - Vulnerable	285,28	22,92	5 - Mildly frail	0
GRP007	5 - Mildly frail	212,32	21,63	5 - Mildly frail	1
GRP008	4 - Vulnerable	521,21	9,23	2 - Well	0
GRP009	3 - Managing well	409,28	12,05	3 - Managing well	1
GRP010	6 - Moderately frail	234,86	33,25	6 - Moderately frail	1
GRP011	4 - Vulnerable	259,86	19,28	5 - Mildly frail	0
GRP012	5 - Mildly frail	308,03	17,63	5 - Mildly frail	1
GRP013	6 - Moderately frail	179,33	23,45	5 - Mildly frail	0
GRP014	3 - Managing well	406,10	11,69	3 - Managing well	1
GRP015	3 - Managing well	375,15	13,95	3 - Managing well	1
GRP016	4 – Vulnerable	282,03	12,16	4 - Vulnerable	1
GRP017	3 - Managing well	381,63	12,23	3 - Managing well	1
GRP018	3 - Managing well	408,39	13,94	3 - Managing well	1
GRP019	2 – Well	341,51	15,59	3 - Managing well	0
GRP020	2 – Well	346,27	11,83	3 - Managing well	0
GRP021	5 - Mildly frail	204,53	24,97	5 - Mildly frail	1
GRP022	4 - Vulnerable	342,42	14,11	4 - Vulnerable	1
GRP023	2 - Well	378,86	16,92	3 - Managing well	0
GRP024	2 - Well	437,16	8,8	2 - Well	1
				Total coherence	16/24
				Reliability %	66,7%

2) The hospital use of this technology and related methodology offer new insights of the simple functional score, so to have a more detailed description of the progression of the PD and its influence on the ability of the subjects;
3) The study applies easy-to-use wearable sensors to offer a domiciliary solution to carry-out standardized tests for periodic and continuous follow-ups, that are so important in the management of the pathology.

The applied classification model is very basic and future work is dedicated to the evaluation of the other tests that were proposed to the PD subjects (10-m and 50-m) and to the development of a set of weighting coefficients to increase the reliability of the classification. Searching for a reliability of the system better than 66.7% we need to consider that our algorithm works on the basis of motor symptoms but the physiatrist diagnoses the pathology using also many co-factors that are non-motor manifestations such as

olfactory disturbances, autonomic dysfunction, sleep fragmentation, depression, bladder disturbances, gastrointestinal symptoms, and dementia (17,18). The clinical scale is subjective with high inter-rater variability evaluation over physiatrists and time. The algorithm proposed can help to have a controlled variability over the clinical evaluation frailty scale.

The weights used in the construction of the evaluation scale of the two gait tests could be further optimized, for example through machine learning [20]. Deep learning techniques offer a high potential to autonomously detect motor states of patients with PD [22]. This should be done using a larger number of observed cases. The evaluation could be explored also using repeated assessment in protocol setup. About TUG test, the system produces also fraction time of execution (time of sit to stand, time of walking and time of stand to sit). We are exploring if the use of these fraction times gives a better result in CFS prediction [23].

4 Conclusions

The wearable actigraphy system is able to allow for the evaluation of the clinical frailty status of subjects both to clinical operators and familiar caregivers. The first results with simplest summative linear method is has a reliability of 66,7%. The usability assessment is still under evaluation but the two users (therapists and patients) have demonstrated high compliance and easiness of use.

A larger court is under recruitment for hospital evaluation so to improve the dataset; this greater number of subjects analyzed will allow to better define the algorithm and its reliability.

The same tests could be performed by the patient at home. This will be the second exploitation direction. We will soon make available a semi-commercial solution based on a COTS (commercial-off-the-shelf) device properly programmed to expand the research with the domiciliary follow-ups. If the data transmission and their analysis led to evidence of a regularity or variation in the classification of fragility, there could be continuous monitoring of the patient which could prevent risk situations or require an urgent clinical re-assessment before the three-monthly scheduled check.

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