Physical Disability and Subclinical Pulmonary Dysfunction in Different Stages of Parkinson's Disease

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ABSTRACT

Background: *Morbidity and mortality are usually caused by respiratory disorders in Parkinson's diseases (PD) because of pulmonary function impairments. Patients with PD have musculoskeletal impairments affecting both axial and appendicular skeletons, that affect physical performance of tasks. So the purpose of this study was to determine the pattern of subclinical pulmonary dysfunction in PD patients and to determine the effect of PD severity on ventilatory and physical dysfunctions.* ***Methods and Results:*** *Thirty patients of idiopathic PD (males), age 55-67 years with mean age 62.383 ± 4.274 and 10 normal matched control subjects with mean age 63.75 ± 3.25, were enrolled in the present study. Patients were assigned into three study groups: first group had stage I, and the second had the stage II, the third had stage III. Clinical disability was indicated by a Hoehn-Yahr (H-Y) scale and they assigned into groups according to their stage (1-3). None of the patients or the control group was smoker patients. All groups underwent pulmonary function testing to measure ventilatory pattern as reflected by forced expiratory volume in first second divided by forced vital capacity (FEV_1/FVC), upper airway obstruction as reflected by forced expiratory volume in first second divided by forced expiratory volume in 0.5 sec. ($FEV_1/FEV_{0.5}$), Peak expiratory flow divided by forced expiratory flow at 50% of forced vital capacity ($PEF/FEF_{50\%}$). Maximal voluntary ventilation (MVV) was measured to reflect respiratory muscle endurance. Functional capacity was measured through cardiopulmonary exercise testing. Finally, all groups performed six minutes walk test and timed up and go test to determine their physical function. The results of the study revealed a statistical significant differences among patients within different stages of Parkinson's disease and the healthy age and sex matched control. Maximal Oxygen consumption (VO_{2max}) and MVV showed an inverse strong correlation with PD severity.* ***Conclusion:*** *The severity of PD had a great impact on ventilatory functions specially MVV which may serve as a useful indicator of the patient's Neurophysiological condition for the purpose of anticipating and preventing pulmonary complications. Also the PD severity had a great impact on VO_{2max} and physical function.*

Key words: *Parkinson's Disease, Ventilatory Dysfunction, Physical Dysfunction.*

INTRODUCTION

Parkinson's disease (PD) is a slowly progressive neurologic disorder by degeneration of dopaminergic neurons in the substantia nigra. Tremors, bradykinesia, rigidity, postural instability, flexed posture and gait disturbance are cardinal features of Parkinson's disease[12].

Muscle strength is usually normal but the ability to perform rapid successive movement is impaired. So they are usually able to perform single motor acts but have difficulties performing more complex, repetitive ones[26].

Although there is physiological evidence of potentially severe pulmonary dysfunction, most patients don't report respiratory symptoms until the final stages of the disease[23]. Probably this disturbance remain unnoticed because physical disability in PD often makes a patient leads a sedentary life and limits the activities where respiratory problem can become manifested[7].

Pulmonary dysfunctions of obstructive, restrictive, and mixed pattern have been described in patients with advanced Parkinson's disease[22], but its prevalence in early PD is not known.

Pulmonary function abnormalities were initially attributed to an obstructive defect caused by an increased parasympathetic activity. More recently, a dysfunction of the upper airway muscles was suggested to be responsible for upper airway obstruction (UAO)[28].

It has been suggested that losses of spinal flexibility in PD patients may contribute to difficulty with balance control and physical limitations[24].

PD patients often complain of fatigue that limit their physical activities and functions[8]. The poor performance of fatigued patients on tests of physical function reflects the known interrelationship between physical fitness, physical activity, and physical function, for example a lack of physical activity will result in a lower functional capacity and a decrement in physical function when functional capacity reaches a critically low level. The more sedentary habits of the more fatigued patients likely had a mediating effect on the relationship between fatigue and test performance[9].

The present study was conducted to determine the pattern of pulmonary dysfunction in PD patients and to characterize the relationship between disease severity and $VO_{2\ max}$ as measure of functional capacity and the relation between disease severity and MVV as a measure of respiratory muscle endurance.

MATERIAL AND METHOD

This study involved 30 patients with idiopathic PD diagnosed by a consultant neurologist . They were selected consecutively after referring to the neurology department at Kasr Al-Aini hospital, Cairo University. Their age ranged from 55 to 67 years and the average age was 62.383 ± 4.274 years, ten healthy age and sex matched volunteers, aged 63.75 ± 3.246 years participated in this study, the duration of PD was 5.87 ± 2.26 years.

None of the patients or the control group was smoker. The severity of disability of the patients was assessed according to the scale of Hoehn and Yahr (H–Y) whereby stage I, is mild unilateral parkinsonism, stage II, is mild bilateral parkinsonism, stage III; includes postural instability, stage IV; is marked incapacitation with the ability to walk still preserved, and stage V; is confinement to bed or wheel chair . Patients were assigned into the three groups according to the disease severity (from stage I to III); each group included 10 patients. Inclusion criteria were clinical stability, no fluctuating, classified in Hoehn and Yahr stage 3 and lower, absence of past smoking history, absence of chronic respiratory disease or cardiac disorders. Exclusion criteria were: severe cognitive impairment, dementia, (mini mental state examination score < 24), concomitant severe neurological, cardiopulmonary or orthopedic disorders that may affect the execution of cardiopulmonary exercise testing and medications that might result in pulmonary dysfunction.

The following data collection was realized at the same day time for each subject, all tests was performed in the same order, with patients in their best medical condition.

1- Pulmonary function testing:

All patients read and signed an informed consent prior to participation in the study.

Pulmonary function tests included spirometry with standard spriometer and maximal inspiratory and expiratory flow–volume curves[12].

At least three reproducible flow –volume curves were obtained values of FVC, FEV_1, PEF/FEF_{50}, $FEV_1/FEV_{0.5}$ and MVV, patient was placed in correct sitting position and made sure that nose clip in place. Patient was instructed to place mouthpiece and close lips around it . Patient was instructed to take tidal breathing and inhale completely to total lung capacity, then exhale maximally with out holding breath and encouraged to force air out as rapidly as possible. For measurement of MVV, the patient breathed in and out through the Spirometer, as rapidly and deeply as possible for 12 seconds.

Each patient had to do the testing three times at least at 1-minute Interval between each test. The best of three technically accepted tests was used to determine Pulmonary function testing parameters. In order to detect upper air way obstruction (UAO), the following ratios were also calculated: FEV_1 / PEF , FEV_1 / $FEV_{0.5}$, FEF_{50} / FEF_{50}, and PEF /FEF_{50}. UAO was considered to be present if at least four of the six following criteria were present at base line[18]. A flow volume curve with a characteristic saw tooth sign, i.e., flow oscillations of flow – volume loop tracing, PIF < 3L/S, FEV_1 /PIF ratio >8.5ml/l/min, a FEV_1 / $FEV_{0.5}$ ratio >1.5, a FEF_{50} /FIF_{50} ratio > 1 and PEF / FEF_{50} ratio <2.

2- Cardiopulmonary exercise testing:

All patients underwent a familiarization with the cardiopulmonary exercise testing unit 4 to 5 days before the test was conducted. After 2 minutes of rest and 3 minutes of unloaded pedaling (warming up), the test was conducted using stationary cycle ergometer. Ramp protocol was selected as the work rate was increased at 10 watt / minute to allow maximum exercise capacity to be reached between 6 to 12 minutes[5]. Patients were instructed to pedal at 50 to 60 revolutions per minute and verbally encouraged through out the test to continue cycling until they couldn't longer cope with the work load.

Exercise difficulty was measured using the Borg Rating of perceived exertion (RPE) scale[6], which is a 20 -point scale ranking the perceived difficulty from very light to maximal exertion. For safety during exercise, three ECG leads (lead 1, AVF, and V_5) were monitored continually and the 12-Lead ECG was recorded at rest. Blood pressure was measured by auscultation after rest before testing, every other minute during exercise, and 5 minutes after exercise. Breath by breath measurements of oxygen up take and carbon dioxide production were made during exercise. The accurate determination of VO_{2max} required patient motivation to exercise to a maximal level of exercise. A respiratory exchange ratio (RER;VCO_2/O_2) ≥ 1.0 combined with the perception of "very hard" exertion on the Borg scale.

3- Six-minute walk test (6 MWT):

The test was applied as a test of fitness for daily physical activities. This test measures the maximal distance a patient can walk at a self-paced velocity (as fast as possible) on a flat hard surface over a period of 6 minutes. It evaluates the global and integrated responses of all systems involved during exercise including motor units and muscle metabolism. The test was performed according to the six-minutes walking test Guideline[3]. The test was administered on a 40-foot–long segment of a quiet hallway and the patient was not allowed to rest or stop before 6 minutes, as desired, during the test.

4- Timed Up and Go (TUG) test:

This test assess the functional balance during gait and standing. The patient sat in a study chair with armrests, placed against a wall to prevent sliding. On the command "go", the patient arose from the chair, walked to a designed spot 3 meters away, turned around, walked back to the chair and sat down. After an initial practice run to allow for task familiarization, the subject repeated the task, and the time took by the subject to complete the task was recorded. The up and go test reflectes muscular strength, balance and agility[4].

Data collection and stasitical procedures data were expressed as mean ± SD. Comparison between patients with different stages of Parkinson's disease and control group was performed using one way ANOVA. Sperman correlation was used to investigate the relationship between the disease severity and functional capacity as measured by VO_{2max} and respiratory muscle endurance as measured by MVV.

RESULTS

Statistical analysis showed no significant difference between all groups in age, duration of illness and BMI, as shown in table (1).

Table (1): General characteristic of patients.

	Age (Years)				Duration of illness (Kg)			Body mass index (Kg / m2)			
	Control	Stage I	Stage II	Stage III	Stage I	Stage II	Stage III	Control	Stage I	Stage II	Stage III
Mean	63.9	63.6	62.05	61.5	5.5	5.8	6.3	24.3	24.92	25.1	24.66
SD	2.66	4.51	4.09	4.37	2.17	2.44	2.31	2.89	2.06	1.94	1.97
F	0.862				0.306			0.237			
P-value	0.469				o.739			0.87			

The following results were obtained from 30 patients with Parkinson's disease and 10 sex and age matched normal control group. The effect of different stages of Parkinson's disease on pulmonary ventilation, respiratory muscle endurance, physical activity and functional capacity were evaluated. The patients were subdivided into three equal groups according to the severity of disability as was assessed according to the scale of Hoehn and Yahr.

The statistical evaluation (ANOVA) of the differences among the different groups (stage I, stage Π, stage III of Parkinson's disease and control group) across the studied parameters (FEV1 / FVC%, FEV_1 / $FEV_{0.5}$, PEF / FEF_{50}, MVV, $VO_{2\ MAX}$, 6 MWT, and timed up and go test), i.e. comparing each intensity versus the other. The results revealed a statistical significant differences among groups. Pulmonary dysfunction was found to be increased according to the severity of the disease. Most of patients in group Π and III showed FEV_1 / $FVC_{0.5}$ ratio > 1.5 and PEF / FEF_{50} ratio <2 which reflects upper airway obstruction (fig. 1, 2, 3 and 4), MVV which reflects respiratory muscle endurance was the most affected parameter according to the disease severity (r = -0.944, P<0.0001). Also VO_{2MAX} showed a strong inverse relationship with the disease severity (r = -0.971, P<0.0001). As shown in table (2a,b) and fig (1-4).

Table (2a): Statistical evaluation of the differences among PD patients with different stages and control groups across pulmonary function testing parameters, functional capacity and physical function.

Variable			Control	Stage I	Stage II	Stage III	F-value	P-value
			Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD		
I	Ventilatory pattern	FEV_1/FVC_{ratio}	70.99 ± 3.54	80.76 ± 4.16	86.75 ± 1.20	91.05 ± 3.60	68.39	0.0001***
II	Upper airways obstruction	FEV1/FEV0.5	1.42 ± 0.15	1.53±0.16	1.72±0.12	1.89±0.09	25.159	0.0001***
		$PEF/FEF_{50\%}$	2.23± 0.57	1.95 ± 0.20	1.57 ± 0.22	1.19 ±0.16	20.433	0.0001***
III	Respiratory muscle endurance	MVV (L/min.)	90.30 ± 4.92	75.1 ± 3.25	50.9 ± 2.64	35.2 ± 5.98	311.551	0.0001***
IV	Functional capacity	VO_{2MAX} (ml/kg/min.)	23.34± 0.97	21.97 ± 0.30	19.05 ± 0.78	12.88 ± 0.42	478.706	0.0001***
V	Physical function	Six minutes walk test (meter)	505.9± 3.60	443.4 ± 2.91	385 ± 2.87	331.8 ± 2.15	6558.36	0.0001***
		TUGO (second)	9.2 ± 1.32	29.40±3.24	43.40±2.84	51.10±5.22	285.01	0.0001***

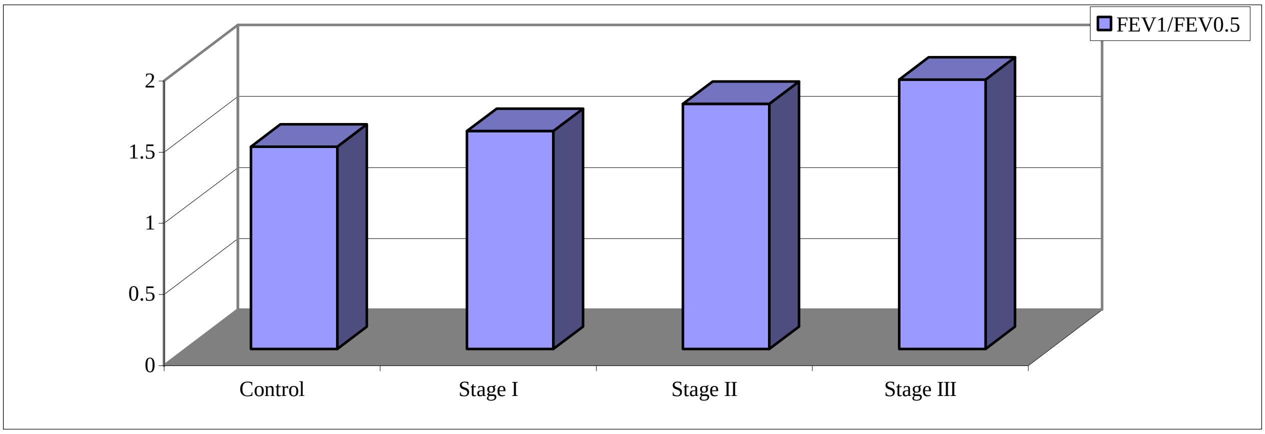

Fig. (1): Mean of $FEV_1/FEV_{0.5}$ in different stages of PD patients and control.

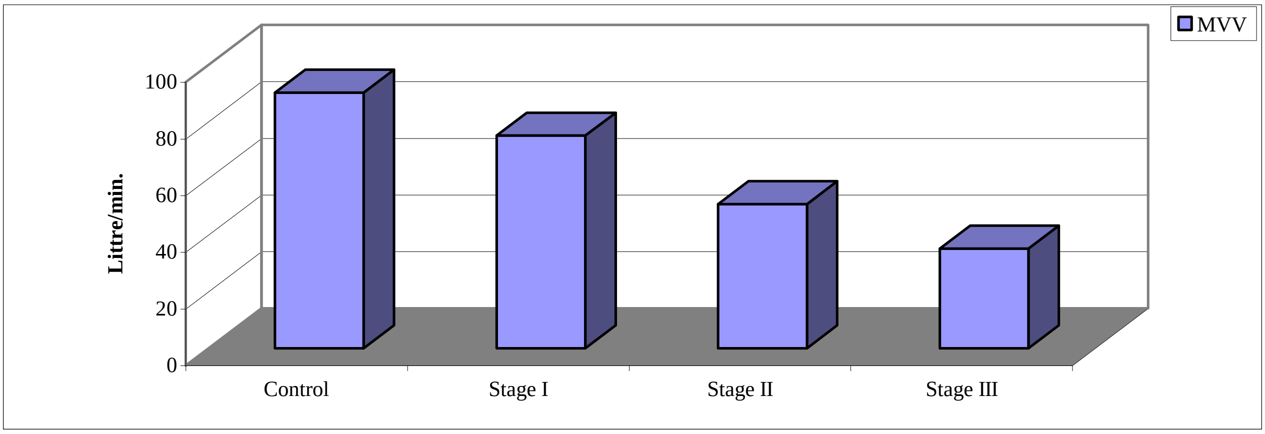

Fig. (2): Mean of MVV in different stages of PD patients and control.

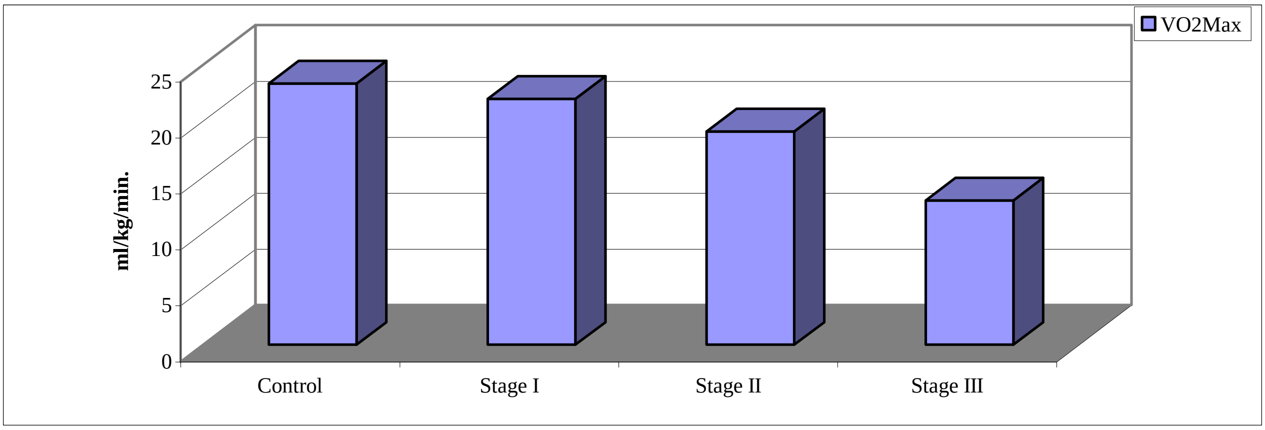

Fig. (3): Mean of VO_{2max} in different stages of PD patients and control.

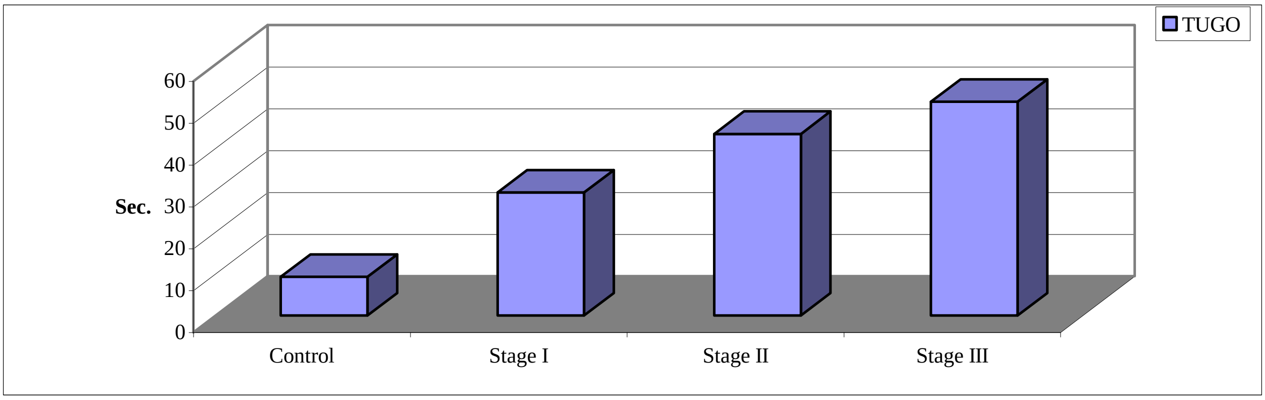

Fig. (4): Mean of TUGO in different stages of PD patients and control.

Table (2b): Statistical evaluation of the differences among PD patients with different stages and control groups across pulmonary function testing parameters, functional capacity and physical function. Each group versus the others.

Variable	P – value					
	I , II	I , III	I , control	II , III	II , control	III, control
FEV_1/FVC_{ratio}	0.0001	0.0001	0.0001	0.007	0.0001	0.0001
$FEV_1/FEV_{0.5}$	0.002	0.0001	0.067	0.008	0.0001	0.0001
$PEF/FEF_{50\%}$	0.01	0.0001	0.06	0.011	0.0001	0.0001
MVV	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
VO_{2MAX}	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
Six M walk test	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
TUGO	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001

DISCUSSION

The present study was conducted to investigate the effect of Parkinson's disease sevirty as classified by Hoehn and Yahr on pulmonary and physical dysfunction. The results of this study confirmed earlier observations of pulmonary dysfunction in PD [22,25,27], Based on the results of spirometry (80.76%±4.16% in stage I, 86.75%±1.20% in stage II and 91.05%±3.60% in stage III), the dysfunction was predominantly restrictive without any significant peripheral air way obstruction (FEV_1 / FVC > 80%).

The results of the present study go hand by hand with the findings of Depandis et al. (2002)[7] who stated that their patients, like those in the present study, were asymptomatic for respiratory dysfunction . Since restrictive pulmonary disease manifests predominantly as dyspned on exertion in early stages, it is possible that reduced physical activities resulting from motor dysfunction could have minimized the perception of dyspnea.

The involvement of upperairways in causing pulmonary dysfunction has been reported previously[12,13,28].

The results of the present study showed that PD stage 1; had no upper airways obstruction; while patients with stages 2, 3 showed upper airway obstructions as revealed by PEFR reduction and PEFR / FEF_{50} reduction less than 2 (1.95±0.20 in stage I, 1.57±0.22 in stage II and 1.19±0.16 in stage III).

The results also revealed that with increasing PD severity, the obstruction increases. Reduced PEFR can result from a combination of upper airways obstruction and lack of coordination of respiratory muscles. Since the decrease in PEFR was not associated with a decrease in FEV_1, lower airway obstruction is unlikely.

The results of the present study are supported by Izquierdo et al. (1994)[14] who found that patients with severe PD had lower PEFR as compared with moderate or mild PD.

The mechanism of UAO is poorly understood. Parkinson's disease symptoms affect various groups of muscles, including upper airway muscles. A saw tooth pattern of flow–volume curve may correspond to upper airway muscles tremor. Moreover, the muscle dysfunction is often asymmetrical and the lack of coordination between the numerous pharyngeal and laryngeal muscles may lead to distortion of upper airway geometry[29].

Maximum voluntary ventilation (MVV) is a sensitive indicator of neuromuscular disorders that impair the strength and endurance of ventilatory muscles. A significant and greater impairment of MVV indicates an impaired performance of repetitive respiratory motor acts as a result of bradykinesia and rigidity of the respiratory muscles[11].

The results of the present study revealed a reduction of MVV in PD patients in comparison with the control (75.1±3.25 in stage I, 50.9±2.64 in stage II, 35.2±5.98 in stage III and 90.30±4.92 in control) and the reduction was increased by increasing the disease severity [16] when measured muscle strength at two speeds of movement in PD with symptoms mainly to one side. They found the affected side was weaker than the other in both slow and fast movements early in the disease, whereas in the advanced disease, the difference between sides remained significantly only at the faster speed. If applicable to respiratory muscles, this observation supported the finding of the present study about MVV.

It can be summarized from the present study that pulmonary function was found to be decreased in patients with PD with increasing clinical disability. A simple spirometric measurements may be used in PD for anticipating and preventing complications because of pulmonary impairment.

The results of the present study also showed a reduction in physical function of PD patients as measured by 6-minute walk test (443.4±2.91 in stage I, 385±2.87 in stage II and 331.8±2.15 in stage III) and timed up and go test (29.40±3.24 in stage I, 43.40±2.84 in stage II and 51.10±5.22 in stage III).

The results also showed a reduction of functional capacity in PD patients as measured by maximal oxygen consumption (21.97±0.30 in stage I, 19.05±0.78 in stage II and 12.88±0.42 in stage III).

The phenomenon of hypokinesia or akinesia is expressed most clearly in the PD patients and takes the form of extreme poverty of the entire musculature. Bradykinesia, which is the slowness in the performance of rapid alternating movements, is probably another aspect of the same physiological difficulty. The velocity of movement, or the time form onset to completion of movement is slower than normal. Rigidity usually involves all muscle groups both flexor and extensor[1].

The more sedentary habits of PD patients had a greater effect on the lack of physical activity that will result in a lower functional capacity and a decrement in physical function when functional capacity reaches a critically low level. Functional capacity (measured most accurately by $VO_{2\,max}$) is a physiologic–health attribute that is affected by regular physical activity or inactivity [10].

Physical function on the other hand refers to the assessment of the capacity to a complete a specific task and is believed to reflect the ability to carry out activities of daily living. Poor performance of PD patients on the six minutes walk test would result from several potential factors, including poor cardiorespiratory fitness and gait or balance abnormalities. It can be concluded that the more sedentary habits of PD patients result in reduced muscular strength, agility, balance and lower cardiorespiratory endurance, attributes that are important determinants of performance on six minutes walk test and the maximal oxygen consumption[9].

The increased time taken during the timed up and go test in PD patients as compared with the control group may be attributed to decreased quadriceps strength, hip extensor muscles to arise from a chair. Parkinson's patients have been reported to have increased muscular fatigability and decreased muscular strength, both of which could affect the muscular action required during the test. This may also related to fatigue which is a common symptom affecting patients with idiopathic PD. Whether fatigue is a case or effect of inactivity and its physiological sequelae is an important factor in decreased physical function, as assessed by time up and go test in Parkinson patients[17].

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الملخص العربي

العجز الوظيفي والخلل الرئوي تحت التشخيص في المراحل المختلفة من مرض الشلل الرعاش

في الآونة الأخير ازداد معدل الوفيات والتدهور الصحي لدى مرضى الشلل الرعاش نتيجة لاضطرابات الوظائف الرئوية ، لذا كان الهدف الأساسي من هذه الدراسة هو تحديد تأثير المراحل المختلفة من هذا المرض على اختلال الوظائف الرئوية وكذلك تأثيره على الكفاءة البدنية والوظيفية ، تم اختيار ثلاثون مريضا مصابين بالشلل الرعاش يتراوح أعمارهم ما بين 55-67 سنة وتم تقسيمهم إلى ثلاث مجموعات باستخدام مقياس (هوهن وياهر) وتم مقارنتهم بالمجموعة الضابطة . وقد تم قياس معدل خروج الزفير في أول ثانية ، تحديد وجود انسداد بالشعب الهوائية العليا و أقصى معدل للتنفس الإرادي . كما تم قياس الكفاءة الوظيفية من خلال قياس أقصى معدل لاستهلاك الأوكسجين وكذلك قياس الكفاءة البدنية من خلال قياس المسافة المقطوعة في زمن قدره 6 دقائق . وقد أظهرت النتائج اختلافات ذات دلالة إحصائية ما بين المجموعة الضابطة ومرضى الشلل الرعاش في المراحل المختلفة للمرض . كما أظهرت النتائج وجود ارتباط عكسي قوي ما بين مرحلة المرض وأقصى معدل لاستهلاك الأوكسجين وكذلك أقصى معدل للتنفس الإرادي . أوصت الدراسة بأهمية اختبار الوظائف الرئوية كمؤشر لتوقع ومنع المضاعفات الرئوية في المراحل المختلفة لمرض الشلل الرعاش .